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Novel nanostructured lipid carriers as a promising food grade delivery system for rutin

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ABSTRACT

The aim of the present study was to encapsulate rutin by nanostructured lipid carriers (R-NLCs), as a solution to eliminate the fortification difficulties and provide healthier functional foods. Rutin was loaded into food grade NLCs in different rutin to lipid ratios using high shear rate homogenization method. Colloidal properties of R-NLCs such as particle size, poly dispersity index, encapsulation efficiency, loading capacity, and encapsulation stability were studied. R-NLCs with a rutin to lipid ratio of 10% were selected as an optimum formulation. Morphological studies have shown that R-NLCs are round shaped particles with smooth surfaces. The R-NLC fortified food samples and models were subjected to pH, physical and thermal stability, and turbidity analysis. The results indicated that the developed R-NLCs could provide a method for designing new functional foods based on nanocarriers.

1. Introduction

Nanotechnology has been introduced into food science in various fields, such as nanobiosensors, nanodelivery systems, and nanocomposite packaging. Nanodelivery systems have increased the safety, shelf life, and development of new food formulations (Huang, Yu, & Ru, 2010; Troncoso, Aguilera, & McClements, 2012). In this case, food-grade delivery system can be defined as the entrapment of a bioactive ingredient in a food grade carrier to protect and improve its functionalities (Wani et al., 2014).

Nowadays, the demand for food is not limited to only satisfaction of hunger. Consumers are becoming more cautious about the relationship between their nutritional habit and their general health. Thus, they appreciate foods that can provide multifunctional ingredients beside the necessary nutrients. Functional foods are defined as foods that can provide more health benefits besides their basic nutritional values (Chen, Jiao, & Ma, 2008; Loveday & Singh, 2008). On the other hand, reducing fatty foods in the diet of consumers may cause a deficiency in fat-soluble nutraceuticals such as vitamins, carotenoids, essential fatty acids, phytosterols, some flavonoids, and other lipophilic nutraceuticals. Therefore, it seems that the enrichment of foods with these health promoting compounds is required. However, there are some problems associated with these compounds such as the low solubility in aqueous medium and low stability during the processing and storage time. Thus, using nanodelivery systems such as food grade nanostructured lipid carriers can potentially provide a solution.

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Nanostructured lipid carriers (NLCs) are a type of lipid based nanocarriers, which can be used for the encapsulation of different bioactive compounds such as plant originated nutraceuticals (i.e. rutin) (Beloqui, Solinís, Rodríguez-Gascón, Almeida, & Préat, 2016). They are composed of solid and liquid lipids, which exhibit higher nutraceutical loading capacity than solid lipid nanoparticles (SLN) (Madane & Mahajan, 2014). The NLC has been regarded as an alternative to SLNs and other carriers such as liposomes due to its enhanced properties such as easy manufacturing, high nutraceutical loading capacity, and more aptitude in controlling the release rate of nutraceuticals. Furthermore, easy dispersion in an aqueous medium, nanoscale size, and biocompatibility enhances the ability of NLCs to deliver nutraceuticals to the body. Moreover, the ability of NLC to improve the delivery of the phyto-active compounds is favourable for the short half-life bio-active compounds such as silybin (Fang et al., 2015; Jia et al., 2010).

Flavonoids are one class of secondary plant metabolites, which have many advantages such as multiple nutritional values, therapeutic, and antimicrobial effects that can be used in food fortification, preservation, and designing of healthy food products. However, there are several problems, such as low stability, solubility, and undesirable sensorial features, associated with the direct addition of polyphenols into foods or beverages (Bilia, Isacchi, Righeschi, Guccione, & Bergonzi, 2014; Heim, Tagliaferro, & Bobilya, 2002). The application of NLCs as the novel food-grade delivery system could potentially reduce these problems; hence, the NLC technology can be applied in the development of healthy and functional foods. Furthermore, as flavonoids have high antioxidant and antimicrobial properties, they can be used as natural preservatives. NLC can increase the preservation potential by protecting the encapsulant against the environmental destructive agents and controlling its release rate. There are some successful attempts in producing NLCs that are loaded with phyto-active compounds such as quercetin, green tea extracts, silymarin, and curcumin. NLCs have been reported to be an effective method for enhancing the healthier effects of quercetin (Sun et al., 2014). NLCs can enhance the antioxidant and antimicrobial effects of green tea extracts (Manea, Vasile, & Meghea, 2014).

Rutin is a glycoside form of quercetin and belongs to the flavonols. It has a rutinose disaccharide in its structure and is naturally found in fruits and plants such as potatoes, onions, tomatoes, vegetables, and vegetable drinks like tea (Kamalakkannan & Prince, 2006; Kreft, Knapp, & Kreft, 1999; Santos et al., 2011). Myricetin and some other flavonoids act as a pro-oxidant agent (compounds that accelerate the lipid oxidation processes) and catalyse the oxygen radical productions in some circumstances, whereas rutin does not have a pro-oxidant activity. This is an important feature that makes rutin superior to them. Rutin has a significant radical scavenging activity besides its nutritional and health promoting effects (Prince & Kamalakkannan, 2006). The protective effects of rutin against oxidizing species such as hydroxyl, superoxide, and peroxyl radicals are derived from its antioxidative and radical-scavenging activity (Hooresfand, Ghanbarzadeh, & Hamishehkar, 2015). Therefore, the use of nanotechnology for encapsulating health promoting phyto-constituents (i.e. rutin) could provide new methods for designing novel functional foods. According to the literatures, daily intake value of rutin is about 1.5 to 70 mg/kg, which varies by country and nutritional habit (Kreft et al., 1999; Nakamura, Ishimitsu, & Tonogai, 2000). The main disadvantages associated with rutin are very low solubility in an aqueous phase and polarity that both reduce the biological access to this phyto-active compound (Sharma, Ali, Ali, Sahni, & Baboota, 2013; Tranchimand, Brouant, & Iacazio, 2010). Thus, in this research, food grade NLC was prepared to encapsulate rutin for food fortification and development of new functional foods, which according to the authors' knowledge has not been conducted before.

2. Materials and methods

2.1. Materials

Rutin (quercetin-3-rutinoside hydrate) was purchased from Sigma-Aldrich (St. Louis, MO, USA). Cacao butter was a gift from Shirin Asal Corporation (Tabriz, Iran). Cacao butter is listed by the FDA as a food additive (21CFR172.861) (Kim, Na, & Choi, 2005). Oleic acid, citric acid, and Tween 80 were purchased from Merck Chemicals (Darmstadt, Germany). Oleic acid is a constituent of many natural edible lipids. Fatty acids manufactured from fats and oils derived from edible sources are included in the FDA list of food additives and are permitted for direct addition to foods (21CFR172.860) (Lopez-Huertas, 2010). Tween 80 is a water-soluble and non-ionic surfactant that is suitable for stabilization of NLC. The non-ionic surfactants, especially Tween series, have low toxicity or irritation potential as compared to the ionic ones. Tween 80 is a direct food additive, which is allowed by the FDA (21CFR172.840). Its acceptable daily intake (ADI) is 25 mg/kg body weight/day. The LD50 of Tween 80 ranges from 4500 to 63,840 mg/kg (Hasenhuettl & Hartel, 2008). Double distilled water was purchased from Shahid Ghazi Pharmaceutical Corporation (Tabriz, Iran).

2.2. Methods

2.2.1. Preparation of R-NLCs

In order to produce rutin loaded food grade NLCs (R-NLCs), both the lipid and the aqueous phases were prepared separately. For the production of NLCs, the pre-emulsion (the initial mixtures of the lipids, bioactive compounds, and surfactant agents in an aqueous phase) was prepared. Cooling this pre-emulsion recrystallizes the lipids and forms NLCs. The amounts of excipients were calculated based on the total volume of the pre-emulsion. Moreover, for accurate calculations, the total volume of the pre-emulsions was kept constant (50 cc) in all the formulations. Lipid phase (oleic acid to cacao butter ratio of 15%) containing different amounts of rutin (rutin to lipid ratios (R/L) of 5, 10, and 20%) was prepared at 5 °C above the melting point of the cacao butter. The same temperature aqueous phase (containing 6% of Tween 80) was added to the rutin containing melted lipid phase dropwise using a high shear homogenizer (Heidolph, Kelheim, Germany) at 1478 *g* for 15 min. The prepared formulations were sonicated by using a probe sonicator (UP200H, Hielscher, Germany) at a cycle of 0.5 s and an amplitude of 70% for 10 min. For recrystallization of lipids and NLC formation, the obtained pre-emulsions were cooled