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Preparation of solid lipid nanoparticles containing active compound by electrohydrodynamic spraying

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ABSTRACT

Electrohydrodynamic (EHD) processing and forming has been successfully used to encapsulate a range of active ingredients but its application in flavour enhancement has been very limited. In this study, an EHD method is used for the first time to prepare nanosized particles of solid lipids, i.e. stearic acid and ethylcellulose encapsulating maltol flavour. The weight ratio of stearic acid: ethylcellulose was kept at 5. Particles, which were spherical in shape and 10–100 nm in diameter, were obtained with stable jetting with the applied voltage set to 13–15 kV and using flow rates of 10 and 15 μl/min. The maltol encapsulation efficiency and yield were 69.5% and 69%, respectively. Fourier transform infrared spectroscopy confirmed the presence of maltol within the stearic acid–ethylcellulose matrix, without any chemical interaction between ingredients.

1. Introduction

Nanotechnology is the understanding and control of matter at dimensions of ~1–100 nm. There is a huge demand for nanotechnology in the food industry (Fathi & Mohebbi, 2010; Neethirajan & Jayas, 2011; Rizvi, Moraru, Bouwmeester, & Kampers, 2010). However, many nanotechnological applications in the food sector may be difficult to adopt commercially, owing to high cost and/or scale requirements. Nanotechnology has been used to deliver bioactive ingredients (Chen, Weiss, & Shahidi, 2006; Shimoni, Edited, & Gustavo, 2009) and nanoencapsulation has been exploited in pharmaceutics, cosmetics and food science (Farokhzad & Langer, 2009; Müller, Petersen, Hommoss, & Pardeike, 2007; Risch & Reineccius, 1995; Sagalowicz, Leser, Watzke, & Michel, 2006; Shah et al., 2007; Shimoni, Edited, & Gustavo, 2009) with a variety of polymeric matrices being used, such as sodium alginate, pectin, chitosan and lipids based materials (Chang et al., 2005). Also the properties of bioactive compounds can be improved by encapsulating them, such as their prolonged residence time in the gastrointestinal tract, delivery, solubility, and the efficient absorption through cells (Chen, Remondetto, & Subirade, 2006).

The successful utilisation of nanoparticles in various industries, particularly in biotechnology, is dependent largely on their uptake by body tissue (i.e. via cell membrane), controlled and sustained release of active ingredient through polymeric matrices and their stability. Solid lipid nanoparticles (SLN) are a colloidal carrier system for bioactive compounds. SLN are generally made of a lipid-based matrix (Müller, Mäder, & Gohla, 2000).

Recently SLN have been gaining impetus scientifically and commercially in the pharmaceutical as well as the food industries (Awad et al., 2008; Gallarate, Trotta, Battaglia, & Chirio, 2009; Varshosaz, Tabbakhian, & Mohammadi, 2009; Varshosaz et al., 2010). SLN have been developed as an alternative to conventional carrier systems such as emulsions, liposome, etc. Owing to their unique properties such as high encapsulation efficiency, small size, increased surface area, SLNs have great potential in applications requiring controlled release, variability in active ingredient content and stabilisation, biodegradability and biocompatibility (Cavalli, Caputo, & Gasco, 1993). They are also commercially viable and have gained regulatory approval (Müller, Mäder, & Gohla, 2000; Smith & Hunneyball, 1986). Further, for food applications, the polymeric material which can be designed to encapsulate active ingredient must be edible, biodegradable and able to form a barrier between the internal phase and its surroundings (creating a modified atmosphere restricting the transfer of gases (O_2, CO_2)) and also becoming a barrier for transfer of aromatic flavour compounds (Miller & Krochta, 1997).

The fatty acid nature of the saturated 14, 16 and 18-carbon chain (i.e. stearic acid (SA), butterfat, and palmitic acid) at normal human body temperature is commonly used in selecting the lipid matrix to prepare SLN (Bocca et al., 1998; Cavalli et al., 1997; Gasco, Cavalli, & Carlotti, 1992; Mehnert & Mader, 2001; Zhang, Yie, Li, Yang, & Nagai, 2000). These form the bulk of fatty acid in animal body tissue (Bruss, 1997). SLN prepared using SA, therefore, are approved by regulatory authorities and hence their application for the delivery of active ingredient is acceptable. Furthermore, SA is known to have a neutral effect on the plasma lipid profile as it is rapidly converted to oleic acid within the body (Bonanome, Bennett, & Grundy, 1992) and it does not increase plasma cholesterol concentration like other saturated fatty acids (Hegsted, McGandy, Myers, & Stare, 1965).

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SA has been chosen as the carrier material owing to its excellent entrapment efficiency, biocompatibility and low toxicity (Phadke, Keeney, & Norris, 1994). Due to its hydrophobic nature, SA reduces flavour dissolution and release and slows the release kinetics at higher SA levels (Dave, Amin, & Patel, 2004).

Ethylcellulose (EC) is a water insoluble polymer which can be used in the entire pH range. It forms a non-eroding diffusional barrier and has been widely used to prepare controlled release dosage forms of water soluble material (Al-Omran, Al-Suwayeh, El-Helw, & Saleh, 2002; Fan, Wei, Yan, Chen, & Li, 2001; Alpar and Walters, 1981; Palmieri, Bonacucina, Di Martino, & Martelli, 2001; Rao & Murthy, 2002). EC is one of the most commonly used polymers in coating because of the various advantages it offers to formulations, such as film forming, minimum toxicity, excellent physical and chemical stability (Rao & Murthy, 2002).

If SLN are prepared using a solvent carrier (as in the work described in this paper) their size and shape will be influenced by the rate of evaporation of solvent from droplets, after the droplet shrinkage and the diffusion of the polymer molecules in the droplets (Xie, Lim, Phua, Hua, & Wang, 2006). As EC is a relatively large molecule, its diffusion rate inside the droplets will be very slow, therefore, the presence of EC is confined to their surface. Loss of solvent through surface evaporation shrinks the droplet size and increases EC concentration close to the surface of the droplet, leading to the formation of a shell of solid EC and SA encapsulating the active ingredient (Trotta, Cavalli, Trotta, Bussano, & Costa, 2010). Also, the electrical properties of the solvent carrier has a direct influence on the size of the SLN produced, a higher dielectric constant results in smaller sized SLN (Xie, Marijnissen, & Wang, 2006). Therefore, ethanol having a high dielectric constant (24.3 at ~25 °C) is likely to produce small SLN.

Recently, flavour encapsulation has become a popular technique in the food industry (Karathanos, Mourtzinos, Yannakopoulou, & Andrikopoulos, 2007). Most flavour compounds are highly volatile and chemically unstable as a result of oxidation, chemical interactions and volatilisation. So, encapsulation of flavour compounds is essential to stabilise them and offer their release when required (Choi, Ruktanonchai, Soottitantawat, & Min, 2009).

Currently, several techniques are used for encapsulation including liposome entrapment, coacervation, inclusion complexation, centrifugal extrusion, spray cooling, spray chilling or spray drying, extrusion coating, fluidised bed coating and rotational suspension separation (Dziezak, 1988; Gibbs, Kermasha, Alli, & Mulligan, 1999; Zuidam & Heinrich, 2009).

Electrohydrodynamic (EHD) processing uses the application of an electrical potential to a flowing fluid. Control of the potential and flow rate allows the formation of a jet which subsequently breaks up to generate droplets with diameter in the nanometer to micrometer size range. One of the emerging technologies in food formulations is the application of EHD technology for encapsulating active ingredients such as, emulsifiers, and flavours (Yoshii et al., 2001). EHD spray technology has advantages; scale and morphology can be easily varied according to the requirement of the food materials (Luo, Loh, Stride, & Edirisinghe, 2012). The size distribution of the particles can be near-monodisperse leading to better flavour perception (Gañán-Calvo & Montanero, 2009). EHD spraying technology essentially generates droplets from which solid relics are deposited. Droplet generation and droplet size can be effectively controlled by optimizing the parameters such as voltage at the capillary needle, the flow rate of the solution and distance between needle and collector, this in turn regulates relics.

In this study EHD technology is used to encapsulate water soluble maltol flavour within solid lipid matrices of SA and EC and the process control parameters are optimised to control the particle size of SLN produced. The reason for using a SA–EC matrix to encapsulate maltol was to limit flavour degradation or loss during processing and storage. This solid matrix is able to provide more protection against chemical reactions such as oxidation.

2. Materials and methods

2.1. Materials

Maltol (MAL), stearic acid (SA), ethylcellulose (EC) in powder form, were purchased from (Sigma–Aldrich, Poole, UK). 95% ethanol was also obtained from Sigma-Aldrich. All materials were used without further purification. Doubled distilled water was used in all the experiments.

2.2. Characterisation of solvents and solutions

Viscosity, surface tension and density of the solvents and solutions were measured using a U-tube viscometer (75 mL Cannon-Fenske Routine Viscometer, Cannon Instruments, USA), plate method, Kruss tensiometer (Model-K9, Kruss GmbH, Germany), and standard 25 ml density bottle method (VWR, Lutterworth, UK), respectively. Each equipment was calibrated using ethanol prior to the measurements.

2.3. Preparation and characterisation of the polymeric solution

SA and EC were dissolved using a magnetic stirrer in different concentrations (10–50 mg/ml) in ethanol, keeping the total polymeric concentration as 5% w/v. To each of these polymeric solutions was added (1.2–2.5 mg/ml) of maltol and stirred again until a clear solution was obtained (Fig. 1a). All the polymeric solutions (i.e. SA + EC) with and without maltol were characterised by measuring the surface tension, viscosity and density at the ambient temperature 25 ± 2 °C.

2.4. Preparation of solid lipid nanoparticles (SLN)

SLN were prepared using a single-needle EHD spraying setup as shown in Fig. 1b. The spraying system consisted of a high voltage electrical power source (Glassman Europe Ltd., Tadley, UK), with a mechanical syringe pump (PHD 4400, Harvard Apparatus, Edenbridge, UK) with high precision and adjustable flow rate and a stainless steel needle set into an epoxy resin and connected to the high voltage supply. The inner and outer diameters of needle were 450 μm and 870 μm, respectively. The polymeric solutions containing the active ingredient, i.e. maltol, were loaded into a 10 ml plastic syringe (BD Plastic, Sunderland, UK). This syringe was mounted on the Harvard syringe pump and was connected to the stainless steel needle at one end via silicone tubing. The syringe pump controlled the flow rate of the spraying solution into the needle. A video camera with an in-built magnifying lens (Leica S6D JVC-color) was used to observe the needle tip at all times during collection of SLN in order to understand the spraying behaviour on the application of applied voltage. The system operating parameters i.e. flow rate, collection distance and voltage, were used to control SLN formation. The SLN were only collected at the applied voltages which furnished a stable cone-jet. The SLN generated (Fig. 1d) from the jet were collected onto a microscopic slide containing distilled water. The particles were then left to dry in a desiccator under vacuum. All five samples were sprayed at varying flow rate (10–25 μl/min), with the collection distance kept between 100 and 150 mm from the needle end and with the applied voltages between 0 and 20 kV. All the experiments were repeated three times.

2.5. Maltol entrapment efficiency and yield

A UV spectrophotometer (Perkin-Elmer, lambda 35, UV/Vis spectrophotometer, Cambridge, UK) was used to measure the absorbance of the solution with a known concentration. A calibration curve was prepared for known concentrations of maltol at a wavelength of 274 nm. The encapsulation efficiency of the SLN was found by quantifying the entrapped maltol in polymeric matrices of SA and EC.