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Mechanistic study of carvacrol processing and stabilization as glassy solid solution and microcapsule

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ABSTRACT

Essential oils and other liquid active pharmaceutical ingredients (APIs) are frequently microencapsulated to improve shelf life, handling, and for tailoring release. A glassy solid solution (GSS), a single-phase system, where the excipient is plasticized by the API, could be an alternative formulation system. Thus this study focuses on the investigation of two formulation strategies using carvacrol as a model compound, namely a microcapsule (MC) and a glassy solid solution (GSS). Applying the solubility parameter approach, polyvinylpyrrolidone (PVP) was chosen as a suitable matrix material for a GSS system, whereas maltodextrin and sucrose served as excipients for a microcapsule (MC) system. Differential scanning calorimetry (DSC) measurements of the excipients' glass transition temperatures and the melting point of carvacrol verified plasticizing properties of carvacrol on PVP. Batch mixing processes, as preliminary experiments for future extrusion processes, were performed to prepare GSSs and MCs with various amounts of carvacrol, followed by crushing and sieving. Maximally 4.5% carvacrol was encapsulated in the carbohydrate material, whereas up to 16.3% were stabilized as GSS, which is an outstanding amount. However, grinding of the samples led to a loss of up to 30% of carvacrol.

1. Introduction

Essential oils belong to the group of liquid lipophilic active pharmaceutical ingredients (API), but are also of high interest as flavours in foods, as fragrances in cosmetics and home care products, and as insecticides in agricultural products. Various techniques within pharmaceutical technology, e.g. coacervation, complexation with cyclodextrins, and spray drying, are common methods for microencapsulation of these oils in solid materials to increase shelf life, improve safety, simplify handling, and for tailoring release. Another potential processing technique – extrusion – has only recently become of interest in the pharmaceutical technology for microencapsulation of essential oils and liquid APIs (Tackenberg et al., 2015). However, within the food science industry, microencapsulation of essential oils/flavours via extrusion has been used intensively for many years (Madene et al., 2006; Porzio, 2008; Risch, 1988; Uhlemann and Reiß, 2010). In order to improve the extrusion process and its products, the structure(s) of the solidified liquid APIs must be studied in detail.

Abbreviations: API, active pharmaceutical ingredient; DCM, methylene chloride/dichloromethane; DE, dextrose equivalent; $\Delta\delta$, Euclidean distance; δ_d, dispersion parameter; δ_p, polarity parameter; δ_h, hydrogen bonding parameter; DSC, differential scanning calorimetry; F_d, contribution to cohesive energy from dispersion forces; F_p, contribution to cohesive energy from polarity; E_h, contribution to cohesive energy from hydrogen bonds; GSS, glassy solid solution; Δh, specific enthalpy of fusion (J/g); ΔH, enthalpy of fusion/melt enthalpy (mJ); i, structural group; IUPAC, international union of pure and applied chemistry; MC, microcapsule; μ-CT, X-ray micro computerised tomography; n_i, number of structural groups; PVP, polyvinylpyrrolidone; R^2, coefficient of determination; r. h., relative humidity; SP, solubility parameter; Tg, glass transition temperature (°C); V, molar volume at the liquid state (cm^3/mol).

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Thus, this study focuses on the identification and characterisation of the solid-state properties of processed essential oils when applying a batch mixing technique. For decades small-scale batch mixing processes have been used for pre-extrusion studies in polymer science, and also in recent years for pharmaceutical extrusion processes (Liu et al., 2010), because the process parameters could be varied without influencing other parameters, which is not possible in continuous extrusion processes (Schuchmann, 2008).

The microencapsulated food products using extrusion are described frequently as a binary-phase system of liquid oil droplets in a solid shell material, and are called microcapsules, microspheres, matrix (micro) particles, multi-core and multi-wall particles, and matrix microcapsules depending on the materials and techniques used (Gibbs et al., 1999; Madene et al., 2006; Uhlemann and Reiß, 2010; Versic, 1988). For such formulations in the pharmaceutical field, the nomenclature is not consistent. In this study, a binary-phase system with a liquid core substance in a solid matrix is called a microcapsule (MC) according to the IUPAC definition (Vert et al., 2012). However a MC is not necessarily the obtained system in a pharmaceutical batch mixing or extrusion process. A wide spectrum of suitable excipients can be used as matrix material. Depending on its chemical nature, plasticizing effects of the API on the applied excipient must be considered (Andrews et al., 2009; Liu et al., 2010). The result is a single-phase system of excipient and API, a glassy solid solution (GSS) (Fig. 1).

Thus, this study focuses on two main goals. Firstly, the identification of a suitable excipient for obtaining a GSS with an essential oil (EO), and secondly the comparison of MC and GSS samples, obtained by batch mixing. The monoterpenoid carvacrol was used as the model substance for EOs and other liquid lipophilic APIs. It is a main component of the essential oil of thyme and oregano and has antimicrobial properties (Baydar et al., 2004). Extrusion and batch mixing processes with carvacrol have been described previously (Tackenberg et al., 2014b; Topolkaraev et al., 2013).

The carbohydrates sucrose, maltodextrin, and a batch mix of both substances (1:1 by mass) served as excipients for a microcapsule system. These substances were selected due to their wide use as shell materials in flavour encapsulation in food science (Gunning et al., 1999). The physical processes during batch mixing of these carbohydrates have already been investigated (Tackenberg et al., 2014a). Another previous study (Tackenberg et al., 2014b) indicated no plasticizing properties of carvacrol on the carbohydrate matrix. This topic was investigated further in this study.

Initial investigations dealt with a carrier screening for carvacrol, based on the concept of solubility parameters. These theoretical calculations should be verified by two differential scanning calorimetry (DSC) methods. In the main part of this study, batch-mixing processes were used to combine carvacrol with both a miscible and immiscible carrier. The obtained samples were characterised by DSC and visualized via X-ray micro computerised tomography (μ-CT). The retained carvacrol content was tested via gas chromatography (GC).

2. Experimental

2.1. Materials

Carvacrol (Sigma Aldrich Chemie GmbH, Schnelldorf, Germany), deionized water, maltodextrin DE 12 and DE 17 (Glucidex® 12 D and 17 D, Roquette Frères, Lestrem, France), methylene chloride (VWR International GmbH, Darmstadt, Germany), polyvinylpyrrolidone (PVP) K 12 and K 17 (Kollidon® 12 PF and 17 PF, BASF, Ludwigshafen, Germany), sodium hydroxide (AppliChem GmbH, Darmstadt, Germany), and sucrose (Bäko Puderzucker, BÄKO Marken und Service eG, Bonn, Germany) were used in this study.

2.2. Batch mixing process

2.2.1. Preparation of the material

A 1:1 mass ratio of maltodextrin DE 12 and sucrose was mixed in a bin blender (LM20, Bohle, Ennigerloh, Germany) at a rotation speed of 25 min^{-1}, for 10 min. PVP K 12 was dried at 45 °C and 300 mbar for at least 8 h to remove the adsorbed water. The true densities of the carbohydrate mixture (1.5058 g/ml) and PVP K 12 (1.2039 g/ml) were determined by a helium pycnometer (AccuPyc 1330, Micromeritics, Norcross, GA 30093, USA). The density of carvacrol (0.9751 g/ml) was taken from literature (Carpenter and Easter, 1955). A value of 1.0 g/mL was used as the density of deionized water.

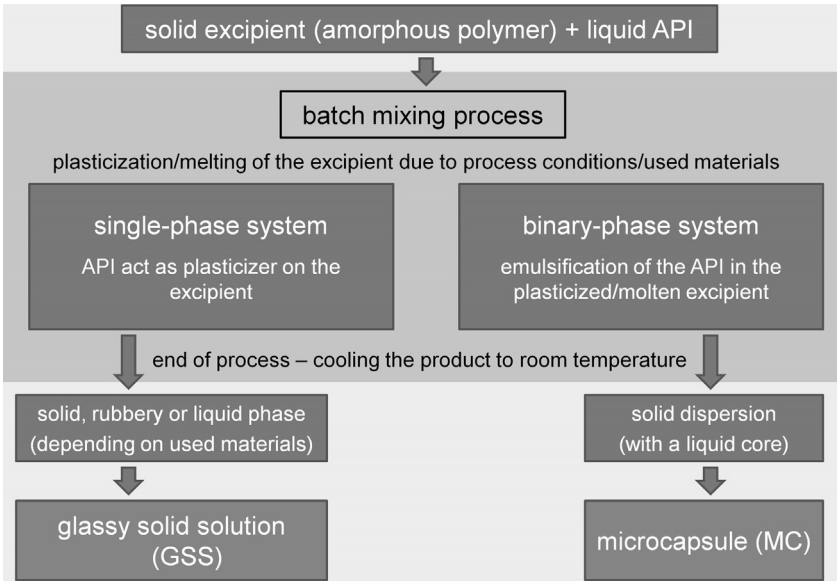

Fig. 1. Batch mixing of a solid excipient with a liquid API at elevated temperature could lead to a single-phase (glassy solid solution – GSS) or binary-phase (microcapsule – MC) system.