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A gas phase method for the generation of aqueous submicron suspensions of poorly water soluble organic substances

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ABSTRACT

This work presents a novel process for the production of vapor-borne submicron organic particles and their transfer into an aqueous environment. A mixture of water and the organic substance is totally evaporated in a micro-structured evaporator. In a second step, the hot vapor mixture is rapidly cooled down inside a quench cooler so that the organic component gets into a supersaturated state and fine particles are formed due to homogenous nucleation. The rapid cooling is realized by the injection of liquid water into the hot vapor atmosphere. The liquid water evaporates and thereby cools down the vapor mixture. Water as one component of the vapor mixture remains in the vapor phase and acts as a carrier for the generated organic particles. The generation of the aqueous suspension is realized by the total condensation of the water vapor atmosphere directly after the quench cooler. The condenser is continuously supplied with surfactant solution. This prevents agglomeration as soon as the particles get transferred from the vapor into the liquid environment. The process has been realized successfully in a lab-scale plant. First results with Tocopheryl acetate and Myristyl myristate as model substances are presented in this work.

1. Introduction

The production of submicron particles of organic substances has become an important issue in many industrial applications in the recent years. Regarding organic substances for pigment and color technology, the reduction of the particle size can improve pigment performance parameters or optical properties (Hao and Iqbal, 1997). Another important field for the application of submicron organic particles is the production of pharmaceutical and cosmetic drugs. A considerable number of organic drugs offer only a low or almost no solubility in water, which limits their bioavailability significantly (Lipinski, 2000; Hu et al., 2004). The reduction of the particle size is one approach well established to increase the bioavailability (Hu et al., 2004; Müller et al., 2001). Reducing the particle size means increasing the surface area per volume, which leads to higher dissolution rates (mass dissolved per time) despite the low solubility of the substance (Hu et al., 2004). The techniques to generate nanoparticles of organic substances can generally be divided into two classes: top-down and bottom-up process (Horn and Rieger, 2001). A top-down process is characterized by breaking up the substance from an initial state like granulate or coarse powder until the desired particle size is reached. Typical top-down processes are dry or wet milling (Merisko-Liversidge et al., 2003) and high pressure homogenization processes (Müller et al., 2001). These processes require high energy input causing sometimes problems like high mechanical and thermal stress or erosion from pearls in case of milling processes (Buchmann et al., 1996).

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Nomenclature

S_i	saturation ratio of the organic component *i* (–)
p_i	partial pressure of organic component *i* (mbar)
$p_{i,s}$	saturation vapor pressure of organic component *i* (mbar)
p	pressure (mbar)
T	temperature (K)
S_{th}	theoretical saturation ratio (–)
S_{crit}	critical saturation ratio (–)
J	nucleation rate ($cm^{-3}\,s^{-1}$)
K	kinetic factor ($cm^{-3}\,s^{-1}$)
ΔG^*	Gibbs free energy of formation (J)
k	Boltzmann constant ($J\,K^{-1}$)
σ	surface tension ($N\,m^{-1}$)
V_L	molar volume ($m^3\,mol^{-1}$)
R	universal gas constant ($J\,mol^{-1}\,K^{-1}$)
c	concentration of surfactant ($g\,l^{-1}$)
w	mass fraction of organic component (–)

Subscripts

TA	Tocopheryl acetate
MM	Myristyl myristate
Tween 80	Tween® 80
SDS	Sodium dodecyl sulfate

In contrast to that, in bottom-up processes particles are generated either by chemical reactions (Pavel, 2004) or by homogenous nucleation in a supersaturated phase. In liquid phase based processes, the organic substance has to be dissolved and supersaturation is established by reducing the solubility of the specific substance in its solvent (D'Addio and Prud'homme, 2011). Cooling the solution (Worlitschek and Mazzotti, 2004; Chew et al., 2007) or adding an antisolvent (Johnson and Prud'homme, 2003; Matteucci et al., 2006; Reverchon, 1999) are the most common methods in this field to create a supersaturated state and to initiate homogenous nucleation. The application of microemulsions for precipitation processes is another possibility. The nucleation of the dissolved organic substance occurs in a disperse phase (Lawrence and Rees, 2000; Margulis-Goshen and Magdassi, 2012) and particles grow inside solvent droplets. The advantage of this path is that the limited reservoir of organic molecules inside such a droplet prevents their growth to too large sizes.

The advantage of liquid phase based nucleation is the possibility of adding surfactants to the liquid in order to prevent agglomeration. On the other hand, solvents or reactants required for those processes usually need to be separated afterwards especially concerning substances for pharmaceutical or cosmetic applications. In order to avoid liquid solvents, the nucleation process can also be performed in a supersaturated gas phase. In this case a saturation ratio S_i of the organic component i in the gas phase can be defined as:

$$S_i = \frac{P_i}{P_{i,s}(T)} \tag{1}$$

p_i is the partial pressure of the organic substance and $p_{i,s}$ its corresponding saturation pressure at a given temperature. According to classical nucleation theory, highly supersaturated phases ($S_i \gg 1$) favor the generation of high number concentrations and consequently small particles. This can be achieved by the rapid formation of supersaturated states, i.e. high rates of supersaturation, which guarantee the generation of high saturation ratios despite incipient particle growth.

Particle formation processes using rapid expansion of supercritical fluids (RESS) are promising ones in this field (Türk et al., 2002; Jung and Perrut, 2001). The main disadvantage of all gas phase based particle formation processes is the fact that the particles must be deposited on a filter or another separator after their generation. Agglomeration of these small particles to larger structures in such a separation step is unavoidable. Agglomerates have to be redispersed in further process steps to produce a consumer product. Redispersion is energy intensive and a particle size distribution similar to that directly after the particle formation process is very difficult or almost impossible to regain. A modification of the RESS process, the RESOLV (Meziani et al., 2004; Sane and Thies, 2005) or RESSAS (Young et al., 2000; Türk and Lietzow, 2008) process faces this problem by expanding the supercritical solution containing the dissolved organic substance into an aqueous surfactant solution in order to precipitate and to stabilize the particles therein directly after their formation. That means the gas borne particles are separated from the inert carrier gas in a bubble column. Typical particle separation efficiencies in such devices are always considerably lower than 100% depending on the actual system and process conditions (Koch and Weber, 2014).

This new process presented in this work also combines the advantages of both the gas phase based and the liquid phase based particle production routes: The particle formation takes place in a gaseous environment so that liquid solvents can be avoided. Directly after the formation process the particles are transferred into a liquid environment, where they are stabilized by surfactants. The combination of these two aspects is achieved by the use of a second condensable substance beside the organic one as a carrier medium: water. Water is able to form both the gaseous environment for the particle formation process and the liquid environment for the stabilization and storage of the produced particles. Both procedures can easily be connected by simple total condensation within a single process. Thus, in contrast to the processes mentioned above, the particle transfer efficiency into the liquid environment is 100%. This new process, illustrated in Fig. 1, consists of three main steps:

I. Total evaporation of water and the organic substance.
   The poorly water soluble organic component is, if necessary, melted, mixed with water and then injected into an evaporator to be evaporated totally so that a vapor mixture is formed. Therefore, the organic substance needs to provide a certain volatility to be evaporated totally.
II. Quenching of the vapor-mixture.
   After the evaporator the vapor mixture is cooled down rapidly in a quench cooler by injecting liquid water. Because of the rapid temperature drop, a high supersaturation as a necessary precondition for homogenous nucleation and consequently particle growth is achieved. The water still remains in the vapor phase in this step. Thus, this system may be termed as a vaporosol, according to the term aerosol for particles formed and borne in an inert gas.
III. Total condensation of the water-vapor atmosphere.
   The water vapor atmosphere is totally condensed in a condenser in the last step. The main part of the system,