



Air-jet atomization for preparation of lipid nanoparticles: Dependence of size on solute concentration



Mahak Sapra^a, Y.S. Mayya^{b,*}, Chandra Venkataraman^{a,b}

^a Centre for Research in Nanotechnology and Science, Indian Institute of Technology Bombay, Powai, Mumbai, Maharashtra 400076, India

^b Department of Chemical Engineering, Indian Institute of Technology Bombay, Powai, Mumbai, Maharashtra 400076, India

ARTICLE INFO

Article history:

Received 14 January 2016

Received in revised form

17 May 2016

Accepted 21 May 2016

Available online 26 May 2016

Keywords:

Scaling law exponent

Solid lipid nanoparticles

Solute diffusion model

Spray-drying

Droplet size

Solute effects

ABSTRACT

Engineering nanoparticles for applications such as drug delivery, needs understanding of dependence of particle size on process and precursor parameters. The size of nanoparticles prepared through the aerosol route using solution droplet drying technique is traditionally governed by a 1/3rd scaling law between dry particle diameter and precursor solute concentration. Here, we experimentally investigate this relationship, for precursor solutions of lipids in organic solvents. Nanoparticles were prepared using air-jet atomization of precursor solutions of stearic acid in organic solvents (acetone, chloroform, methanol and ethanol), in a pulse heat aerosol reactor, at a process temperature of 50 °C. The relationship between median mobility diameter of prepared nanoparticles (40–155 nm) and solute concentration was governed by a scaling law exponent (SLE) in the range 0.104–0.182. The observed exponents showed significant deviations from the classical 1/3rd law. The experimental investigation indicated an unexpected increase in particle number concentration with increasing solute concentration for all solvents studied. Simulations with a critical super saturation based solute diffusion model and theoretical calculations of size dependent external factors such as coagulation and wall losses during transit, could not explain the deviation in SLE, nor the increased number concentrations. These considerations point to possible effects of solute concentration on the mechanism of droplet formation during the atomization process. A preliminary model based on an area conservation law has been proposed to explain the twin effects of deviation in SLE and increased droplet number concentration with increasing solute concentration. The present study provides empirical data on the relationship between dry particle diameter and solute concentration in the selected lipid-organic solvent systems. Also, it opens avenues for further understanding nanoparticle formation by air-jet atomization.

© 2016 Elsevier Ltd. All rights reserved.

1. Introduction

Nanoparticles with controlled properties, made of organic, inorganic or magnetic materials, have been explored as promising vehicles for the delivery of drugs to target sites through parenteral routes (Bamrungsap et al., 2012; Moghimi, Hunter, & Andresen, 2012; Wissing, Kayser, & Muller, 2004). The highest potential for prolonged drug release has been observed for nanoparticles in the size range of 100–200 nm. Nanoparticle size plays a critical role in the delivery of therapeutic agents

* Corresponding author. Tel.: +91 22 2576 7228; fax: +91 22 2572 6895.

E-mail address: ysmayya@iitb.ac.in (Y. Mayya).

(drug/gene) and their in-vivo fate (Petros & DeSimone, 2010). Thus, it is important to be able to relate nanoparticle size to process parameters and conditions in methods used for their preparation.

Aerosol based methods (electrospray and air jet atomization) offer the advantage of being single-step, continuous processes that can produce free nanoparticles for therapeutic applications. Drying of submicron solution aerosols, generated using air-jet atomization, has recently been used to make nanoparticles with controlled size, structure and crystallinity (Pawar, Chen, & Venkataraman, 2012; Pawar & Venkataraman, 2011; Raula, Eerikainen, & Kauppinen, 2004). Traditionally, the output specifications of historically developed atomizers and nebulizers have been characterized based on the 1/3rd scaling law, the power with which diameter of the nanoparticle obtained varies as a function of precursor solute concentration (Raabe, 1976). In an early review of air jet atomizers, it was observed that “The size distribution of the residual particles after complete drying can be obtained by multiplying the drop size by the cube root of the fractional concentration of the solute by weight of the solute and the cube root of the ratio of the densities of the solution/residual particles” (May, 1973).

The argument for 1/3rd scaling law proceeds from the fact that in the course of drying of solution droplets, the solute material precipitates almost uniformly throughout the droplet volume to its crystalline density. The residual moisture present within the precipitate evaporates slowly allowing the formation of a well solidified solute structure. In that case, solid density of the dry particle would be equal to the crystalline density, which is independent of original concentration. The solute mass contained in the precipitate is then proportional to the cube of the dry particle diameter and since this mass should be the same as the amount of solute contained originally in the droplet, the 1/3rd scaling law is written as Eq. (1)

$$D_p = D_d \left(\frac{C}{\rho} \right)^{1/3} \quad (1)$$

where D_d is the droplet diameter, C the precursor solute concentration, D_p the particle diameter (after drying), and ρ is the constant dry particle density/crystal density.

The simplicity and elegance of 1/3rd scaling law has led to its use for determination of droplet diameter from ultrasonic nebulizers (Rodes, Smith, Crouse, & Ramachandran, 1990), as a tool for parameter selection in process development (Dobry et al., 2009) and for estimating droplet sizes from different nebulizers (Zarrin, Kaufman, & Socha, 1991). However, it is now widely accepted that drying of submicron solution droplets involves several complex stages, such as, solute diffusion, formation of a crust (which defines the particle diameter), its thickening to form a shell and drying of liquid inside the crust giving rise to hollow or solid dry particles (Bandyopadhyay, Pawar, Venkataraman, & Mehra, 2015; Jayanthi, Zhang, & Messing, 1993). Thus, tailored engineering of nanoparticles is possible by identifying factors that govern dependence of size on process parameters and conditions, which may cause deviation from the classical 1/3rd scaling law.

Important evidence for possible deviation from 1/3rd law came in context of electrospray atomization. A modeled scaling law for highly conducting liquids was proposed (Fernández de la Mora & Loscertales, 1994) to deviate from the classical 1/3rd law. Competing models for simple electrospray predict the same expression for the emitted current except for a non-dimensional constant which either depends on dielectric constant of the liquid (Basak, Chen, & Biswas, 2007; Fernández de la Mora & Loscertales, 1994; Ganan-Calvo, Davila, & Barrero, 1997), or is independent of it (Ganan-Calvo, 1998). Experimental determination of scaling laws for coaxial electrospray demonstrated dependence of current (I) on the driving (outer capillary) flow rate (Q) to be 1/2th law (Lopez-Herrera, Barrero, Lopez, Loscertales, & Marquez, 2003). The effect of conductivity of the precursor solutions was incorporated to obtain modified scaling laws for both weak and strong electrolytes (Basak et al., 2007). Thus, electrospray system has been characterized in terms of determining a scaling law to predict particle size and has been shown to deviate from the classical 1/3rd law but, its application for therapeutic purposes is limited by the conductivity of the solution and low generation rates (Gomez, Bingham, de Juan, & Tang, 1998).

The size and internal structure of nanoparticles prepared by drying of submicron solution droplets produced by air-jet atomization, is governed by solvent physical properties such as vapor pressure, solute concentration, droplet temperature (Pawar et al., 2012; Pawar & Venkataraman, 2013), effect of solute on surface tension (Steckel and Eskandar, 2003), Peclet number (Vehring, Foss, & Lechuga-Ballesteros, 2007) and critical supersaturation ratio (CSS) (He, Bhamidi, Tan, Kenis, & Zukoski, 2006). CSS in turn depends upon solute molecular volume, interfacial tension and solubility characteristics of solute in the solvent. The complicated mathematical theory of CSS based models (Bandyopadhyay et al., 2015; Eslamian, Ahmed, & Ashgriz, 2006; Jayanthi et al., 1993) renders it difficult to predict the dependence of diameter on the initial solute concentration. A priori, it questions the constant density assumption and hence the basis of the 1/3rd law.

In view of the above discussions, the validity of the 1/3rd scaling law between observed dry particle diameters and solute concentration deserves careful examination. The present work investigates this aspect through experiments for stearic acid nanoparticles prepared by drying of submicron solution droplets generated by air-jet atomization. Different organic solvents were chosen to account for the variability in vapor pressure and solubility of stearic acid in the solvent. Significant deviations were observed in the SLE values for all the solvents. In support of providing explanation, several auxiliary parameters were measured and attempt has been made to explain the observations from different perspectives.

Download English Version:

<https://daneshyari.com/en/article/6344250>

Download Persian Version:

<https://daneshyari.com/article/6344250>

[Daneshyari.com](https://daneshyari.com)