Chemical Engineering and Processing 86 (2014) 47–52

Contents lists available at ScienceDirect

Chemical Engineering and Processing: Process Intensification

journal homepage: www.elsevier.com/locate/cep

Review

Particle formation and micronization using non-conventional techniques- review

Fahim T.K. [a], Zaidul I.S.M. [a,*], Abu Bakar M.R. [a], Salim U.M. [a], Awang M.B. [b], Sahena F. [c], Jalal K.C.A. [c], Sharif K.M. [a], Sohrab M.H. [d]

[a] Faculty of Pharmacy, International Islamic University Malaysia, Kuantan Campus, 25200 Kuantan, Pahang, Malaysia
[b] Faculty of Pharmacy, Cyberjaya University College of Medical Sciences, 63000 Cyberjaya, Selangor Darul Ehsan, Malaysia
[c] Faculty of Science, International Islamic University Malaysia, Kuantan Campus, 25200 Kuantan, Pahang, Malaysia
[d] School of Industrial Technology, Universiti Sains Malaysia, 11800 Pulau Pinang, Malaysia

ARTICLE INFO

Article history:
Received 17 August 2014
Received in revised form 4 October 2014
Accepted 15 October 2014
Available online 22 October 2014

Keywords:
Micronization
Particle formation
Dissolution rate
Encapsulation efficiency
Supercritical fluid

ABSTRACT

Due to growing concerns regarding health, safety and the environment, non-conventional methods for particle formation and micronization that are either solvent-less or use environmentally acceptable solvents such as carbon dioxide have come into favor. Supercritical CO_2 (sc CO_2) ($T > 31.1\,^{\circ}C$, $P > 7.3$ MPa) has been used in food and pharmaceutical industries to minimize the use of organic solvents, produce new food products, produce environmentally superior food products and to process and micronize (0.1–5 μm) pharmaceuticals. Control of particle size increases the dissolution rate of drugs into the body. Techniques that use sc CO_2 eliminate inherent drawbacks of conventional methods such as thermal or mechanical degradation of the product, poor control of the particle size and morphology, lack of brittleness of some polymers and low encapsulation efficiency. Several techniques have been reported for the particle formation and micronization using supercritical fluids that have been successfully scaled up for commercial use. Supercritical CO_2 has also been used to develop applications for medicines, essential oils, vitamins, food grade polymers, catalysts and pigments. This review highlights the process mechanism of supercritical fluid based techniques as well as some applications on particle formation and micronization.

Contents

1. Introduction

The demands for processing fine particles with a biocompatible or biodegradable carrier material to produce micron-sized and nanosized paritcles are growing and is being applied in the pharmaceutical, cosmetic and food industries [1,2]. Various techniques can be used to produce micro and nanoparticles. Conventional techniques use freeze drying, spray-cooling, spray-drying, fluidized bed coating, air micronization, coacervation, recrystallization from the liquid solution and sublimation [3]. Non-conventional techniques use supercritical fluid technique that can be divided into three groups according to their role in the

* Corresponding author. Tel.: +60 9 5714841; fax: +60 9 5706775.
E-mail address: zaidul@iium.edu.my (I.S.M. Zaidul).

http://dx.doi.org/10.1016/j.cep.2014.10.009
0255-2701/

processing; (a) Supercritical fluid (SCF) as a solvent which include rapid expansion of supercritical solution (RESS), (b) SCF as a solute which include particles form gas-saturated solutions (PGSS) and (c) SCF as a antisolvent which include supercritical anti-solvent (SAS), gas anti-solvent (GAS), aerosol solvent extraction system (ASES), solution enhanced dispersion by supercritical fluid (SEDS) [3,4].

Non-conventional techniques that use supercritical fluids have many advantages compared to the conventional techniques as they do not pollute the extracts, residues, and, in many cases, the environment. The characterization of supercritical fluids are done by a continuous adjustable solvent power/selectivity obtained by different pressure and temperature. Among all the possible supercritical fluids, carbon dioxide is largely used as a lipophilic solvent because it is nontoxic, nonflammable, nonpolluting and relatively cheap. Its critical state of pressure ($Pc = 7.3$ MPa) and temperature ($Tc = 31.1\,^{\circ}C$) are readily accessible in practical applications. Various supercritical fluids-based processes for fine particles have been developed for taking advantages of their properties. Recent reviews on micronization with non-conventional techniques are highlighted in the literature [5–14]. The focus is more on the recent development in the practical applications, especially the pharmaceutical and nutraceutical applications of this technology as well as the fundamentals and description of the main features and mechanisms of some of the most relevant supercritical fluid techniques used for this purpose. The review also highlights the comparison between the different supercritical fluid techniques in respect to their advantages and limitations.

1.1. Micronization using supercritical fluid techniques

1.1.1. Rapid expansion of supercritical solution (RESS)

The concept of RESS was proposed as a supercritical nucleation by Krukonis in 1984 and the technique became very popular for particle design because of its simplicity [1]. Solutes are dissolved into supercritical fluid and the fluid is expanded through depressurization to produce fine particles. This process is based on the solubility of the polymer or solute (from which particles are formed) in the SCF [15]. In detailed description of RESS, the solute is first dispersed in the SCF such as carbon dioxide and the high pressure solution is expanded adiabatically within a nozzle to gaseous condition creating high super-saturation and thereby causing rapid nucleation and the desired product will be precipitated as fine particles into the collector (Fig. 1). This concept has been demonstrated for a materials including polymers, oils and some pharmaceutical substances [5,7,8,12].

The advantage of the RESS process for producing fine particles is that materials can be formed with a narrow size of distribution and it is a single step process where the organic solvents are eliminated [4]. The disadvantages of RESS process are high fluid consumption especially if there is a compound of low solubility in supercritical fluid and it suffers from the operational and scale-up problems related with nozzle plugging due to accumulation of the particles in the fluid nozzle [16]. Beside the solubility limitations, there are some major problems regarding the extremely fast precipitation by this technique. As a result, it becomes very difficult to control the loading and shape of the particles, as these parameters are very sensible to the degree of supersaturation [15]. To overcome this problem, the carrier can be precipitated over previously formed microparticles of the active substance. By implementing this procedure, it is becoming easier to control the loading and morphology of the particles by varying the feed parameters, as long as the substance to be coated and the polymer is homogenously dispersed in the precipitation chamber. To minimize this homogeneity problem, Mishima [17] proposed a high shear mixer into the expansion vessel which helps in circulating the particles improving the homogeneity of the process. In general, the micronization process that exhibit a good solubility in CO_2 have very promising applications due to the simplicity and immaculateness of this process.

1.1.2. Particles from gas saturated solution (PGSS)

The very first application of the PGSS concept related mostly to paint and polymer industry particularly to powder coating [18]. Since the solubilities of compressed gases in liquids and solids like polymers are usually much higher than those of such liquids and solids in the compressed gas. That is why, this method is proved to be more advantageous over RESS.

PGSS process is based on the formation of the particles that absorb supercritical fluid at high concentration because of the insolubility in supercritical fluids [15] and is highly suitable for the micronization of liquids, suspensions and emulsions. PGSS process consist of solubilizing a supercritical fluid into a liquid suspended solution or into a melting material and then the gas containing solution is rapidly expanded through a nozzle into a high pressure vessel leading to the precipitation of the fine particles [19] (Fig. 2). This process is very useful for the permeation of active ingredients in polymer matrices. Some of the published reports regarding PGSS process are highlighted in this review [13,14]. To date, more than 100 substances have been encapsulated with the PGSS process and some of them are shown in Table 1.

The advantages of PGSS are low fluid consumption and low to medium pressure process [4]. Because of simplicity of this process, the processing cost is very low compare to other processes. It can be used with suspensions or emulsion of active ingredients in polymers or other carrier substances leading to composite particles. The disadvantages of PGSS process include the difficulty

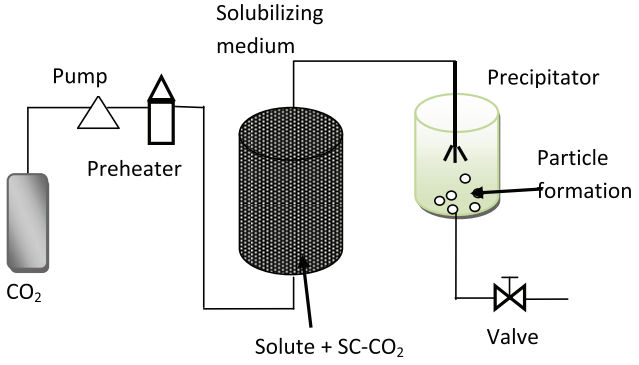

Fig. 1. Schematic diagram of RESS process (Adapted from Ref. [41]).

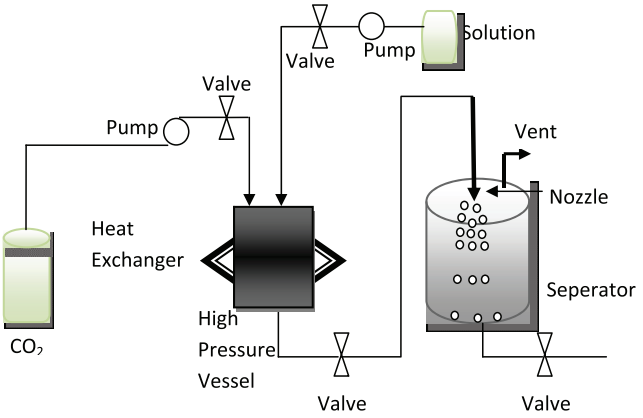

Fig. 2. Schematic diagram of PGSS process (Adapted from Ref. [13]).