

Review

Production of micro- and nano-composite particles by supercritical carbon dioxide

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Abstract

Carbon dioxide is the only fluid which has been applied in producing composite particles by supercritical fluid methods. In the present paper, design of composite particles by supercritical carbon dioxide (SCO₂) will be reviewed. The production processes of composite particles by SCO₂ are classified based on fluid roles, which are solvent, anti-solvent, solute and reaction medium. In addition, these processes are sub-categorized based on the fluid flow and contact pattern.

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1. Introduction

Composite particles are produced for many purposes such as controlling the release of active material in a desired quantity and

location, increasing the dissolution rate of slightly water-soluble materials and modifying the surface properties of particles used in pharmaceuticals, catalysts, cosmetics, printing industry and energetic materials. Composite particles are defined as either the dispersion of one (or more) solid phase(s) in another continuous solid phase, called matrix structure, or a core of a material coated by another solid phase, called reservoir structure (Fig. 1). Matrix and reservoir structures have been called by

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Nomenclature

BSA	bovine serum albumin
CBZ	carbamazepine
CD	cyclodextrin
CLSM	confocal laser scanning microscopy
D	diameter of expansion device
DCR	dechlorane
DSC	differential scanning calorimetry
DMSO	dimethyl sulfoxide
EE	encapsulation efficiency, ratio of loaded drug weight to theoretical drug weight
FITC	fluorescein isothiocyanate
GAS	gas anti-solvent
HPBCD	hydroxypropyl- β -cyclodextrin
HPC	hydroxypropyl cellulose
HPGCD	hydroxypropyl- γ -cyclodextrin
IY	inclusion yield (total drug content – free drug content)/total drug content
L	length of expansion device
MBCD	methyl- β -cyclodextrin
MC	methylene chloride or dichloromethane
MW	molecular weight
<i>p</i> -HBA	<i>para</i> -hydroxybenzoic acid
PCA	compressed anti-solvent
PDMS-g-PA	polydimethylsiloxane-graft-polyacrylate
PEG	poly ethylene glycol
PGMA	poly glycidyl methacrylate
PGSS	particle from gas saturated solution/suspension
PLA	poly lactic acid
PLGA	poly D,L-lactide- <i>co</i> -glycolide
PMMA	poly methyl methacrylate
PPG	poly propylene glycol
PS	poly styrene
PVB	poly 4-vinylbiphenyl
PVCVA	poly vinyl chloride- <i>co</i> -vinyl acetate
PVDF	poly vinylidene fluoride
PVP	poly vinyl phenol
RESS	rapid expansion of supercritical solution
RESS-N	rapid expansion of supercritical solution with a non-solvent
SAS	supercritical anti-solvent
SEDS	solution enhanced dispersion by supercritical fluids
TSZnPc	zinc phthalocyanine tetrasulfonic acid
XRD	X-ray diffraction

Greek letter

η	coating efficiency, ratio of coating material on the particle to theoretical coating material input
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some researchers microsphere and microencapsule, respectively. Composite particles can be produced by different ways. Among the proposed methods, the supercritical fluid (SCF) method is the most recent one. Supercritical carbon dioxide

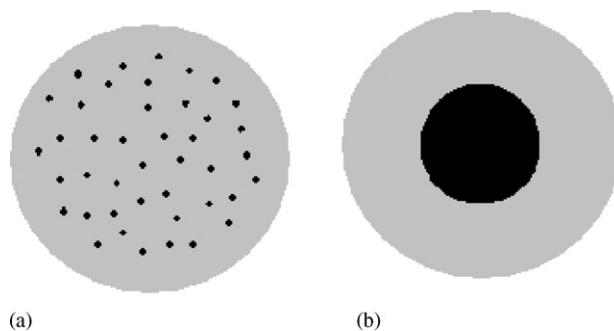


Fig. 1. (a) A matrix structure, microsphere, and (b) a reservoir structure, microencapsule.

(SCO₂) is the only used fluid due to its favourable critical properties, i.e. low critical temperature ($T_C = 304.2$ K) and moderate critical pressure ($P_C = 7.38$ MPa). It is also environmentally suitable, non-toxic, non-flammable, inexpensive and recyclable. The design of particles by SCF method has been commenced by production of single-component particles, followed by more valuable and complicated applications like composite particles.

Several review papers have been published to cover numerous available literatures on particle design by SCF method. Tom and Debenedetti [1] have published the first review article on the application of SCF method in particle design. This paper has focused on rapid expansion of supercritical solution (RESS) method. The RESS method is the first SCF method which has been applied to produce particles. Tom and Debenedetti have reviewed the experimental works done on inorganic and organic systems. Palakodaty and York [2] have studied the effect of phase behaviour on the formation of particles in three groups of processes, in which SCF is acting as solvent, anti-solvent or solute. In 1999, Reverchon [3] has reviewed the application of SCFs as anti-solvents in precipitation of micro- and nano-single-component particles at various industrial fields during 1990s decade. Jung and Perrut [4] have published a review article on different SCF methods developed for manufacturing of particulates during next decade. This paper was followed by another review article published by Shariati and Peters [5]. In 2002, Hay and Khan [6] have summarized a number of applications of RESS and particle from gas saturated solution (PGSS) methods in particles coating. Hauthal [7] has published a tabular survey on application of supercritical fluids in chemistry and chemical engineering. Woods et al. [8] have reviewed the design and application of new surfactants, polymer processing and polymer blend technologies and production of biomedical materials in supercritical carbon dioxide.

Although the production of composite particles has been reviewed in some of the mentioned articles [4–6,8], in none of them a peculiar attention has been made on this subject. In 2005, two review papers were published by Ginty et al. [10] and Yeo and Kiran [9], in which more concentration was made on composite particles. Ginty et al. have summarized the application of SCO₂ in micronization of drug and production of composite particles and matrices. Yeo and Kiran have focused on works related to design of pure polymeric and composite par-

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