Available online at www.sciencedirect.com
ScienceDirect
Advanced Drug Delivery Reviews 58 (2006) 1688–1713
Advanced DRUG DELIVERY Reviews
www.elsevier.com/locate/addr

Freeze-drying of nanoparticles: Formulation, process and storage considerations ☆

Wassim Abdelwahed [a], Ghania Degobert [a,*], Serge Stainmesse [b], Hatem Fessi [a]

[a] *Laboratoire d'Automatique et de Génie des Procédés (LAGEP) UMR-CNRS 5007 CPE Lyon, ISPB, Université Claude Bernard Lyon 1, 43, Boulevard du 11 Novembre 1918, 69622 Villeurbanne cedex, France*

[b] *Conservatoire National des Arts & Métiers-Chaire des Techniques Pharmaceutiques, 292, rue Saint Martin, 75141 Paris, Cedex 03, France*

Received 14 September 2006; accepted 29 September 2006
Available online 6 October 2006

Abstract

Freeze-drying has been considered as a good technique to improve the long-term stability of colloidal nanoparticles. The poor stability in an aqueous medium of these systems forms a real barrier against the clinical use of nanoparticles. This article reviews the state of the art of freeze-drying nanoparticles. It discusses the most important parameters that influence the success of freeze-drying of these fragile systems, and provides an overview of nanoparticles freeze-drying process and formulation strategies with a focus on the impact of formulation and process on particle stability.

Keywords: Nanoparticles; Freeze-drying; Stability; Freezing; Cryoprotectant; Glass transition; Physical and chemical characterization; Formulation

Contents

☆ This review is part of the *Advanced Drug Delivery Reviews* theme issue "2006 Supplementary Non-Thematic Collection", Vol. 58/15, 2006.

* Corresponding author. Tel.: +33 472 431 874; fax: +33 472 431 874.
E-mail address: degobert@lagep.cpe.fr (G. Degobert).

0169-409X/$ - see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.addr.2006.09.017

1. Introduction

In the last decade, significant effort has been done to develop nanoparticles for drug delivery [1–5]. The colloidal systems offer a suitable means for delivering as well as small molecules than macromolecules such as proteins or peptides by either localized or targeted delivery to the tissue of interest. These systems in general can be used to provide targeted (cellular/tissue) delivery of drugs, to improve oral bioavailability, to sustain drug effect in target tissue, to solubilize drugs for intravascular delivery, and to improve the stability of therapeutic agents against enzymatic degradation [6–9].

Nanoparticles are submicron sized colloidal polymeric systems. According to the process used in preparing nanoparticles, nanospheres or nanocapsules can be obtained [1–4,10]. Nanocapsules are vesicular systems in which a drug is confined inside a cavity surrounded by a polymeric membrane, whereas nanospheres are matrix systems in which a drug is dispersed throughout the particles.

The submicron size of nanoparticles offers a numerous advantages over microparticles. Nanoparticles have in general relatively higher intracellular uptake compared to microparticles. It was demonstrated that nanoparticle size of 100 nm showed 2.5 fold greater uptake compared to 1 μm and 6 fold higher uptake compared to 10 μm microparticles in Caco-2 cell line [8]. Similar results were obtained when these formulations of nano- and microparticles were tested