Available online at www.sciencedirect.com
ScienceDirect
Advanced Drug Delivery Reviews 59 (2007) 379–402
Advanced DRUG DELIVERY Reviews
www.elsevier.com/locate/addr

Characterization of lipid nanoparticles by differential scanning calorimetry, X-ray and neutron scattering ☆

Heike Bunjes [a,*], Tobias Unruh [b]

[a] *Institut für Pharmazeutische Technologie, Technische Universität Braunschweig, Mendelssohnstr. 1, 38106, Braunschweig, Germany*
[b] *Forschungsneutronenquelle Heinz Maier-Leibnitz, Technische Universität München, Lichtenbergstr. 1, 85747 Garching, Germany*

Received 9 May 2006; accepted 24 April 2007
Available online 17 May 2007

Abstract

Differential scanning calorimetry and X-ray diffraction play a prominent role in the characterization of lipid nanoparticle (LNP) dispersions. This review shortly outlines the measurement principles of these two techniques and summarizes their applications in the field of nanodispersions of solid lipids. These methods are particularly useful for the characterization of the matrix state, polymorphism and phase behavior of the nanoparticles which may be affected by, for example, the small particle size and the composition of the dispersions. The basics of small angle X-ray and neutron scattering which are also very promising methods for the characterization of LNPs are explained in some more detail. Examples for their use in the area of solid LNPs regarding the evaluation of particle size effects and the formation of superstructures in the nanoparticle dispersions are given. Some technical questions concerning the use of the different characterization techniques in the field of LNP research are also addressed.
© 2007 Elsevier B.V. All rights reserved.

Keywords: Colloidal drug carriers; Glycerides; Cholesterol esters; Fatty acids; Physicochemical characterization

Contents

☆ This review is part of the Advanced Drug Delivery Reviews theme issue on "Lipid Nanoparticles: Recent Advances".

* Corresponding author. Tel.: +49 531 3915657; fax: +49 531 3918108.
E-mail address: Heike.Bunjes@tu-braunschweig.de (H. Bunjes).

0169-409X/$ - see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.addr.2007.04.013

1. Introduction

As for all drug delivery systems detailed characterization is a major part of the research and development work on lipid nanoparticle (LNP) dispersions to ensure the generation of systems with the desired properties. Among the multitude of analytical techniques employed for that purpose, differential scanning calorimetry (DSC) and X-ray diffraction (XRD) play a prominent role because they are able to provide structural information on the dispersed particles. Moreover, the use of these two techniques often leads to complementary information on the systems of interest. The background of these methods will be outlined in this review in a relatively brief way since DSC and XRD are well-known standard techniques in the area of pharmaceutics and since data evaluation from these methods is usually straightforward. In addition to XRD, the related techniques of small angle X-ray and neutron scattering (SAXS and SANS, respectively) can give very interesting additional information on the structure of the systems. Because these techniques are less frequently employed for the study of lipid nanoparticle dispersions, a more detailed introduction into their theoretical basics and their measurement principles will be given with special regard to their application in lipid nanoparticle research. In particular, we will consider the specific technical challenges arising from the investigation of LNP dispersions with these methods.

The second part of the review focuses on the characterization of specific properties of lipid nanoparticles that can be studied with DSC and XRD and also demonstrates the advantages of combining the two techniques. Moreover, we would like to focus the attention of the reader on some peculiarities of the use of DSC and XRD on LNP dispersions as the investigation of nanoparticulate material in liquid dispersion is not a common part of the technical literature.

This article will only cover investigations on nanodispersions based on solid lipids (in some cases with the admixture of liquid ones) which may, however, form solid, liquid as well as liquid crystalline particles in the dispersed state. Moreover, to limit the scope of our contribution, we will only consider matrix-type LNPs (e.g., emulsion droplets, suspension particles) although the analytical techniques under discussion here have important applications for the characterization also of membrane-type lipid particles (e.g., liposomes, dispersions of bicontinuous cubic phases) [1–5].

It should be emphasized that nanoparticulate lipids are not only of high interest as drug carrier systems but also play an important role in other fields of science. As a prominent example, dispersions of glycerides, in particular of triglycerides, are important research subjects in food technology (e.g., with respect to the behavior of milk and cream). Therefore, much basic work on the behavior of such systems originates from that area, providing a valuable resource on basic questions in this field. Often DSC and XRD are employed as major analytical techniques in these studies [6–10]. Another example is investigations on biological systems such as lipoproteins for which also a wealth of information has been collected by the techniques presented here [11–14].

2. X-ray and neutron scattering

2.1. Some considerations on the methods

The properties of formulations of LNPs are determined mainly by the manifold structures formed by the different components of the dispersions (lipid, drug, stabilizers, dispersion medium) and their interactions. Characteristic lengths d of these structures range from sub-atomic distances ($d < 1$ Å) important for e.g. crystal structure determination up to the μm range corresponding to the size of large particles or particle assemblies. The whole size range can be investigated by means of X-ray and neutron scattering. In general those methods detect electron (X-ray scattering) and nucleus (neutron scattering) density fluctuations, respectively, on a length scale d according to Bragg's law

$$2d \sin\theta = \lambda. \quad (1)$$

Considering the experimentally available wavelength range 0.5 Å < λ < 20 Å for neutrons and 0.5 Å < λ < 2.5 Å for X-rays the scattering angles 2θ corresponding to the size range of interest are between 0.01° and 180°. Several other properties of X-rays and neutrons such as their non-destructive nature with respect to the sample structure, their high penetration capability for organic systems allowing bulk property determination, their sensitivity to small structural changes and the variety of their applications which will be highlighted in the following give the reason for the use of these probes in LNP research.

Download English Version:

https://daneshyari.com/en/article/2072331

Download Persian Version:

https://daneshyari.com/article/2072331

Daneshyari.com