Journal of Drug Delivery Science and Technology 46 (2018) 259–267

Contents lists available at ScienceDirect

Journal of Drug Delivery Science and Technology

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

Novel drug delivery systems based on the encapsulation of superparamagnetic nanoparticles into lipid nanocomposites

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ARTICLE INFO

Keywords:
Magnetite
Solid lipid nanoparticles
Nanocapsules
Nanocomposite
Drug
Delivery
SPION
Nanomedicine

ABSTRACT

Hydrophobic superparamagnetic iron oxide nanoparticles (SPIONs) with an average size of 13 nm prepared by the salt co-precipitation method were included into solid lipid nanoparticles (SLN) and oily-core polymeric nanocapsules (NC) using the emulsification-diffusion technique to form novel lipid-magnetic drug delivery systems. Microscopy showed spherical-shaped composites with a hydrodynamic diameter between 300-400 nm and 450–500 nm for the NC/SPIONs and SLN/SPIONs composites, respectively. The entrapment efficiency (EE) of SPIONs into the NC/SPIONs composite was calculated as 49.0% and 55.7% for batches prepared with 25% and 12.5% (w/w) of SPIONs, respectively. EE for the SLN/SPIONs was calculated as 40.8% and 59.1%, respectively, for batches prepared with 25% and 12.5% SPIONs (w/w). Magnetic measurement revealed that the saturated magnetization of the NC/SPIONs and SLN/SPIONs reached values of 6–12 and 5–9 A m^2/Kg, respectively. Also, the remanent magnetization and coercivity was almost zero, suggesting characteristics of superparamagnetism that may have important implications for drug delivery. The *in vitro* release profiles showed that a model drug could be slowly released from the nanocomposite without interference of SPIONs.

1. Introduction

During the last decades, there has been an increased interest in the synthesis and application of superparamagnetic iron oxide nanoparticles (SPIONs), and other inorganic nanoparticles due to their extensive applications in various scientific fields, including biotechnology and medicine. In nanomedicine, SPIONs have been shown to provide a versatile platform for developing systems with biomedical applications; for example, controlled drug delivery systems [1], contrast agents for magnetic resonance imaging [2], theranostics agents [3], agents for hyperthermia in cancer therapy [4], separation and purification of biomolecules [5], and as a support in solid-phase extraction in analytical applications [6].

Studies have shown that the direct incorporation of uncoated SPIONs into biological systems decreases biocompatibility [7,8]. Also, uncoated SPIONs have lower physical stability due to interactions among the particles in colloidal dispersions [7,9]. Adding SPIONs can reduce efficacy when intended for use as drug-delivery carriers, and may also affect the results of drug-loading due to the decreased surface area that comes with larger size [7]. However, reducing cytotoxicity and extending the lifetime of SPIONs in suspension may be achievable through adequate chemical functionalization of their surface, have been reported the use of polymeric dispersants with Mw > 10 kDa and with low Mw < 10 kDa, the last consisting of a polymer spacer with a covalently bound anchor that has high affinity for the NP surface [10]. In recent years, has been proposed the coating of SPIONs with chitosan a biocompatible material able to electrostatically stabilize aqueous dispersions of the nanoparticles [11,12].

A potential alternative to functionalization would consist incorporating SPIONs into biodegradable or biocompatible matrices, preferably in the range of 100–1000 nm, to form nanocomposites with applications as drug-carrier systems. Without question, the chemical nature of the support matrices is one of the key elements that determine the effectiveness of such applications, as they play a major role in encapsulation efficiency (EE), biodegradability and biocompatibility. The search of optimal materials for incorporating SPIONs has led to the development of several organic composites that are classified according to their composition as either biodegradable polymer-based or lipid-

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https://doi.org/10.1016/j.jddst.2018.05.032
Received 14 December 2017; Received in revised form 19 May 2018; Accepted 21 May 2018
Available online 22 May 2018
1773-2247/