Colloids and Surfaces A: Physicochem. Eng. Aspects 416 (2013) 32–42

Contents lists available at SciVerse ScienceDirect

Colloids and Surfaces A: Physicochemical and Engineering Aspects

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

Engineering of a nanostructured lipid carrier for the poorly water-soluble drug, bicalutamide: Physicochemical investigations

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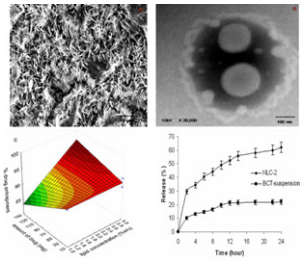
HIGHLIGHTS

- We developed a nanostructured lipid carrier (NLC) for the poorly water-soluble drug, bicalutamide (BCT).
- BCT phase transition occurred during the NLC processing and was subsequently studied by DSC, PXRD and Raman analysis.
- The presence of hydrophilic surfactants was significant to modulate BCT release from NLC.
- Developed NLC showed potential to entrap the poorly water-soluble BCT and revealed good stability for six months.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 13 July 2012
Received in revised form 14 October 2012
Accepted 18 October 2012
Available online 26 October 2012

Keywords:
Nanostructured lipid carrier
Bicalutamide
Poorly water-soluble
High-pressure homogenization
Crystalline Form I
Raman analysis

ABSTRACT

The purpose of this study was to develop an optimized nanostructured lipid carrier (NLC) for bicalutamide (BCT), a poorly water-soluble drug, and to investigate its phase transition behavior during the NLC processing. BCT loaded NLCs (BCT-NLCs) were prepared using a hot high-pressure homogenization (HPH) technique. Factorial design (2^3) was used to identify the key formulation variables influencing particle size, percent drug encapsulation, and zeta potential of the NLC. The optimized batch (NLC-2) revealed spherical morphology with a smooth surface under scanning electron microscopy (SEM). NLC-2 achieved a high drug encapsulation of $98.48 \pm 0.70\%$ and demonstrated good stability for six months. Drug–lipid interaction was investigated using Fourier transform infrared spectra (FT-IR) and proton nuclear magnetic resonance (^{1}H NMR). BCT phase transition occurred during the NLC processing and BCT crystalline Form I was identified in NLC-2. The same was confirmed by differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD), and Raman analysis. The *in vitro* release study of NLC-2, revealed peppas release kinetics with Fickian diffusion ($n < 0.5$) as drug release mechanism. The presence of hydrophilic surfactants was significant to modulate BCT release from NLC-2. Finally, NLCs made of Precirol® ATO 5 (solid lipid) and triacetin (oil) posses the potential to entrap the poorly water-soluble drug, bicalutamide and the system can be tailor-made to meet the desired drug release. This may provide better prospects for the oral delivery of bicalutamide.

1. Introduction

Prostate cancer is the second most common type of newly diagnosed cancer and the sixth leading cause of cancer deaths among men worldwide [1]. The treatment of prostate cancer generally includes surgery, radiation therapy, and the hormonal therapy [2]. Bicalutamide [BCT] is an orally active non-steroidal antiandrogen

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http://dx.doi.org/10.1016/j.colsurfa.2012.10.031