Colloids and Surfaces B: Biointerfaces 218 (2022) 112763

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

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

Functionalized bosutinib liposomes for target specific delivery in management of estrogen-positive cancer

Priya Singh, Neelu Singh, Nidhi Mishra, Raquibun Nisha, Alka, Priyanka Maurya, Ravi Raj Pal, Samipta Singh, Shubhini A. Saraf *

Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University, Vidya Vihar, Raebareli Road, Lucknow 226025, India

ARTICLE INFO

Keywords:
Estrogen-positive
Bosutinib
Breast cancer
Liposomes

ABSTRACT

This study was designed to create surface-functionalized bosutinib liposomes that could be used for the management of estrogen-positive cancers. The novelty of this work was the anti-cancer activity of bosutinib-loaded liposomes (Bos-LPs) in estrogen-positive cancer via estrogen response elements, responsible for the malignancy of cancer cells. Biotin effectively delivers active moiety to tumor tissues because it interacts with the biotin receptor and operates through the Sodium-dependent multivitamin transporters (SMVT) transporter. The prepared liposomes had a 257.73 ± 4.50 nm particle size, − 28.07 ± 5.81 mV zeta potential, 87.78 ± 1.16 % encapsulation efficiency and 85.56 ± 0.95 % drug release for 48 h. The surface architecture of biotin-modified bosutinib-loaded liposomes (b-Bos-LPs) was confirmed using scanning electron and transmission electron microscopies. In-vitro experiments revealed that b-Bos-LPs outperformed Bos and Bos-LPs in terms of significantly reduced cell viability in MCF-7 cells. According to biodistribution and pharmacokinetic studies, b-Bos-LPs have a higher Bos concentration in tumor tissues as compared to the other organs and also possess better pharmacokinetic activity, indicating that they can be used to treat carcinogen-induced estrogen-positive cancers. This is the first study to show that b-Bos-LPs can display activity against estrogen-positive cancer via biotin targeting. As evidenced by various parameters, b-Bos-LPs showed improved anticancer targeting, therapeutic safety and efficacy in carcinogen-induced estrogen-positive cancer. The receptor protein estrogen, which is primarily responsible for this cancer was downregulated by b-Bos-LPs in an immunoblotting assay. The results showed that biotinylated distearoylphosphatidylcholine (DSPC) augmented LPs loaded with Bosutinib can cause apoptosis in estrogen-positive breast cancer and be an effective way to treat estrogen-positive cancer.

1. Introduction

Bosutinib is an SRC tyrosine kinase inhibitor and small-molecule BCR-ABL used in leukemia and promising in patients with breast cancer, and has shown effectiveness in chemotherapy via extension in time for cancer progression [1]. Bosutinib and exemestane were used in hormone-positive breast cancer treatment where bosutinib showed synergistic activity with the drug exemestane. Meanwhile, bosutinib activity in breast cancer has entered clinical trials [2]. It has proven effective in various types of solid tumors and breast cancers. Some of these are in clinical trials [3]. Bosutinib is an anticancer drug which is classified as BCS Class IV, comprising low solubility and permeability and shows poor bioavailability (33.58 %). Therefore, there is an unmet need to develop an appropriate nanocarrier to deliver the active moiety to the specific tumor site, resulting in the use of a lower dose and fewer undesirable responses. Through the design and development of nanoformulations, superior performance is achieved via higher concentrations in target tissues. Lipid-based nanosystems displayed improved efficacy because of their potential for hydrophobic drug delivery to the target site. Liposomes are used as carriers to improve oral drug bioavailability and biocompatibility [4]. Biotin is one of the safest and most suitable targeting ligands for tumor cells among the many targeting moieties like proteins, antibodies, peptides, ligands based on nucleic acids and tiny molecules. Recent researches revealed that overexpressed biotin-selective transporters can be used to target cancer cells effectively. Biotin is required for gene regulation, cell signaling and chromatin structure at the cellular level. Sodium-dependent multivitamin transporters (SMVT) and biotin transporters are both used by mammalian cells to absorb biotin. SMVT is the primary active transporter for biotin absorption and it is elevated in different malignancies [5]. One of

* Corresponding author.
E-mail address: shubhini.saraf@gmail.com (S.A. Saraf).

https://doi.org/10.1016/j.colsurfb.2022.112763
Received 15 June 2022; Received in revised form 27 July 2022; Accepted 5 August 2022
Available online 6 August 2022