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RESEARCH ARTICLE

Successful delivery of docetaxel to rat brain using experimentally developed nanoliposome: a treatment strategy for brain tumor

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Abstract

Docetaxel (DTX) is found to be very effective against glioma cell *in vitro*. However, *in vivo* passage of DTX through BBB is extremely difficult due to the physicochemical and pharmacological characteristics of the drug. No existing formulation is successful in this aspect. Hence, in this study, effort was made to send DTX through blood–brain barrier (BBB) to brain to treat diseases such as solid tumor of brain (glioma) by developing DTX-loaded nanoliposomes. Primarily drug-excipients interaction was evaluated by FTIR spectroscopy. The DTX-loaded nanoliposomes (L-DTX) were prepared by lipid layer hydration technique and characterized physicochemically. *In vitro* cellular uptake in C6 glioma cells was investigated. FTIR data show that the selected drug and excipients were chemically compatible. The unilamellar vesicle size was less than 50 nm with smooth surface. Drug released slowly from L-DTX *in vitro* in a sustained manner. The pharmacokinetic data shows more extended action of DTX from L-DTX in experimental rats than the free-drug and Taxotere®. DTX from L-DTX enhanced 100% drug concentration in brain as compared with Taxotere® in 4 h. Thus, nanoliposomes as vehicle may be an encouraging strategy to treat glioma with DTX.

Keywords

Blood–brain barrier, nanoliposomes of Docetaxel, glioma, C6 cells, brain distribution

History

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Introduction

Astrocytoma (commonly known as glioma) is most prevalent among three different types of brain tumors, namely astrocytomas, oligidendrogliomas and oligoastrocytomas, in adults. This aggressive malignant form of cancer accounts for ~45–50% of all primary tumors resulting in death of patients within a couple of years (Guo et al., 2011; Nance et al., 2014). The characteristic features such as lack of sharp border, infiltration ability of the tumor cells in the brain of glioma as well as their wide distribution restrict their treatments by surgery and radiotherapy (Guo et al., 2011). Further, due to the strategic location of the blood–brain barrier (BBB) that allows a selective transport of drugs into the brain, chemotherapy becomes an auxiliary treatment for malignant glioma. In the last few decades, many drugs have been or being explored for the treatment of glioma. Most of them including docetaxel (DTX) are large hydrophobic molecules, which are unable to cross the BBB easily (Asperen et al., 1997) and may become an effective candidate for efflux by various efflux pumps governed by BBB as well as tumor cells (Beaulieu et al., 1997).

Docetaxel (DTX) is a complex diterpene alkaloid, isolated from the bark of *Texas baccata*, congener of paclitaxel. It has an efficient antineoplastic effect against a wide spectrum of solid tumors, such as ovarian, breast and lung cancer. It is found to be effective in the treatment of glioma *in vitro* but its *in vivo* efficacy is highly compromised due to its poor aqueous solubility and high molecular weight (Banks, 2009; Liu et al., 2011; Tan et al., 2012). Therefore, suitable design and development of appropriate vehicle for the transport of therapeutic payload is of prime importance in order to develop an effective therapy against glioma. In this context colloidal drug carrier especially nanoliposomes have gained significant interest among the researchers around the globe (Jain, 2012; Zhang & Zhang, 2013; Hao et al., 2015; Sonali et al., 2016a; Sonali et al., 2016b; Sonali et al., 2016c).

Liposomes, the small spherical vesicle with single or multiple lipid bilayers, made from natural and/or synthetic lipids have been widely exploited due to their unique characteristics such as high biocompatibility, biodegradability, and non-immunogenicity (Laouini et al., 2012; Akbarzadeh et al., 2013). They usually improve biodistribution and pharmacokinetic profile of the therapeutic payload by sustained drug release from the formulation and

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