

Physicochemical characterization, cytotoxic effect and toxicity evaluation of nanostructured lipid carrier loaded with eucalyptol

ABSTRACT

Background: Eucalyptol is an active compound of eucalyptus essential oil and was reported to have many medical attributes including cytotoxic effect on breast cancer cells. However, it has low solubility in aqueous solutions which limits its bioavailability and cytotoxic efficiency. In this study, nanostructured lipid carrier loaded with eucalyptol (NLC-Eu) was formulated and characterized and the cytotoxic effect of NLC-Eu towards breast cancer cell lines was determined. In addition, its toxicity in animal model, BALB/c mice was also incorporated into this study to validate the safety of NLC-Eu. Methods: Eucalyptol, a monoterpene oxide active, was used to formulate the NLC-Eu by using high pressure homogenization technique. The physicochemical characterization of NLC-Eu was performed to assess its morphology, particle size, polydispersity index, and zeta potential. The in vitro cytotoxic effects of this encapsulated eucalyptol on human (MDA MB-231) and murine (4T1) breast cancer cell lines were determined using the MTT assay. Additionally, acridine orange/propidium iodide assay was conducted on the NLC-Eu treated MDA MB-231 cells. The in vivo sub chronic toxicity of the prepared NLC-Eu was investigated using an in vivo BALB/c mice model. Results: As a result, the light, translucent, milky-colored NLC-Eu showed particle size of $71.800 \pm 2.144\text{nm}$, polydispersity index of 0.258 ± 0.003 , and zeta potential of $-2.927 \pm 0.163\text{mV}$. Furthermore, the TEM results of NLC-Eu displayed irregular round to spherical morphology with narrow size distribution and relatively uniformed particles. The drug loading capacity and entrapment efficiency of NLC-Eu were 4.99 and 90.93%, respectively. Furthermore, NLC-Eu exhibited cytotoxic effects on both, human and mice, breast cancer cells with IC₅₀ values of $10.00 \pm 4.81\mu\text{g}/\text{mL}$ and $17.70 \pm 0.57\mu\text{g}/\text{mL}$, respectively at 72h. NLC-Eu also induced apoptosis on the MDA MB-231 cells. In the sub chronic toxicity study, all of the studied mice did not show any signs of toxicity, abnormality or mortality. Besides that, no significant changes were observed in the body weight, internal organ index, hepatic and renal histopathology, serum biochemistry, nitric oxide and malondialdehyde contents. Conclusions: This study suggests that the well-characterized NLC-Eu offers a safe and promising carrier system which has cytotoxic effect on breast cancer cell lines.