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Development and comparison of Docetaxel lipid nano-emulsions by different strategies for tumor targeting

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The aim was to develop tumor targeted docetaxel lipid nano-emulsions with four strategies for improving the antitumor activity and compare their targeting efficiencies. The O/W lipid nano-emulsions (LNEs) were prepared by homogenization followed by ultra-sonication process. The size of globules and zeta potential were measured by Malvern Zetasizer. The drug content and entrapment efficiencies for the LNEs were determined by HPLC. The in vitro cytotoxic studies of the delivery systems were performed on MCF-7 and HeLa cells. The IC50 values of targeted LNEs on both the cell lines were statistically significant ($P<0.05$) when compared to DS (docetaxel solution) and DLNE (docetaxel LNE). The in vivo antitumor activity was tested on solid tumors induced in C57BL/6 mice. This study revealed that the percentage tumor inhibition when compared with the control (untreated) were found to be 55.62%, 70.80%, 89.31%, 54.25%, 80.0% and 84.66% for the DLNE, PLNE, FLNE, SALNE, ALNE and TFLNE formulations, respectively. Further, in vivo distribution studies were carried out in breast cancer MDA-MB231 induced tumors in Balb/c mice. The LNEs were loaded with fluorescent DiD oil and the distribution in different organs after 6 hours was tracked by small animal in vivo imaging system. When compared with the DLNE the average radiance values at the tumor site for the formulations PLNE, FLNE, SALNE, TFLNE and ALNE were found to be increased by 2.31, 4.81, 1.35, 3.54 and 3.04 folds, respectively. The tumor targeting efficiency was found to be in the order FLNE>TFLNE>ALNE>PLNE>SALNE>DLNE by imaging study. The results indicated that the prepared LNEs with four different approaches are capable of delivering docetaxel to tumors. When compared, FLNE, TFLNE, ALNE and PLNE produced the antitumor activities in decreasing order. To conclude, the results demonstrated great future potential for targeted LNEs as a prospective drug delivery system for docetaxel and other lipophilic drugs which are tumor selective.

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