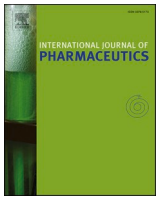
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Co-Delivery of erlotinib and resveratrol via nanostructured lipid Carriers: A synergistically promising approach for cell proliferation prevention and ROS-Mediated apoptosis activation

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ABSTRACT

Cancer treatments are always associated with various challenges, and scientists are constantly trying to find new therapies and methods. Erlotinib (ELT) is a well-known medicine against non-small cell lung cancer (NSCLC). However, treatments by ELT disrupt therapy due to drug resistance and pose severe challenges to patients. To achieve high-performance treatment, we gained nanostructured lipid carriers (NLCs) to evaluate synergistic anticancer effects of co-delivery of ELT and resveratrol (RES), a natural herbal derived phenol against NSCLC. NLCs are prepared via the hot homogenization method and characterized. *In vitro* cytotoxicity of formulations were evaluated on adenocarcinoma human alveolar basal epithelial (A549) cells. Prepared NLCs showed a narrow particle size (97.52 ± 17.14 nm), negative zeta potential (-7.67 ± 4.55 mV), and high encapsulation efficiency (EE%) was measured for the prepared co-delivery system (EE% 89.5 ± 5.16 % for ELT and 90.1 ± 6.61 % for RES). *In vitro* outcomes from cell viability study (12.63 % after 48 h of treatment), apoptosis assay (85.50%.), cell cycle (40.00% arrest in G2-M), and western blotting investigations (decreasing of protein expression levels of survivin, Bcl-2, P-Caspase 3P-caspase 9, and P-ERK 1/2, and additionally, increasing protein levels of BAX, P53, C-Caspase 3 and 9), DAPI staining, and colony formation assays showed the augment cytotoxic performances for co-delivery of ELT and RES loaded NLCs. Our study introduced the co-delivery of ELT and RES by NLCs as a novel strategy to elevate the efficacy of chemotherapeutics for NSCLC.

Abbreviations: ELT, erlotinib; RES, resveratrol; NLCs, nanostructured lipid carriers; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; MTT, 3- (4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; DMSO, dimethyl sulfoxide; FBS, fetal bovine serum; DAPI, 4′,6-diamidino-2- phenylindole; TEM, transmission electron microscopy; HPLC, high-performance liquid chromatography; LE, loading efficiency; EE, encapsulation efficacy; A549, adenocarcinoma human alveolar basal epithelial cells; ROS, reactive oxygen species; MDR, Multiple drug resistance; DPI, dry powder inhalation.

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