

Antitumor and anti-metastatic effects of citral loaded nanostructured lipid carrier in 4T1 induced breast cancer mouse model

ABSTRACT

Cancer nano-therapy has been progressing rapidly with the introduction of many novel drug delivery systems. The previous study has reported on the in vitro cytotoxicity of citral-loaded nanostructured lipid carrier (NLC-Citral) on MDA-MB-231 cells and some preliminary in vivo antitumor effects on 4T1 breast cancer cells challenged mice. However, the in vivo apoptosis induction and anti-metastatic effects of NLC-Citral have yet to be reported. In this study, the in vitro cytotoxic, anti-migration, and anti-invasion effects of NLC-Citral were tested on 4T1 breast cancer cells. In addition, the in vivo antitumor effects of oral delivery of NLC-Citral was also evaluated on BALB/c mice induced with 4T1 cells. In vitro cytotoxicity results showed that NLC-Citral and citral gave similar IC₅₀ values on 4T1 cells. However, wound healing, migration, and invasion assays reflected better in vitro anti-metastasis potential for NLC-Citral than citral alone. Results from the in vivo study indicated that both NLC-Citral and citral have anti-tumor and anti-metastasis effects, whereby the NLC-Citral showed better efficacy than citral in all experiments. Also, the delay of tumor progression was through the suppression of the c-myc gene expression and induction of apoptosis in the tumor. In addition, the inhibition of metastasis of 4T1 cells to lung and bone marrow by the NLC-Citral and citral treatments was correlated with the downregulation of metastasis-related genes expression including MMP-9, ICAM, iNOS, and NF-κB and the angiogenesis-related proteins including G-CSF alpha, Eotaxin, bFGF, VEGF, IL-1alpha, and M-CSF in the tumor. Moreover, NLC-Citral showed greater downregulation of MMP-9, iNOS, ICAM, Eotaxin, bFGF, VEGF, and M-CSF than citral treatment in the 4T1-challenged mice, which may contribute to the better anti-metastatic effect of the encapsulated citral. This study suggests that NLC is a potential and effective delivery system for citral to target triple-negative breast cancer.

Keyword: Citral; Murine model; Breast cancer; Nanocarrier