# C4 Apoptosis effect of aloe-emodin on human skin cancer cells and efficacy assessment of liposomes encapsulated aloe-emodin

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## ABSTRACT

The cytotoxicity results show that aloe-emodin expressed less cytotoxicity to human skin fibroblast Hs68 cells than the human skin A431 and SCC25 cancer cells. aloe-emodin-treated skin cancer cells displayed several features of apoptosis, including morphological changes of chromatin condensation, DNA fragmentation and arrest of cells in the S-$G_2$/M phase along with increase in the sub-$G_1$ population. Aloe-emodin revealed dose-dependent upregulation the death receptor-mediated pathway proteins expressions by upregulation of tumor necrosis factor-α (TNF-α) and FasL and their cognate receptors (TNFRs and Fas) and downstream adaptors TNF-R1-associated death domain (TRADD) and Fas-associated death domain (FADD), and activation of executing caspase-8. Additionally, aloe-emodin-displayed apoptosis is associated with mitochondria-mediated pathway, including upregulation of p53, increase the intracellular reactive oxygen species (ROS) levels, deplete the intracellular-reduced GSH, upregulation of cytochrome *c* and Bax, downexpression of Bcl-2, and activation of executing caspase-9 and -3 in A431 and SCC25 cells. The combinatory use of non-toxic liposome with the low concentrations of aloe-emodin ($IC_{20}$ and $IC_{50}$) accelerated greater cell death than aloe-emodin did alone for short times (24 and 48 h) in A431 and SCC25 cells. These data demonstrate positive cooperation of liposome and aloe-emodin and emphasize the potential clinical usefulness of liposome-aloe-emodin combination therapy. Furthermore, results of skin permeation profile suggest that the liposomal formulation could enhance the transdermal delivery of aloe-emodin, which may be useful to increase the efficiency of aloe-emodin delivery.

**Keywords:** aloe-emodin, apoptosis, transdermal, skin cancer