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Methanolic extract from aerial parts of *Artemisia annua* L. enhances sensitivity of pre-b acute lymphoblastic leukemia cell lines to vincristine

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Purpose: Vincristine (VCR) is a widely used chemotherapy drug in the treatment of Acute Lymphoblastic Leukemia (ALL). Clinical use of VCR is highly limited by its neurotoxicity and dose-limiting effects. Combination therapy with natural products can be an efficient therapeutic approach to reduce adverse effects of chemotherapy drugs. The aim of the present study is to investigate the synergistic effect of methanolic extract from aerial parts of *Artemisia annua* in combination with VCR on leukemic cell death *in vitro*

Methods: MTT assay was carried out to determine the cytotoxicity activity of the extract and VCR. Combination Index was evaluated to assess the synergism/antagonism effect of two agents. Apoptosis was analyzed by flow cytometry and Caspase 3 activity assay. mRNA expressions of Caspase 3, Bax, Bcl-2 were quantified using RT-PCR. One-way ANOVA and post hoc Tukey multiple comparison tests were used for statistical analysis.

Results: Our results showed that the combination of *Artemisia annua* and VCR caused time and dose-dependent decrease in cell viability and induced apoptosis in both cell lines. Lower doses of VCR and the extract displayed significant synergistic inhibition of Nalm-6 and Reh cell growth ($P < 0.001$). Interestingly, concurrent use of *A. annua* and VCR resulted in Caspase 3 and Bax gene upregulation and Bcl-2 gene downregulation ($P < 0.05$).

Conclusion: From the results presented here, the extract of *Artemisia annua* substantially increased sensitivity of leukemic cells to VCR, suggesting that this combination could potentially decrease VCR drug side effects.

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