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Título	Reversal of Ovarian Cancer Cell Lines Multidrug Resistance Phenotype by the Association of Apiole with Chemotherapies
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Resumo	Multidrug resistance (MDR) is the main obstacle in anticancer therapy. The use of drug combinations to circumvent tumor resistance is a well-established principle in the clinic. Among the therapeutic targets, glycoprotein-P (P-gp), an energy-dependent transmembrane efflux pump responsible for modulating MDR, is highlighted. Many pharmacological studies report the ability of calcium channel blockers to reverse tumor resistance to chemotherapy drugs. Isolated for the first time from parsley, the phenylpropanoid apiole is described as a potent calcium channel inhibitor. Taking this into account, herein, the ability of apiole to potentiate the action of well-established chemotherapeutics in the clinic, as well as the compound's relationship with the reversal of the resistance phenomenon by blocking P-gp, is reported. The association of apiole with both chemotherapeutic drugs doxorubicin and vincristine resulted in synergistic effect, in a concentration-dependent manner, as evaluated by the concentration reduction index. Molecular docking analysis demonstrated the affinity between apiole and the active site of P-gp, corroborating the inhibitory effect. Moreover, apiole demonstrated druglikeness, according to ADME analysis. In conclusion, apiole possibly blocks the active P-gp site, with strong binding energy, which, in turn, inhibits doxorubicin and vincristine efflux, increasing the antiproliferative response of these chemotherapeutic agents.
Fomento	