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Computational investigation of selected flavonoids as caspase-3 inducers in multidrug-resistant leukemia

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Leukemia is one of the most common forms of cancer worldwide, particularly in children. Multidrug-resistant leukemia remains a significant challenge in cancer therapy due to resistance mechanisms, including drug efflux pumps. Apoptosis, particularly *via* caspase-3 activation, is a key target to overcome this resistance. This study aims to explore and assess the mechanisms of flavonoids CPD5, CPD7, and doxorubicin as potential agents against multidrug-resistant leukemia. Key molecular targets identified include JNK1, AKT1, MAPK3, TP53, NFKB1, and CREB1, linked to apoptosis signaling. Molecular docking with the caspase-3 structure (PDB ID: 4JJE) reveals that CPD5 and doxorubicin exhibit more stable binding energies and better localization within the protein 4JJE compared to CPD7. Molecular dynamics simulation over 100 ns confirms stable binding interactions for all compounds. *In silico* ADMET predictions have assessed oral bioavailability, showing CPD7 meets all pharmacokinetic criteria, being non-toxic, with superior distribution capacity and high absorption. These findings suggest CPD7 as a promising future drug for treating multidrug-resistant leukemia by inducing apoptosis through caspase-3 activation.

Keywords: ADMET, apoptosis, caspase-3, flavonoids, multidrug-resistant leukemia