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Optimizing the design and potency of diterpenic acid derivatives to improve cell membrane permeability and Hsp27 targeting characteristics

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Abstract

Heat shock protein 27 (Hsp27) acts as a protective protein allowing it to play an integral role in aiding cancer cell resistance. Stress-induced Hsp 27 overexpression aids in the stabilization of partially denatured proteins to establish protein refolding resulting in thermotolerance, inhibition of apoptosis, cytoprotection, etc. As a result of rapid proliferation and general instability, cancer cells exhibit increased dependency on the support of Hsp 27 and it's chaperone proteins, therefore generating an ideal target for anticancer therapy. Copalic acid, a clerodane diterpenoid, has already been confirmed in effective chaperone inhibition and antiproliferative synergistic effect. We hypothesize that by optimizing the structure of Copalic acid derivatives to increase solubility and drug potency we will increase anti-chaperone activity thereby hindering phosphorylation of Hsp27 affecting cell proliferation and stability. combinatorial chemistry strategies were used to develop and modify Copalic acid derivatives while synthesizing various dimers to enhance potency. Through utilizing NMR to identify synthesis alterations and MTT colorimetric assay we will continue to monitor and optimize the derived compounds.

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