NEW HYBRID ANTITUMOUR AGENTS AGAINST DRUG RESISTANCE: DESIGN, SYNTHESIS, AND NMR ANALYSIS

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Protulactone A and asperilactone C are natural compounds isolated from a marine-derived Aspergillus species, has demonstrated moderate cytotoxic activity.[1-2] Goniofufurone and its structural analogues, have shown potent antiproliferative effects against various cancer cell lines.[3] In this study, guided by a molecular hybridization approach, we designed and synthesized a novel hybrid analogues integrating a bicyclic lactone core−characteristic of protulactone A−and a phenyl moiety commonly found in styryl lactones. Comprehensive structural elucidation of synthesized molecules was performed using 1D and 2D NMR spectroscopy. The resulting compounds (**1**-**4**) were evaluated for their cytotoxic potential across a panel of human cancer cell lines, including drug-resistant variants. Tested compounds reduced MRP1 levels and moderately increased Caspase-3 levels in K562 cells, indicating anti-MDR and pro-apoptotic activity. No Caspase-3 activation was detected in MRC-5 cells, confirming the selective cytotoxicity of these compounds toward cancer cells.

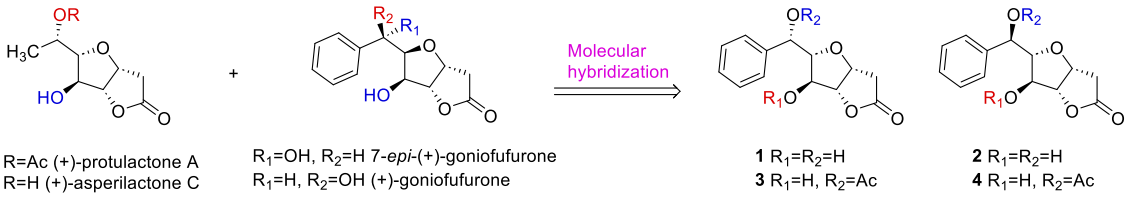

Figure 1. Design of new hybrid antitumour agents.

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