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Synthesis and biological evaluation of new a-ring modified asiatic acid derivatives as anticancer agents

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Cancer is one of the leading causes of mortality and morbidity worldwide. Despite major advances in diagnostics and therapeutics of cancer, the the outcome for many patients remains limited. Thus, there is a constant demand for the search of new, safer and effective pharmacological treatments to fight cancer. Asiatic acid (AA) is an pentacyclic triterpenoid that exhibited promising anticancer effects in both *in vitro* and *in vivo* studies. In addition, this compound exhibited a relatively safe profile, and is readily availability in nature, which support the contention that AA is an interesting compound for the design of new leads aimed at the development of new anticancer agents. Hence, in the present work, a series of new lactol and A-nor AA derivatives were prepared, and their antiproliferative activities were evaluated against several human cancer cell lines. Among all the derivatives tested, compound 1 exhibited the best antiproliferative profile, with IC50 values ranging from 0.11 μM to 0.65 μM for cancer cells. The results of the preliminary mechanistic studies suggest that compound 1 induced cell cycle arrest at G0/G1 phase and apoptotic HeLa cell death. In light of this results, compound 1 might represent a promising drug candidate for the development of new anticancer agents.

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