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CYTOTOXIC POTENTIAL OF *α,β*-UNSATURATED KETONES OF 3*β*-[(*α*-L-ARABINOPYRANOSYL)OXY]OLEAN-12-EN-28-OIC ACID IN HUMAN NON-SMALL CELL LUNG CANCER (NCI-H292) CELLS USING SULFORHODAMINE B ASSAY

J.M.J. Jayasundara[1], A. Wickramasinghe[2], D.N. Karunaratne[2], N.S. Wickramaratne[3], S.R. Samarakoon[3] and J.M.S. Jayasingha[2*]

[1]*Postgraduate Institute of Science, University of Peradeniya, Peradeniya, Sri Lanka*
[2]*Department of Chemistry, Faculty of Science, University of Peradeniya, Peradeniya, Sri Lanka*
[3]*Institute of Biochemistry, Molecular Biology and Biotechnology, Colombo, Sri Lanka*
[*]*susanthij@pdn.ac.lk*

Lung cancer is the leading cause of cancer deaths throughout the world. Non-small cell lung cancers (NSCLC) are the most prevailing lung cancers, accounting for about 80% of all lung cancers. Undesirable side effects and rapid development of resistance for chemotherapeutic drugs have increased the demand for novel alternative therapeutics. A number of new drugs with greater pharmacological activity have been obtained from natural sources by modification of functional groups of leading natural compounds. Therefore, synthesis of natural product derived compound libraries in the search for novel drugs is still a priority goal for cancer therapy. 3*β*-[(*α*-L-arabinopyranosyl)oxy]olean-12-en-28-oic acid (APOA) is a triterpenoid saponin with the oleanolic acid aglycone linked to arabinopyranose sugar moiety and can be easily isolated from endemic plant extracts of genus *Schumacheria*. This compound exerts potent cytotoxic and apoptotic potential in human NSCLC cells (NCI-H292) with an IC_{50} value of 5.977 μg mL^{-1} while exhibiting a comparable toxicity value (IC_{50}=5.702 μg mL^{-1}) against normal lung (MRC-5) cells. The objective of this study was to synthesize structural analogues at C11 position of the APOA and to study the effect of those on anti-cancer activity. Sulforhodamine B (SRB) assay is used to evaluate *in-vitro* cytotoxic efficacy of the synthesized analogues on NCI-H292 cells and MRC-5 cells. The methylene group at the C-11 position of the APOA, acetylated APOA (Ac-APOA) and ethyl ester of Ac-APOA were oxidized to afford respective *α,β*-unsaturated ketones, and their structures were confirmed. Comparative cytotoxic effects of the synthesized analogues were assessed using SRB assay against APOA. The results indicated that all the oxidized derivatives exerted potent cytotoxic activity against NCI-H292 cells while being less toxic to normal lung (MRC-5) cells compared to the parental saponin indicating better activity. These empirical data suggest that the modification at C-11 of APOA could be a lead to promising new anticancer agents.

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