Synthesis and Cytotoxicity Studies of Derivatives of 3β-[(α-L-arabinopyranosyl) oxy] olean-12-en-28-oic acid

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A number of new commercialized drugs as anti-cancer therapeutics have been obtained from natural sources by structural modification of natural compounds or by synthesis of new compounds following a natural compound as a model. 3β-[(α-L-arabinopyranosyl) oxy] olean-12-en-28-oic acid (3-O-α-L-arabinosyl oleanolic acid) is a natural product possessing cytotoxic activities for several cancer cell lines and isolated from the three species of the genus *Schumecheria*. In the present study structural analogues of the target saponin were synthesized and brine shrimp lethality bioassay was used as a preliminary study to identify the potential cytotoxicity. Air dried, ground stem bark of *S. castaneifolia* was extracted into dichloromethane: methanol (1:1) solution at room temperature using a bottle shaker for 3×24 hours. 3-O-α-L-arabinosyl oleanolic acid was isolated from the crude extracts using column chromatography, in 0.02 % yield and the structure was confirmed by comparing the literature data with observed IR and ^{1}H-NMR data. Five compounds (1,2,3,4 and 5) were synthesized by modifying the target compound by acetylation of sugar hydroxyls (compound 1), allylic oxidation at C12-13 double bond of compound 1 (compound 2), deacetylation of the sugar hydroxyls of compound 2 (compound 3), esterification of the COOH group at C28 (compound 4) and oxidation of C12-C13 olefin of compound 4 (compound 5). Characterization of the synthesized derivatives was done using IR and ^{1}H-NMR spectroscopy. LC_{50} values of compound 1 to 5 are 52.9380 ppm, >1000 ppm, 98.0482 ppm, 304.9670 ppm and >1000 ppm respectively and are higher than that of the original compound (4.36 ppm) which indicates that the cytotoxicity has been decreased for all the synthesized derivatives. However, the cytotoxicity is high in acetylated derivative than the other four derivatives. Hence based on these empirical data it can be concluded that the C12-C13 double bond and COOH group at C28 are important for the reported cytotoxicity.

Key words: *Schumecheria*, 3-O-α-L-arabinosyl oleanolic acid, anti-cancer activities