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SYNTHESIS OF DERIVATIVES OF OLEANOLIC ACID AND THEIR CYTOTOXICITY STUDIES

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Natural products and their modified derivatives act as leading compounds for modern drug discovery due to their broad spectrum of biological activities. Oleanolic acid (3*β*-hydroxyolean-12-en-28-oic acid) is one of the most important pentacyclic triterpenoids known to process several biological activities including cytotoxicity, antibacterial, anti-inflammatory, antioxidant and antidiabetic. Even though several structural analogs of oleanolic acid have been reported, very few reports are found on the synthesis of fluoro analogs of the oleanolic acid. In the present study, the fluoro derivatives of oleanolic acid were synthesized via a new synthetic route and the cytotoxic potential of the synthesized compounds were evaluated using Brine Shrimp Lethality (BSL) assay and Sulforhodamine B (SRB) assay. Clean, air-dried and ground roots of *Lantana camara* were extracted into methanol by maceration. Oleanolic acid was isolated from the roots of *Lantana camara* using flash chromatography in 0.49% yield and the structure was confirmed using FTIR and mass spectroscopy analysis. Seven derivatives of oleanolic acid were synthesized by acetylation of C3-OH group followed by fluorination of C28-COOH, oxidation of C3-OH group followed by fluorination of C28-COOH, esterification of C28-COOH group followed by fluorination of C3-OH and esterification of C28-COOH group followed by oxidation of C3-OH. The synthesized compounds were characterized by using FTIR and ^{1}H-NMR spectroscopy. Cytotoxicity studies were carried out by using BSL assay, and LC_{50} values were calculated by probit analysis. The LC_{50} values of acetylated, oxidized and esterified products obtained indicate a higher cytotoxicity than oleanolic acid and the fluorinated compounds. This shows that the cytotoxicity has been decreased by fluorination at C28-COOH and C3-OH groups. Finally, the IC_{50} values were calculated from the SRB assay. It also showed that the cytotoxicity has been decreased with the fluorination. However, the oxidized product shows higher and lower cytotoxicity for NCI-H292 and MRC 5 cells, respectively, indicating better activity.

Keywords: Cytotoxicity, Fluoro derivatives, *Lantana camara,* Oleanolic acid