DESIGN AND SYNTHESIS OF NOVEL ESTERS OF OLEANONIC AND OLEANOLIC ACIDS WITH ANTIOXIDANT AND ANTI-CANCER ACTIVITIES

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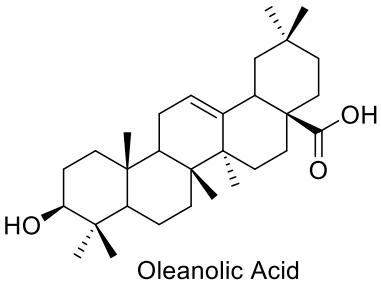
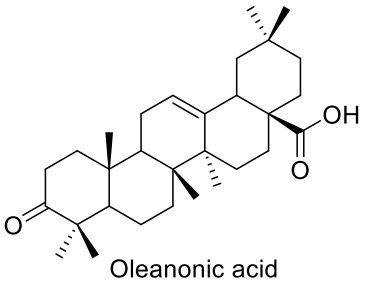
Pentacyclic triterpenic acids comprise a versatile chemical scaffold for the production of semi-synthetic derivatives with a wide spectrum of biological properties. For instance, ursolic, oleanolic and oleanonic acid are triterpenic acids of natural origin with significant anticancer and anti-inflammatory activities [1,2]. A rich source of the two later acids is *Pistacia lentiscus* var. Chia, (Anacardiaceae) and especially its natural resin or Chios mastic gum (CMG). Thus, in the current work the resin was used as a starting material for the isolation of the target compounds using different chromatographic techniques, such as CPC and prep-HPLC-DAD. After purification of oleanolic and oleanonic acid, a series of twelve novel esters were synthesized and evaluated for their antioxidant activity, as well as, their anticancer potential against a panel of four human cancer cell lines. The new analogs found to be more active or with comparable potency than the respective parent compounds against HeLa, HepG2, MIAPaCa2 and PANC.1 cell lines. Specifically, among the derived esters, oleanonic acid ester with 3-keto-hydroxytyrosol exhibits promising anticancer activity against HeLa and PANC.1 cell. It is worth noting that oleanonic acid as well as oleanolic acid esters with 3-keto-hydroxytyrosol as a substitute, showed increased antioxidant activity.



Oleanolic Acid



Oleanonic acid

1. Liu, J. Pharmacology of oleanolic acid and ursolic acid. *J Ethnopharmacol* **49**, 57–68 (1995).

2. Giner-Larza, E. M. *et al.* Oleanonic acid, a 3-oxotriterpene from Pistacia, inhibits leukotriene synthesis and has anti-inflammatory activity. *Eur J Pharmacol* **428**, 137–143 (2001).