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Methanolic extract of *Pistacia lentiscus* (MEPL) as novel therapeutic approach in high-grade serous ovarian cancer

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Ovarian cancer remains the most lethal gynecologic cancer in women. More than 60% were diagnosed at advanced stage and the mortality did not significantly improve over last years. The poor prognosis and high mortality show that the current therapies often fail and novel approaches are urgently required in order to enhance the prognosis of the disease. In our study we investigated the effect of the leaves of *Pistacia lentiscus* and *Fraxinus angustifolia*, two Algerian medicinal plants used in traditional medicine since 15th - 16th centuries in ovarian cancer. The different extracts were obtained in different organic solvents, ethanol, methanol and acetone, and tested towards two ovarian cancer cell lines A2780 and SKOV3. We determine that the methanolic extract of *P. Lentiscus* exhibit a cytotoxic potential in A2780 and SKOV3 cells. The active extract (MEPL) induced apoptosis and cell cycle arrest in these ovarian cancer cell lines. However, the widely used cell lines SKOV-3 and A2780 were implicated as not being representative of the major HGSC subtype because of the wild-type p53 status. In order to investigate the mechanism of action (MoA) of MEPL also in patients with the most common subtype of EOC (HGS), we conducted the preclinical study using newly established primary cell lines from ascites of high grade serous ovarian cancer patients. The results show that MEPL inhibit PI3K/AKT and MAPK/ERK signaling pathways, and decreased release of IL6 and VEGF by the malignant cells. Moreover, treatment with MEPL increased the sensitivity to chemotherapy in our primary cell lines of HGS ovarian cancer patients and might be a promising novel combination therapeutic approach with patients in this histological subtype of ovarian cancer.

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