

***Pistacia atlantica* subspecies kurdica mastic gum resin, a potent and novel natural plant metabolite for cancer treatment**

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The present study is focused on investigating the anticancer effect of *Pistacia atlantica* subspecies kurdica mastic gum resin (MGR) on the proliferation of various cancerous and noncancerous human cell lines exploiting MTT assay, microscopic evaluations, flow cytometry, caspase activity and qPCR. The MTT results showed that the mastic gum resin (0.01-100 μ M) is selectively induced death of cancer cells in a dose and time-dependent manner. Significant suppression of proliferation of human cancerous cells was seen with IC₅₀ value of 15.34 \pm 0.21, 11.52 \pm 0.18, 8.11 \pm 0.23 μ g/mL and 5.2 \pm 0.8 μ g/mL at 72 hours of treatment respectively for bile duct cancer (cholangiocarcinoma) (KMBC), pancreatic carcinoma (PANC-1), gastric adenocarcinoma (CRL-1739), breast adenocarcinoma (MCF-7) and colonic adenocarcinoma (COLO205). On the other hand, normal human colon fibroblasts (CCD-18Co) have not showed

adverse effect after treatment with various doses of a natural resin. The study also showed that a natural resin at a concentration of 5.2 \pm 0.8 μ g/mL for 72 h early signs of apoptosis as evidenced by confocal microscopy imaging. Flow cytometry studies showed that the natural resin significantly ($P < 0.05$) arrests COLO205 cells at G2/M phase of cell cycle. On the other hand, we revealed that, the antiproliferative effect of natural resin on COLO205 cells is through the apoptotic intrinsic pathway via activation of caspases -3 and -9. In conclusion, the results revealed that natural resin can be further developed as chemotherapeutic compound for the treatment of cancers especially colon cancer.

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