Anti-cancer activity of compounds isolated from *Bursera microphylla*

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INTRODUCTION

Bursera microphylla (BM), one of the common elephant trees, is widely distributed in Sonoran Desert in Mexico. Seri ethnic group in Sonoran Desert uses BM as a antinflammatory and painkiller drug for the treatment of sore throath, herpes labialis, abscessed tooth, wound healing and BM dried stems and leaves in a tea to relieve painful urination and to stimulate bronchial secretion. Furthermore, BM was used for fighting venereal diseases. Our aim in this study is to investigate the effects of the whole BM resin and its hexane (HEX-S) and dichloromethane (DCM-S) fractions of resin methanol extract on tumor cell proliferation and cancer progression.

RESULTS

Firstly, the acute myeloid cell line (OCI-AML3) were treated with 3 different concentrations of the whole BM resin. We found that concentrations of 2,5 and 0,25 but not 0,025 μ/mL of BM were able to significantly decrease OCI-AML3 cell number after 24 and 48 hours of treatment. The reduction of cell number resulted in increased cell apoptosis, decreased in S-phase and in a block of G2/M phase of the cell cycle. We also tested the acute myeloid cell line U937 and similar results to those obtained with OCI-AML3 cell line at concentration of 0,25 μg/ml after 24 hours-treatment were observed.

Subsequently, we assessed if the *B. microphylla* HEX-S and DCM-S fractions exert the same anti-proliferative effects of BM resin. We found that HEX-S, but not DCM-S or BM decreased OCI-AML3 cell number at a concentration of 0,025 μg/ml after 24 hours of treatment. Moreover, HEX-S increased apoptosis and inhibited cell division of the same cell line. Same results were obtained in different acute myeloid cell lines (U937, HL-60, K562), in a T-cell lymphoma (Jurkat) and in several solid tumor cell lines such as Anaplastic Thyroid Carcinoma (C643), Breast Carcinoma (MCF-7) and Colon Carcinoma (HCT116).

To dissect the possible molecular mechanism involved in the effects observed in OCI-AML3 cells, we evaluated apoptosis and proliferation pathways. Regarding apoptosis, activation of caspase-3, but not of caspase-8, was detectable at 4, 8, 14 or 24 hours after HEX-S treatment, thus suggesting that the extrinsic caspase-8-dependent pathway is not involved in HEX-S-induced apoptosis. An additional analysis demonstrated that the pro-apoptotic molecules Bim and Puma, and the anti-apoptotic molecule Bcl-2 were not involved in this process.

Regarding cell proliferation, we found that its HEX-S-induced inhibition was due to the up-regulation of the protein p21 in a p53-independent way.

CONCLUSIONS

This data suggest that the *Bursera microphylla*'s HEX-S fraction inhibited cell proliferation of AML cell lines mainly by the involvement of p21-dependent, p53-independent mechanism. Additionally, cell apoptosis was promoted through activation caspase-3, but not caspase-8.

Future experiments will focus on the isolation and identification of single molecules responsible for the antiproliferative effect exerted by the HEX-S fraction of *Bursera microphylla* in order to find a promising drug used in novel antitumor therapeutic strategies.

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