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Umbelliprenin from Ferula szowitsiana inhibits the growth of human M٤Beu metastatic pigmented malignant melanoma cells through cell-cycle arrest in G١ and induction of caspase-dependent apoptosis

Barthomeuf, C.[a] , Lim, S.[a], Iranshahi, M.[b], Chollet, P.[c]

[a] **University** Clermont١, Laboratoire de Pharmacognosie/Biotechnologies, INSERM, U٤٨٤, Clermont-Fd F-٦٣٠٠١, France

[b] Department of Pharmacognosy and Biotechnology, Faculty of Pharmacy, **Mashhad University** of **Medical Sciences**, Iran

[c] Centre Jean-Perrin, INSERM, U٤٨٤, Groupe de Recherche Clinique, Clermont-Fd, France

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Abstract

Metastatic malignant melanoma have a bad prognosis (median survival: ٦-٨ months) mainly due to the development of lung, hepatic and brain metastases. In this study we have used the resazurin reduction test and FACS analysis to assess the cytostatic and cytotoxic effect of umbelliprenin from Ferula szowitsiana (Apiaceae) on human solid cancer cells and human primary fibroblasts. We have observed that the cell susceptibility to umbelliprenin decreases in the order M٤Beu (metastatic pigmented malignant melanoma)>A٥٤٩ (nonsmall cell lung carcinoma)≈PC٣ (androgen-resistant prostate carcinoma)>PA١ (ovary teratocarcinoma)>human primary fibroblasts≈MCF٧ (breast adenocarcinoma)>DLD١ (colon adenocarcinoma). M٤Beu cell-proliferation is inhibited through cell-cycle arrest in G١ and induction of caspase-dependent apoptosis. The finding that the cytotoxic effect of umbelliprenin is markedly more pronounced in M٤Beu cells than in primary fibroblasts, suggests a therapeutic margin. As M٤Beu cell proliferation is more potently inhibited by umbelliprenin ($IC_{٥٠}$ ١٢,٣ μM) than by the citrus coumarin auraptene (٧-geranyloxycoumarin, $IC_{٥٠}$ ١٧,١ μM) previously reported capable of inhibiting the prevalence of lung metastasis in mice bearing B١٦BL٦ murine melanoma, our data suggest that umbelliprenin orally administered and foods and folk medicines containing this coumarin, may afford protection against the development and early recurrence of malignant melanoma. In vivo investigations are needed to test these hypotheses. © ٢٠٠٧ Elsevier GmbH. All rights reserved.

Author keywords

Apoptosis; Cancer; Cell proliferation; Cell-cycle blockade; Coumarin; Ferula szowitsiana umbelliprenin; Malignant melanoma

Indexed Keywords

EMTREE drug terms: auraptene; caspase; cisplatin; coumarin; coumarin derivative; resazurin; sesquiterpene derivative; umbelliprenin; unclassified drug

EMTREE medical terms: animal experiment; animal model; animal tissue; apoptosis; article; cell cycle arrest; cell cycle G١ phase; cell proliferation; cell strain MCF ٧; cell survival; controlled study; cytostasis; drug cytotoxicity; drug structure; fennel; fibroblast; fluorescence activated cell sorting; human; human cell; IC ٥٠; melanoma cell; metastasis; metastasis inhibition; mouse; nonhuman; priority journal; reduction; statistical analysis

MeSH: Antineoplastic Agents, Phytogenic; Apoptosis; Carcinoma; Caspases; Cell Line, Tumor; Cell Proliferation; Cells, Cultured; Cisplatin; Coumarins; Dose-Response Relationship, Drug; Drug Screening Assays, Antitumor; Ferula; Fibroblasts; G١ Phase; Humans; Inhibitory Concentration ٥٠; Melanoma; Plant Roots; Umbelliferones
Medline is the source for the MeSH terms of this document.

Species Index: Apiaceae; Citrus; Ferula; Murinae; Mus