Benzofenantridinas são alcalóides de produtos naturais (sanguinarine, cheleritrine, etc) com potente atividade antiproliferativa no melanoma independente do gene p53

A SANGUINARINE E A CHELERITRINE ambas benzofenatridinas apresentam efeitos: antimicrobiano, antifúngico, antiinflamatório, adrenolítico, simpaticolítico, e anestésico local com citotoxicidade em várias células neoplásicas (câncer) .José de Felippe Junior

Benzo[c]phenanthridine alkaloids exhibit strong anti-proliferative activity in malignant melanoma cells regardless of their p53 status.

Hammerová J, Uldrijan S, Táborská E, Slaninová I.
J Dermatol Sci. 2011 Apr;62(1):22-35.

Source

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Abstract

BACKGROUND:

Search for new substances with antiproliferative activity towards melanoma cells is important since malignant melanoma is notoriously resistant to conventional chemotherapy. Benzo[c]phenanthridine alkaloids (BAs) are natural products with significant anti-proliferative activities, therefore they are considered as agents promising for cancer therapy.

OBJECTIVES:

The effects of five BAs (sanguinarine, chelerythrine, chelidonine, sanguilutine, and chelilutine) on human malignant melanoma cell lines were compared. The study focused on BAs effects on DNA, anti-apoptotic and p53 protein levels; and the involvement of p53 in cellular responses to alkaloids treatment.

METHODS:

Melanoma cell lines, two wild types and two with dysfunctional p53 derived from one of them were used. The mechanism of anti-proliferative and pro-apoptotic effects and the effect on DNA was investigated using MTT assay, flow cytometry, Western blot analysis, fluorescence and electron microscopy.

RESULTS:

All tested alkaloids exhibit strong anti-proliferative activity. CHL, CHE and SA induced apoptosis, which was probably mediated by decreasing levels of anti-apoptotic proteins (Bcl-xL, Mcl-1, XIAP) and was accompanied by mitochondrial membrane potential decrease as well as caspase-3 and PARP cleavage. Although all alkaloids caused DNA damage, which was demonstrated by induction of H2AX phosphorylation, none of the tested alkaloids stabilised p53 and their toxicity in cells with non-functional p53 was comparable to wild type cells.

CONCLUSION:

Despite the profound similarity of BAs molecular structures, it is clear that the mechanism of cell death induction is different for each alkaloid. Our results indicate that BAs could be effective in malignant melanoma treatment, including tumours which have lost wild type p53.

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