

Publication

Anti-proliferative activity-guided isolation of clerodermic acid from *Salvia nemorosa* L.: Geno/cytotoxicity and hypoxia-mediated mechanism of action

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**ID** 4483014**Author(s)** Bahadori, Mir Babak; Eskandani, Morteza; De Mieri, Maria; Hamburger, Matthias; Nazemiyeh, Hossein**Author(s) at UniBasel** [Hamburger, Matthias](#) ; [de Mieri, Maria](#) ;**Year** 2018**Title** Anti-proliferative activity-guided isolation of clerodermic acid from *Salvia nemorosa* L.: Geno/cytotoxicity and hypoxia-mediated mechanism of action**Journal** Food and chemical toxicology**Volume** 120**Pages / Article-Number** 155-163**Mesh terms** A549 Cells; Annexin A5, metabolism; Apoptosis, drug effects; Biological Assay; Carcinogens, pharmacology; Cell Proliferation, drug effects; Down-Regulation; Humans; Hypoxia, metabolism; Hypoxia-Inducible Factor 1, alpha Subunit, metabolism; Inhibitory Concentration 50; Lactones, pharmacology; Magnetic Resonance Spectroscopy; Molecular Structure; Mutagens, pharmacology; Naphthalenes, pharmacology; RNA, Messenger, genetics; Real-Time Polymerase Chain Reaction; *Salvia*, chemistry

The adaptation of solid tumors to the low oxygen/nutrient environment is mediated by the pivotal transcription role of hypoxia-inducible factor-1 (HIF-1). Thus, the HIF-1 and its subunits have been considered to be hopeful anti-cancer targets. Various natural compounds were reported to persuade cell cytotoxicity through targeting and downregulation of the HIF-1. The genus *Salvia* is a rich source of bioactive terpenoids which show promising anti-cancer activities. Here, the identification of natural anti-proliferative compound targeting the HIF-1 α expression was reported. A bioassay-guided isolation was employed for the discovery of natural anti-proliferative compounds from *Salvia* extracts using MTT assay against A549/cells. In this direction, clerodermic acid (CDA) as a potent cytotoxic compound was purified from *Salvia nemorosa* and identified using 1D and 2D NMR analysis. Results indicated that CDA has anti-proliferation activity (IC₅₀ value of 35/ μ g/mL) which was confirmed by genotoxicity and apoptosis detection analyses. The quantitative qPCR analysis showed that the expression level of HIF-1 alpha was strongly inhibited in the hypoxic cells treated with CDA compared to the untreated cells tolerated hypoxia. Findings exhibited that *S. nemorosa* and clerodermic acid have significant potential for reducing HIF-1 α expression and could be considered for further studies for cancer therapy.

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