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Aromatic sulphur compounds from *Allium* species induce antioxidant signaling in human bladder cancer cells

Emil Jivishov[1,2*], Jörg Hänze[3], Pietro Di Fazio[4], Rainer Hofmann[3], Shah Mahmoud Faqiri[5] and Michael Keusgen[1]

[1] *Institute of Pharmaceutical Chemistry, Faculty of Pharmacy, Philipps University of Marburg, Marburg, Germany*
[2] *Department of Chemistry, Azerbaijani-French University (UFAZ-ASOIU), Baku, Azerbaijan*
[3] *Department of Urology and Pediatric Urology, Philipps University of Marburg, Marburg, Germany*
[4] *Department of Visceral, Thoracic and Vascular Surgery, Philipps University of Marburg, Marburg, Germany.*
[5] *Department of Forestry, University of Balkh, Mazar-e Sharif, Afghanistan*

*E-mail: emil.jivishov@ufaz.az

In this study, anticancer effect of ethyl acetate extracts from bulbs and flowers of 68 *Allium* species originated from Southwest Asia to the high mountains of Central Asia were analysed, with many of them being evaluated for the first time. The extracts were analysed dose dependently and compared to two pure known *Allium* compounds namely, 2,2'-dipyridyl disulphide and dipyrithione. Doxorubicin drug was used as a reference. Human bladder cancer cell lines T24 and UMUC3 were tested in comparison to non-cancer primary human foreskin fibroblasts (HFF). The most cytotoxic species were *A. stipitatum* (Afghanistan), and *A. aflatunense* with the LD_{50} values comparable to the doxorubicin's LD_{50} value. Toxicity of the *Allium* extracts against human foreskin fibroblasts (HFF) cells was considerably higher than the toxicity of the doxorubicin. The extracts of *A. stipitatum, A. aflatunense,* and of other species were analysed for effects on cell death and cell cycle. The extracts caused a significant increase of the sub G1 events. Additionally, cyclin dependent kinase inhibitor (CDKN1A) was induced. Using bioassay guided fractionation, aromatic sulphur compounds from *A. stipitatum* and *A. aflatunense* extracts, were identified as active compounds acting as oxidative stress inducers. This suggestion was supported by the observation that the treated cells displayed enhanced antioxidant signaling pathway mediated by Nrf2 as indicated by enhanced HO-1 levels.

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