

24th Scientific Symposium of the Austrian Pharmacological Society Graz, 27–28 September 2018

MEETING ABSTRACT

A4.5

Carvotacetones from *Sphaeranthus africanus* with anti-proliferative activity against several cancer cell lines

Huyen TRAN THI¹, Eva M. PFERSCHY-WENZIG¹, Nadine KRETSCHMER¹, Olaf KUNERT², Loi HUYNH³ and Rudolf BAUER^{1,*}

¹Department of Pharmacognosy, Institute of Pharmaceutical Sciences, University of Graz, Austria; ²Department of Pharmaceutical Chemistry, Institute of Pharmaceutical Sciences, University of Graz, Austria; ³Saigon Pharmaceutical Sciences and Technology Center (SAPHARCEN), University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam

Background: *Sphaeranthus africanus* L. (Asteraceae) has been used in traditional medicine in Vietnam to alleviate swelling and as a sedative. Pressed juice from fresh leaves of *Sphaeranthus africanus* have been used for mouth and throat washes to treat sore throat. The decoction is also used as antitussive and expectorant. The pounded leaves are applied externally to relieve pain and swelling [1]. Chemical investigations of *S. africanus* are scarce. Until now, only two compounds and one mixture of carvotacetone derivatives, chryso-splenol D, squalene, spinasterol, and stigmasterol were reported for this plant [2]. There is no literature dealing with cytotoxic activities of the plant.

Methods: The air-dried and milled leaves and stems of *S. africanus* were percolated with 96% ethanol at room temperature. The crude extract was then partitioned sequentially with *n*-hexane, dichloromethane, ethyl acetate and *n*-butanol. The dichloromethane extracts (SA-DCM) exhibited activity against CCRF-CEM cells. Bioassay-guided fractionation of SA-DCM was performed, and all isolates (1–5) were evaluated for their anti-proliferative activity against CCRF-CEM, MDA-MB-231, U-251, HCT-116 cancer cells and non-tumorigenic HEK 293 cells.

Results: Five carvotacetone derivatives, including two known: 3-angeloyloxy-5-angeloyloxy-7-hydroxycarvotacetone (1), 3-angeloyloxy-5-[2",3"-epoxy-2"-methyl-butanoyloxy]-7-hydroxycarvotacetone (2), along with three new compounds: 3-angeloyloxy-5-[3"-chloro-2"-hydroxy-2"-methyl-butanoyloxy]-7-hydroxycarvotacetone (3), 3-tigloyloxy-5-angeloyloxy-7-hydroxycarvotacetone (4), and 3-angeloyloxy-5-hydroxy-7-hydroxycarvotacetone (5), were isolated from the aerial parts of *S. africanus* collected in Vietnam. Bioassay-guided fractionation was monitored by the anti-proliferative activity on CCRF-CEM human cancer cells. The structures of the compounds were determined on the basis of NMR and mass-spectroscopic data. Activities were evaluated *in vitro* against four human cancer cell lines (CCRF-CEM, MDA-MB-231, U-251, HCT-116). All compounds exhibited significant anti-proliferative activity against all four cell lines. CCRF-CEM was most sensitive to the compounds, with IC_{50} values ranging from 0.6 to 1.5 μ M. Compounds 3 and 4 possessed the highest activity, with IC_{50} values in the four cell lines ranging from 0.6 to 2.9 μ M and 1.3 to 2.5 μ M, respectively. These compounds also showed inhibitory activity towards HEK 293 human embryonic kidney cells, with IC_{50} values ranging from 2.5 to 5.5 μ M.

Discussion: This is the first time that anti-proliferative activity of *Sphaeranthus africanus* extracts and constituents have been reported, and constituents 1–5 are the most cytotoxic carvotacetone derivatives reported so far. Our results have shown that leukemia cells

reacted more sensitive to these compounds than non-tumorigenic cells. Therefore, carvotacetones may be interesting lead compounds in leukemia research.

Acknowledgements: We thank Assoz. Prof. Dr. Beate Rinner, Core Facilities Alternative Biomodels and Preclinical Imaging, Medical University of Graz, Austria, for providing the HEK 293 cells.

References

1. Chi VV: **Từ điển cây thuốc Việt nam [Dictionary of medicinal plants in Vietnam]**. Hà Nội: Y học; 2014. p. 662–663.
2. Ragasa CY, Espineli DL, Raga DD, Shen CC: **Chemical Constituents of *Sphaeranthus africanus***. *J Chem Pharm Res*, 2014; 6(7):2197–2200. <http://www.jocpr.com/articles/chemical-constituents-of-sphaeranthus-africanus.pdf>

*Corresponding author e-mail: rudolf.bauer@uni-graz.at