

Publication

Antiprotozoal Nor-triterpene alkaloids from *Buxus sempervirens* L

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Author(s) Szabó, L. U.; Kaiser, M.; Mäser, P.; Schmidt, T. J.

Author(s) at UniBasel [Mäser, Pascal](#) ; [Kaiser, Marcel](#) ;

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Malaria and human African trypanosomiasis (HAT; sleeping sickness) are life-threatening tropical diseases caused by protozoan parasites. Due to limited therapeutic options, there is a compelling need for new antiprotozoal agents. In a previous study, O-tigloylcyclovirobuxine-B was recovered from a *B. sempervirens* L. (common box; Buxaceae) leaf extract by bioactivity-guided isolation. This nor-cycloartane alkaloid was identified as possessing strong and selective in vitro activity against the causative agent of malaria tropica, *Plasmodium falciparum* (Pf). The purpose of this study is the isolation of additional alkaloids from *B. sempervirens* L. to search for further related compounds with strong antiprotozoal activity. In conclusion, 25 alkaloids were obtained from *B. sempervirens* L., including eight new natural products and one compound first described for this plant. The structure elucidation was accomplished by UHPLC/+ESI-QqTOF-MS/MS and NMR spectroscopy. The isolated alkaloids were tested against Pf and *Trypanosoma brucei rhodesiense* (Tbr), the causative agent of East African sleeping sickness. To assess their selectivity, cytotoxicity against mammalian cells (L6 cell line) was tested as well. Several of the compounds displayed promising in vitro activity against the pathogens in a sub-micromolar range with concurrent high selectivity indices (SI). Consequently, various alkaloids from *B. sempervirens* L. have the potential to serve as a novel antiprotozoal lead structure.

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