ABSTRACT

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Twenty-three monoterpene indole alkaloids of different structural types were isolated by chromatographic techniques from aerial parts of *Vinca minor* L. (Apocynaceae). The alkaloids were identified by a combination of analytical methods (NMR, MS, HRMS, optical rotation). Among obtained compounds, one structure was undescribed so far and was named vincaminorudeine. Eleven alkaloids were isolated for the first time from this species. Obtained compounds that were isolated in sufficient amounts were subjected to *in vitro* tests for the inhibition of *h*AChE, *h*BuChE, POP, and GSK-3β – enzymes that play a key role in the pathophysiology of Alzheimer's disease. The most active alkaloid was (−)-2-ethyl-3[2-(3-ethylpiperidinyl)-ethyl]-1*H*-indole (VR-19) with $IC_{50} = 0{,}65$ μM for the inhibition of *h*BuChE, and with $IC_{50} = 58$ μM for the inhibition of POP. Other alkaloids which exhibited a significant inhibition against *h*BuChE ($IC_{50} < 30$ μM) were vincaminoreine, minovine, 16-methoxyminovine, vincorine, and tubotaiwine. None of the isolated alkaloids were active against *h*AChE. The most active alkaloid VR-19 was further studied for its pharmacokinetic, revealing a reversible competitive type of inhibition for *h*BuChE with $Ki = 55$ nM. A follow-up docking study helped to explain structural aspects responsible for the high activity. This compound can also penetrate the blood-brain barrier by passive diffusion, as was assessed by *in vitro* study. Most of the isolated alkaloids were also tested for the cytotoxicity on ten different cell lines. Except for eburnamonine, none of the alkaloids showed significant inhibition of the growth.