

4th Symposium of Young Researchers on Pharmacognosy

BOOK OF ABSTRACTS

(ed. Judit Hohmann)

Institute of Pharmacognosy, University of Szeged, Szeged, Hungary

22–24 May 2023

Venue:

Szeged Regional Committee of Hungarian Academy of Sciences
H-6720 Szeged, Somogyi u. 7, Szeged



<https://us06web.zoom.us/j/89528815637?pwd=dHk1ODcyaXFicWpRK0xnZXk1QU9tQT09>

Meeting ID: 895 2881 5637, Passcode: 227572

doi: 10.14232/syrmpnpr.2023.af

University of Szeged, Faculty of Pharmacy, Institute of Pharmacognosy
Szeged, 2023

14 – SHORT LECTURE

doi: 10.14232/syrmpr.2023.14

Antioxidant and pharmacokinetic studies on new semi-synthetic nitrogen-containing diarylheptanoids derived from curcumin

Gábor Girst¹, György T. Balogh^{2,3}, Attila Hunyadi¹

¹ Institute of Pharmacognosy, Interdisciplinary Excellence Centre, University of Szeged, Faculty of Pharmacy, Eötvös str. 6, H-6720, Szeged, Hungary (girst.gabor.02@szte.hu, hunyadi.attila@szte.hu)

² Institute of Pharmacodynamics and Biopharmacy, University of Szeged, Faculty of Pharmacy, Eötvös str. 6, H-6720, Szeged, Hungary

³ Department of Chemical and Environmental Process Engineering, Budapest University of Technology and Economics, H-1111 Budapest, Hungary

Hydrocurcumins are the main Phase I metabolites of curcumin, the main bioactive compound of the widely known spice and traditional Asian medicine turmeric. Hydrocurcumins just like the parent compound possess a diverse pharmacological profile but, compared to curcumin, they have a much better bioavailability. Based on its pharmacokinetic properties and antioxidant activity, hexahydrocurcumin (HHC) is the most promising lead among them [1]. A big portion of approved drugs contain nitrogen, in most cases as heterocycle. Nitrones are less apparent, but due to their radical scavenger properties are also being investigated. It has been found that the introduction of nitrone moiety to Trolox increases its antioxidant potential [2].

In this study, we aimed to synthesise new derivatives of hexahydrocurcumin and investigate their antioxidant capacity as well as their pharmacokinetic properties. Along the naturally occurring gingerenone A and dihydrogingerenone A, nitrogen-containing diarylheptanoids were prepared, such as nitrones, oximes and heterocyclic derivatives. The antioxidant properties of the synthesized compound were tested on DPPH and oxygen radical absorbing capacity (ORAC) assay. Solubility and membrane permeability (on PAMPA model) were also measured. Some pharmacokinetic properties were calculated *in silico*.

Diverse results were obtained. Concerning most investigated properties, there were some new compounds more potent than HHC. While on the DPPH assay none of the new derivatives showed significantly better activity compared to HHC, on the ORAC assay several had lower IC₅₀ values. The best activity was found for a methyl-nitronone that had 0.18 µM IC₅₀ value, about half of that of the reference compound. Generally, the nitronone and oxime derivatives showed better water solubility, while the heterocyclic compounds had better membrane permeability compared to HHC. Our results show that some of the new nitrogen-containing diarylheptanoids have comparable potential to that of hexahydrocurcumin, and are worth of further investigation.

References

[1] Girst, G, et al. *Molecules* **2021**, 26(12):3542. doi: 10.3390/molecules26123542

[2] Balogh, GT, et al. *Bioorg. Med. Chem. Lett.* **2005**, 15(12):3012–3015. doi: 10.1016/j.bmcl.2005.04.043

Acknowledgements

This work was supported by NKFI K-134704, TKP2021-EGA-32 and ÚNKP-22-4-SZTE-164 projects.