proceedings

MDPI

Extended Abstract

Antibacterial *N*-Arylcinnamamides as Anti-inflammatory Agents †

Jiri Kos [1,*], Lubos Danisovic [2], Zuzana Varchulova Novakova [2], Radoslav Zamborsky [3], Ferdinand Devinsky [4] and Josef Jampilek [1,5]

[1] Division of Biologically Active Complexes and Molecular Magnets, Regional Centre of Advanced Technologies and Materials, Faculty of Science, Palacky University, Slechtitelu 27, 78371 Olomouc, Czech Republic; josef.jampilek@gmail.com
[2] Institute of Medical Biology, Genetics and Clinical Genetics, Faculty of Medicine, Comenius University in Bratislava, Sasinkova 4, 81108 Bratislava, Slovakia; lubos.danisovic@fmed.uniba.sk (L.D.); zuzana.varchulova@fmed.uniba.sk (Z.V.N.)
[3] Department of Orthopedics, Faculty of Medicine, Comenius University and Children's University Hospital, Limbova 1, 83340 Bratislava, Slovakia; radozamborsky@gmail.com
[4] Faculty of Pharmacy, Comenius University, Odbojarov 10, 83232 Bratislava, Slovakia; devinsky@fpharm.uniba.sk
[5] Department of Analytical Chemistry, Faculty of Natural Sciences, Comenius University, Ilkovicova 6, 84215 Bratislava, Slovakia
* Correspondence: jirikos85@gmail.com
† Presented at the 2nd Molecules Medicinal Chemistry Symposium (MMCS): Facing Novel Challenges in Drug Discovery, Barcelona, Spain, 15–17 May 2019.

Published: 8 August 2019

Keywords: cinnamamides; polypharmacology; anti-inflammatory activity; chondrocytes; cytotoxicity

---

A series of ring-substituted *N*-arylcinnamamides was prepared, characterized, and investigated for their antimicrobial efficacy in detail. Several of these derivatives showed strong activities, especially against Gram-positive bacteria and mycobacteria; they were able to increase the antibacterial activity of clinically used antibiotics with different mechanisms of actions. They were even able to inhibit the growth of staphylococcal biofilm and disrupted mature biofilm in concentrations close to MICs. It was found that the activity of the arylcinnamamides is bactericidal. No cytotoxic effect on human cells was observed for the most effective compounds [1,2]. Thus, the investigated cinnamamides may be considered as promising compounds for future research.

As derivatives of cinnamic acid are known for their anti-inflammatory and antioxidant effects [3,4], the cytotoxicity of the most effective compounds was tested on chondrocytes, and no inhibition of proliferation was found up to 100 μg/mL concentration. Thus, based on the concepts of polypharmacology, multifactorial diseases, and multitarget drugs and the abovementioned results, the compounds were investigated on their ability to inhibit cartilage damage caused by inflammation processes. This contribution is focused especially on the anti-inflammatory investigation of ring-substituted *N*-arylcinnamamides in relation to the induction of apoptosis and expression of pro- and anti-inflammatory markers. Structure–activity relationships and the supposed mechanism of action are discussed.

Acknowledgments: This study was supported by the Ministry of Education, Youth and Sports of the Czech Republic (LO1305), by the Slovak Research and Development Agency (APVV-17-0373 and APVV-17-0318). Knowledge gained within the project Center of Excellence in Security Research (CEBV) ITMS 26240120034 has been used in the results.

References

1. Pospisilova, S.; Kos, J.; Michnova, H.; Kapustikova, I.; Strharsky, T.; Oravec, M.; Moricz, A.M.; Bakonyi, J.; Kauerova, T.; Kollar, P.; et al. Synthesis and spectrum of biological activities of novel *N*-arylcinnamamides. *Int. J. Mol. Sci.* **2018**, *19*, 2318.
2. Pospisilova, S.; Kos, J.; Michnova, H.; Strharsky, T.; Cizek, A.; Jampilek, J. *N*-Arylcinnamamides as antistaphylococcal agents. In the Proceedings of the 4th International Electronic Conference on Medicinal Chemistry (ECMC-4), 1–30 November 2018, doi:10.3390/ecmc-4-05576.
3. Hadjipavlou-Litina, D.; Pontiki, E. Aryl-acetic and cinnamic acids as lipoxygenase inhibitors with antioxidant, anti-inflammatory, and anticancer activity. *Methods Mol. Biol.* **2015**, *1208*, 361–377.
4. Chen, G.; Zhang, Y.; Liu, X.; Fang, Q.; Wang, Z.; Fu, L.; Liu, Z.; Wang, Y.; Zhao Y.; Li, X.; et al. Discovery of a new inhibitor of myeloid differentiation 2 from cinnamamide derivatives with anti-inflammatory activity in sepsis and acute lung injury. *J. Med. Chem.* **2016**, *59*, 2436–2451.

© 2019 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).