

COMMENTARY TO HABILITATION THESIS¹

The adaptation of microorganisms to external influences, and thus the development of their resistance to antimicrobials, is becoming faster and faster over time. The increasing burden caused by cancer is an indisputable fact. Chronic inflammation is a hallmark of many diseases that make life very difficult for the human population. These are the main areas and goals where I try to apply my products of many years of research.

I started studying biologically active amides during my postgraduate studies. First, I focused on simple azanaphthanilides and hydroxy(aza)naphthanides. Due to its electronic properties and certain common features with a peptide bond, the amide (-NHCO-) group is able to interact with a wide range of enzymes and receptors. Through these target sites, they can then trigger an appropriate biological response. The properties of amides can be easily modified by substitution. Even on the basis of these facts, the amide group is found in the scaffolding of many modern drugs and other biologically active compounds such as antimicrobials, antiprotozoals, antivirals, antineoplastic agents, anti-inflammatory agents or herbicides; even in various pharmaceutical excipients. A common disadvantage across all series of hydroxy(aza)naphthanilides was their poor water solubility, which led to limitations in biological activity screening. In optimizing the structure, one of the two rings of the naphthalene segment was removed to give derivatives of the natural substance cinnamic acid.

The synthesis of the final products that are discussed in the habilitation thesis is designed using click chemistry. The traditional drug discovery process based on natural secondary metabolites has often been laborious, expensive, and slow. Click chemistry is a newer approach to drug-like molecules synthesis that can accelerate drug research. The reactions are simple to perform, reaction conditions and stable product isolation are straightforward, starting materials and reagents are readily available, the used solvent can be easily removed, purification processes use benign solvents and avoid chromatography. Microwave-assisted organic synthesis has been used in all of the above work to meet this requirement. This method has revolutionized organic synthesis, which was previously used only to speed up the reaction. It has several advantages over conventional heating (uniform heating occurs throughout the

¹ The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.

material, high purity of the final product, less unwanted side reaction, high efficiency of heating, high reaction rate, low operating cost)

This habilitation thesis is a collection of selected annotated articles that have been published over the last nine years. The articles describe the design, synthesis, structure, physicochemical properties and screening of the biological activity of hydroxyazanaphthanilides / cinnamamides. The obtained results are used to the analysis of the structure–activity relationship (SAR).

č. ²		ISSN	IF _{20xx}	
1	KOS, Jiří and ZADRAŽILOVÁ, Iveta and PEŠKO, Matúš and KELTOŠOVÁ, Stanislava and TENGLER, Jan and GONĚC, Tomáš and BOBÁL, Pavel and KAUEROVÁ, Tereza and ORAVEC, Michal and KOLLÁR, Peter and ČÍŽEK, Alois and KRÁĽOVÁ, Katarína and JAMPÍLEK, Josef. Antibacterial and Herbicidal Activity of Ring-Substituted 3-Hydroxynaphthalene-2-carboxanilides. <i>Molecules</i> 2013, vol. 18, no. 7, 7977-7997	1420-3049	IF ₂₀₁₃ = 2.095	
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	60%	-	50%	-
2	KOS, Jiří and NEVIN, Eoghan and ŠORAL, Michal and KUSHKEVYCH, Ivan and GONĚC, Tomáš and BOBÁL, Pavel and KOLLÁR, Peter and COFFEY, Aidan and O'MAHONY, Jim and LIPTAJ, Tibor and KRÁĽOVÁ, Katarína and JAMPÍLEK, Josef. Synthesis and Antimycobacterial Properties of Ring-Substituted 6-Hydroxynaphthalene-2-carboxanilides. <i>Bioorg. Med. Chem.</i> 2015, vol. 23, no. 9, 2035-2043	0968-0896	IF ₂₀₁₅ = 2.923	
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	60%	-	50%	-
3	KOS, Jiří and ZADRAŽILOVÁ, Iveta and NEVIN, Eoghan and ŠORAL, Michal and GONĚC, Tomáš and KOLLÁR, Peter and ORAVEC, Michal and COFFEY, Aidan and O'MAHONY, Jim and LIPTAJ, Tibor and KRÁĽOVÁ, Katarína and JAMPÍLEK, Josef. Ring-substituted 8-Hydroxyquinoline-2-carboxanilides as Potential Antimycobacterial Agents. <i>Bioorg. Med. Chem.</i> 2015, vol. 23, no. 15, 4188-4196	4188-4196	IF ₂₀₁₅ = 2.923	

² Bibliographic record of a published scientific result, which is part of the habilitation thesis.

	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	60%	30%	50%	40%
4	PEŠKO, Matúš and KOS, Jiří and KRÁĽOVÁ, Katarína and JAMPÍLEK, Josef. Inhibition of Photosynthetic Electron Transport by 6-Hydroxynaphthalene-2-carboxanilides. <i>Indian J. Chem. B</i> 2015, vol. 54B, no. 12, 1511-1517		0376-4699	IF ₂₀₁₅ = 2.486
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	50%	30%	50%	40%
5	JAMPÍLEK, Josef and KRÁĽOVÁ, Katarína and PEŠKO, Matúš and KOS, Jiří . Ring-substituted 8-Hydroxyquinoline-2-carboxanilides as Photosystem II Inhibitors. <i>Bioorg. Med. Chem. Lett.</i> 2016, vol. 26, no. 16, 3862-3865		0960-894X	IF ₂₀₁₅ = 2.486
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	40%	20%	40%	20%
6	KAUEROVÁ, Tereza and KOS, Jiří and GONĚC, Tomáš and JAMPÍLEK, Josef and KOLLÁR, Peter. Antiproliferative and Pro-Apoptotic Effect of Novel Nitro-Substituted Hydroxynaphthanilides on Human Cancer Cell Lines. <i>Int. J. Mol. Sci.</i> 2016, vol. 17, no. 8, 1219		1422-0067	IF ₂₀₁₆ = 3.226
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	40%	-	30%	-
7	KUSHKEVYCH, Ivan and KOS, Jiří and KOLLÁR, Peter and KRÁĽOVÁ, Katarína and JAMPÍLEK, Josef. Activity of ring-substituted 8-hydroxyquinoline-2-carboxanilides against intestinal sulfate-reducing bacteria <i>Desulfovibrio piger</i> . <i>Med. Chem. Res.</i> 2018, vol. 27, no. 1, 278-284		1054-2523	IF ₂₀₁₈ = 1.720
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	50%	-	30%	30%
8	KOS, Jiří and KAPUSTÍKOVÁ, Iva and CLEMENTS, Carol and GRAY, Alexander I. and JAMPÍLEK, Josef. 3-Hydroxynaphthalene-2-carboxanilides and Their Antitrypanosomal Activity. <i>Monatsh. Chem.</i> 2018, vol. 149, no. 5, 887-892		0026-9247	IF ₂₀₁₈ = 1.501

	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	50%	40%	60%	50%
9	DOLAB, Juan G. and LIMA, Beatriz and SPACZYŃSKA, Ewelina and KOS, Jiří and CANO, Natividad H. and FERESIN, Gabriela and TAPIA, Alejandro and GARIBOTTO, Francisco and PETENATTI, Elisa and OLIVELLA, Monica and MUSIOL, Robert and and JAMPÍLEK, Josef and ENRIZ, Ricardo D. Antimicrobial Activity of <i>Annona emarginata</i> (Schltdl.) H. Rainer and Most Active Isolated Compound Against Clinically Important Bacteria. <i>Molecules</i> 2018, vol. 23, no. 5, 1187		1420-3049	IF ₂₀₁₈ = 3.060
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	20%	-	20%	-
10	KUSHKEVYCH, Ivan and VÍŤEZOVÁ, Monika and KOS, Jiří and KOLLÁR, Peter and JAMPÍLEK, Josef. Effect of Selected 8-Hydroxyquinoline-2-carboxanilides on Viability and Sulfate Metabolism of <i>Desulfovibrio piger</i> . <i>J. Appl. Biomed.</i> 2018, vol. 16, no. 3, 241-246		1214-021X	IF ₂₀₁₈ = 1.573
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	50%	-	30%	30%
11	POSPÍŠILOVÁ, Šárka and KOS, Jiří and MICHNOVÁ, Hana and KAPUSTÍKOVÁ, Iva and STRHÁRSKY, Tomas and ORAVEC, Michal and MÓRICZ, Ágnes M. and BAKONYI, József and KAUEOVÁ, Tereza and KOLLÁR, Peter and ČÍŽEK, Alois and JAMPÍLEK, Josef. Synthesis and Spectrum of Biological Activities of Novel <i>N</i> -arylcinnamamides. <i>Int. J. Mol. Sci.</i> 2018, vol. 19, no. 8, 2318		1422-0067	IF ₂₀₁₈ = 4.183
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	50%	30%	40%	40%
12	KOS, Jiří and KU, Chuen Fai and KAPUSTÍKOVÁ, Iva and ORAVEC, Michal and ZHANG, Hong-Jie and JAMPÍLEK, Josef. 8-Hydroxyquinoline-2-carboxanilides as Antiviral Agents against Avian Influenza Virus. <i>ChemistrySelect</i> 2019, vol. 4, no. 15, 4582-4587		2365-6549	IF ₂₀₁₈ = 1.716
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)

	60%	30%	50%	60%
13	CAMPOS, Ludmila E. and GARIBOTTO, Francisco M. and ANGELINA, Emilio and KOS, Jiří and TOMASIC, Tihomir and ZIDAR, Nace and KIKELJ, Danijel and GONĚC, Tomáš and MARVANOVÁ, Pavlína and MOKRÝ, Petr and JAMPÍLEK, Josef and ALVAREZ, Sergio E. and ENRIZ, Ricardo. Searching New Structural Scaffolds for BRAF Inhibitors. Integrative Study using theoretical and experimental techniques. <i>Bioorg. Chem.</i> 2019, vol. 91, 103125		0045-2068	IF ₂₀₁₈ = 3.926
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	30%	-	20%	-
14	HOŠEK, Jan and KOS, Jiří and STRHÁRSKY, Tomáš and ČERNÁ, Lucie and ŠTARHA, Pavel and VANČO, Ján and TRÁVNÍČEK, Zdeněk and DEVÍNSKY, Ferdinand and JAMPÍLEK, Josef. Investigation of Anti-Inflammatory Potential of <i>N</i> -Arylcinnamamide Derivatives. <i>Molecules</i> 2019, vol. 24, no. 24, 4531		1420-3049	IF ₂₀₁₈ = 3.060
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	40%	50%	50%	60%
15	BAK, Andrzej and KOS, Jiří and MICHNOVÁ, Hana and GONĚC, Tomáš and POSPÍŠILOVÁ, Šárka and KOZIK, Violetta and ČÍŽEK, Alois and SMOLÍNSKI, Adam and JAMPÍLEK, Josef. Consensus-Based Pharmacophore Mapping for New Set of of <i>N</i> -(disubstituted-phenyl)-3-hydroxynaphthalene-2-carboxamides. <i>Int. J. Mol. Sci.</i> 2020, vol. 21, no. 18, 6583,		1422-0067	IF ₂₀₁₉ = 4.556
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	50%	30%	50%	40%
16	KOS, Jiří and BAK, Andrzej and KOZIK, Violetta and JANKECH, Timotej and STRHÁRSKY, Tomáš and ŚWIETLICKA, Aleksandra and MICHNOVÁ, Hana and HOŠEK, Jan SMOLÍNSKI, Adam and ORAVEC, Michal and DEVÍNSKY, Ferdinand and HUTTA, Milan and JAMPÍLEK, Josef. Biological Activities and ADMET-related Properties of Novel Set of Cinnamanilides. <i>Molecules</i> 2020, vol. 25, no. 18, 4121		1420-3049	IF ₂₀₁₉ = 3.267
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	60%	60%	50%	60%

17	CAMPOS, Ludmila E. and GARIBOTTO, Francisco M. and ANGELINA, Emilio and KOS, Jiří and GONĚC, Tomáš and MARVANOVA, Pavlína and VETTORAZZI, Marcela and ORAVEC, Michal and JENDRZEJEWSKA, Izabela and JAMPÍLEK, Josef and ALVAREZ, Sergio E. and ENRIZ, Ricardo. Hydroxynaphthalenecarboxamides and Substituted Piperazinypropandiols, Two New Series of BRAF Inhibitors. A Theoretical and Experimental Study. <i>Bioorg. Chem.</i> 2020, vol. 103, 104145.	0045-2068	IF ₂₀₁₉ = 4.831	
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	30%	-	20%	-
18	KOS, Jiří and GONĚC, Tomáš and ORAVEC, Michal and JENDRZEJEWSKA, Izabela and JAMPÍLEK, Josef. Photosynthesis-Inhibiting Activity of <i>N</i> -(Disubstituted-phenyl)-3-hydroxynaphthalene-2-carboxamides. <i>Molecules</i> 2021, vol. 26, no. 14, 4336.	1420-3049	IF ₂₀₂₀ = 4.411	
	Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
	60%	60%	50%	60%