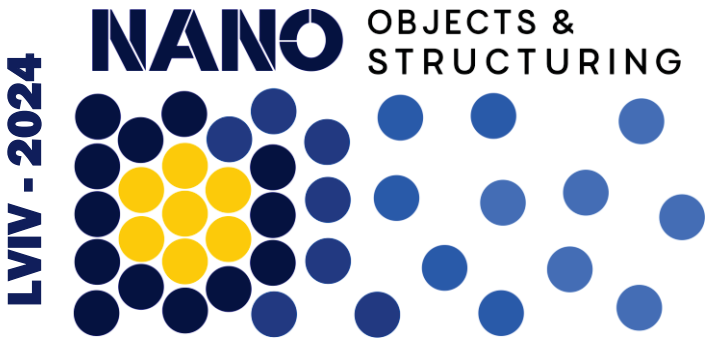
Ministry of Education and Science of Ukraine

Ivan Franko National University of Lviv
Faculty of Chemistry

Shevchenko Scientific Society

The National Academy of Sciences of Ukraine



III[rd] INTERNATIONAL RESEARCH and PRACTICE CONFERENCE «NANOOBJECTS & NANOSTRUCTURING» (N&N–2024)

October 7–10, 2024, Lviv, Ukraine

PROCEEDINGS

of such sulphides is the capacity to perform hydrogenation of aromatic halogen-containing compounds without cleavage of C-Hal bond, as well as to catalyze hydrogenation of thiophene without cleavage of the heterocyclic ring.

COMPUTATIONAL STUDY OF LINKER COMPOSITION IMPACT ON CONFORMATIONAL BEHAVIOR OF DUAL-TARGET CK2/HDAC INHIBITORS

Klenina Olena [1, 2], *Márquez-Cantudo Laura* [1], *Coderch Claire* [1], *de Pascual-Teresa Beatriz* [1]

[1] Departamento de Química y Bioquímica, Facultad de Farmacia, Universidad San Pablo CEU, CEU Universities, 28668, Madrid, Spain
[2] Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
olena_klenina@yahoo.com

Multitarget directed ligands as a modern approach for drug design has gained increasing attention in the recent decades as a more effective therapeutic strategy, especially in the framework of multifactorial diseases including cancer, leading to synergistic anti-tumor effects and reduced drug-drug interactions [1].

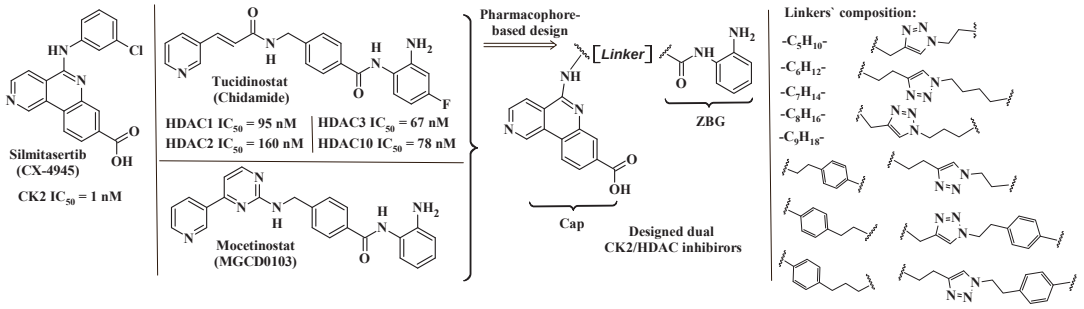


Fig. 1. Pharmacophore-based design of dual CK2/HDAC inhibitors

The systematic development of CK2/HDAC dual inhibitors [2] held by Drug Design and Synthesis Research Group at San Pablo CEU University led to novel dual-target ligands construction through the pharmacophores combining of Tucidinostat as zinc-binding group (ZBG) chelating Zn^{2+} cation at the catalytic domain of HDAC1, and CX-4945 as the competitive CK2 inhibitor, which also acts as Surface Recognition Domain (Cap group) in HDACs. Alkyl linear chains of varying length and alkyl chains incorporating phenyl or/and triazole motifs were introduced as the Linkers to connect the Cap structure to the ZBG (Fig. 1).

The objective was to discover the impact of the linkers` composition on the conformational behavior of the dual inhibitors in explicit water and chloroform

environments. The workflow included the geometry optimization with Gaussian16 [3] followed by 100 ns MD simulations using Amber 16 suite [4]. Trajectory analysis with cpptraj allowed to retrieve the molecular descriptors which are essential to predict cell permeability and characterize conformers' shape (radius of gyration), polarity (Polar surface area) and the ability to fold (the number of intramolecular hydrogen bonds and ZBG-Cap mass-centered distance). Clustering analysis of generated conformers resulted in 10 clusters which represent the most probable and stable conformations.

Acknowledgements. Financial support from MICINN for PID2021-123786OB-I00 project is kindly acknowledged. O. K. thanks Universidad San Pablo CEU for a Postdoctoral Contract for Ukrainian Researchers 2022-2024. L. M.-C. thanks Universidad San Pablo CEU and Banco Santander for a Young Researcher contract.

[1] V. Lembo, G. Bottegoni. Systematic Investigation of Dual-Target-Directed Ligands // J. Med. Chem. – 2024. – 67(12). – P. 10374–10385.
[2] L. Rangasamy, I. Ortín, J.M. Zapico *et al*. New Dual CK2/HDAC1 Inhibitors with Nanomolar Inhibitory Activity against Both Enzymes // ACS Med. Chem. Lett. – 2020. – 11(5). – P. 713-719.
[3] M. J. Frisch, G. W. Trucks, H. B. Schlegel *et al.* (2016) Gaussian 16.
[4] D.A. Case, R.M. Betz, D.S. Cerutti *et al.* AMBER 2016, University of California, San Francisco; San Francisco, CA: 2016.

THE INFLUENCE OF COMPOSITION AND STRUCTURE OF COBALT-CONTAINING COMPOSITES ON THEIR CATALYTIC PRODUCTIVITY IN THE PROCESS OF QUINOLINE HYDROGENATION

Arabadzhy Mykola [1, 3], Gryn Svitlana [2], Alekseev Sergei [2], Pashkevych Vyacheslav [1, 3], Subotin Vlad [1, 3], Ostapchuk Yevgen [1], Melnychenko Oleksiy [4], Pariiska Olena [3], Kurmach Mykhailo [3], Kolotilov Sergey [3]

[1] Enamine Ltd, Kyiv, Ukraine
[2] Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
[3] L.V.Pisarzhevsky Institute of Physical Chemistry of NAS of Ukraine, Kyiv, Ukraine
[4] State Enterprise "Radma" of L.V. Pisarzhevsky Institute of Physical Chemistry of the NAS of Ukraine, Kyiv, Ukraine
kolkamessi3@gmail.com

Development of hydrogenation catalysts, which do not contain metals of platinum group, is actual task of modern physical chemistry. In this study three types of catalysts were examined: the systems containing Co nanoparticles and car-