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RATIONAL DESIGN, SYNTHESIS AND IN VITRO TESTING OF SELECTIVE HDAC6 AND SIRT2 INHIBITORS

Dusan Ruzic (1), Nemanja Djokovic (1), Milos Petkovic (2), Danica Agbaba (1), Sheraz Gul (3), Maija Lahtela-Kakkonen (4), A. Ganesan (5), Juan F. Santibanez (6), Tatjana Srdic-Rajic (7), Katarina Nikolic (1)

1) Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Belgrade, Vojvode Stepe 450, 11000 Belgrade, Serbia; E-mail of the presenting author: knikolic@pharmacy.bg.ac.rs
2) Department of Organic Chemistry, Faculty of Pharmacy, University of Belgrade, Vojvode Stepe 450, 11000 Belgrade, Serbia
3) Fraunhofer-IME SP, Hamburg, Germany
4) School of Pharmacy (Pharmaceutical Chemistry) University of Eastern Finland, Kuopio, Finland
5) School of Pharmacy, University of East Anglia, Norwich Research Park, NR4 7TJ Norwich, United Kingdom
6) Group for Molecular Oncology, Institute for Medical Research, University of Belgrade, Dr. Subotića 4, 11129 Belgrade, Serbia
7) Department of Experimental Oncology, Institute for Oncology and Radiology of Serbia, Pasterova 14, 11000 Belgrade, Serbia

Histone deacetylases (HDACs) are epigenetic enzymes involved in regulation of histone posttranslational modifications and gene expression. Since changed function of HDACs is involved in pathogenesis of cancer [1-3], the HDAC inhibitors are extensive examined as promising anticancer agents. In our *in silico* study we have combined structure-based, ligand-based, and fragment-based methodologies to design selective inhibitors against cytoplasmic isoforms of HDAC, such as histone deacetylase 6 inhibitors (HDAC6) and SIRT2. The drug design study has defined several promising selective HDAC6 and SIRT2 inhibitors for further synthesis and *in vitro* testing. Based on the *in vitro* activities of the novel compounds in a panel of biochemical HDAC assays as well as various cell-based assays were selected the most promising candidates for further investigation.

References

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