26th Congress of SCTM

Sept. 20-23, 2023, Metropol Lake Resort, Ohrid, N. Macedonia

Synthesis, *In silico*, and *In vitro* Biological Testing of Novel 19-halogenated D-homo Lactone Steroids as Potential Antitumor Compounds

I. Kuzminac,[a,*] S. Bekić,[a] A. Ćelić,[b] D. Jakimov,[c] M. Sakač[a]

[a] *University of Novi Sad, Faculty of Sciences, Department of Chemistry, Biochemistry, and Environmental Protection, Trg Dositeja Obradovića 3, 21000 Novi Sad, Serbia*

[b] *University of Novi Sad, Faculty of Sciences, Department of Biology and Ecology, Trg Dositeja Obradovića 2, 21000 Novi Sad, Serbia*

[c] *Oncology Institute of Vojvodina, Faculty of Medicine, University of Novi Sad, Put Dr Goldmana 4, 21204 Sremska Kamenica, Serbia*

*ivana.kuzminac@dh.uns.ac.rs

Multiple tumors have been proven to be hormone-dependent, meaning that their development and growth are induced by endogenous human hormones. This fact was the basis for the design and development of antitumor steroidal drugs such as testolactone and exemestane. With the same goal in mind, we have performed a synthesis of C19-halogenated steroidal D-homo lactones. Previously synthesized 5α-bromo-6β-hydroxy D-homo lactone derivative[1] was used as a starting compound. It was transformed into a 19-hydroxy derivative through two synthetic steps: 6,19-epoxidation and reductive epoxide opening. Next synthetic steps led to the synthesis of two new halogenated derivatives as well as one intermediate and two side products. All novel synthesized compounds, halogenated, intermediate and side products, were tested *in silico* for their ADME properties (SwissADME Prediction), and *in vitro* for their cytotoxicity against a panel of cancer cell lines (MTT). Their relative binding affinities to the ligand-binding domains of androgen receptor and estrogen receptor α and β isoforms, were measured using a fluorescence-based assay in yeast.

Keywords: androstane, cytotoxicity, hormone derivatives

References

1. Kuzminac, I., Klisurić, O., Škorić, D., Jakimov, D., Sakač, M., Structural analysis and antitumor potential of novel 5,6-disubstituted-17a-homo-17-oxa-androstane derivatives, *Struc. Chem.* **2017**, 28, 567–576. DOI: 10.1007/s11224-016-0815-9