MedChem 2022 Barcelona

XI Paul Ehrlich Euro-PhD Network

BOOK OF ABSTRACTS

Institut Químic de Sarrià – Universitat Ramon Llull (IQS-URL)

Barcelona, July 14th-16th 2022

www.pehrlichmedchem.eu

medchem2022@iqs.url.edu

Poster Communication 1 (FP-1)

Design of novel dual COX-2 and 5-LOX inhibitors using quantitative structure-activity relationships analysis

Jelena Bošković, Vladimir Dobričić, Dušan Ružić, Katarina Nikolić, Olivera Čudina

Department of Pharmaceutical Chemistry, University of Belgrade – Faculty of Pharmacy

Vojvode Stepe 450, Belgrade, Serbia

jelena.boskovic@pharmacy.bg.ac.rs

Inflammation is a part of immune system's response to harmful intrinsic and extrinsic stimuli, such as infection or injury. It has an important role in progression of some diseases, such as cancer, arthritis, stroke [1]. It is considered that inhibition of COX-2 and 5-LOX pathways of production of inflammation mediators provides a new strategy for development of more effective anticancer drugs [2]. The aim of this study was designing of novel COX-2/5-LOX inhibitors with improved activity towards both enzymes using quantitative structure-activity relationships (QSAR). QSAR modeling was applied on a literature data set consisting of 28 dual COX-2/5-LOX inhibitors and obtained pharmacophoric features were used in design of novel compounds. Regarding prediction of activity of novel COX-2 and 5-LOX inhibitors, two models were developed. Based on values of Q^2 (0.53 (COX-2 model) and 0.71 (5-LOX model)) and R^2_{pred} (0.85 (for both COX-2 and 5-LOX models)), developed models have good predictive ability and can be used for activity prediction of novel designed compounds. Obtained values of r_m^2, $r_m'^2$ and $\overline{r_m^2}$ were higher than 0.5 and Δr_m^2 was lower than 0.2 indicating high predictive quality of developed models. Applicability domain (AD) was defined using Leverage approach and all compounds were inside the AD. In order to get more potent dual inhibitors of COX-2 and 5-LOX enzymes, compounds with high pIC_{50} values were chosen for design of novel compounds. As a result, 32 novel compounds were designed and according to predicted pIC_{50} values can be considered promising dual COX-2 and 5-LOX inhibitors.

———

[1] Ricciotti, E.; Fitzgerald, G. A., *Arteriosclerosis, Thrombosis, and Vascular Biology*, **2011**, *31*(5), 986–1000.

[2] Charlier, C.; Michaux, C., *European Journal of Medicinal Chemistry*, **2003**, *38*(7-8), 645–659.