EuroSciCon

Euroscicon Conference on

Medicinal Chemistry and Biosimilars

March 25-26, 2019
Budapest, Hungary

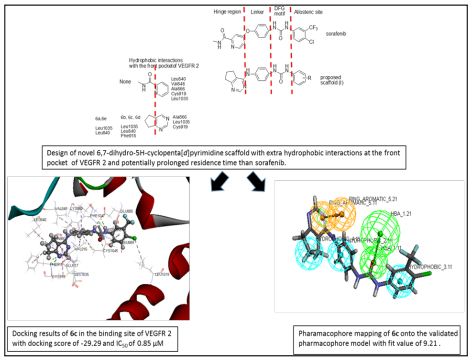
Nahla A Farag et al., Der Pharmacia Sinica 2019, Volume:10
DOI: 10.21767/0976-8688-C1-003

3D-QSAR PHARMACOPHORE MODELING, VIRTUAL SCREENING AND DOCKING STUDIES FOR LEAD DISCOVERY OF NOVEL SCAFFOLD FOR VEGFR 2 INHIBITORS: DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION

Nahla A Farag[1], Mahitab K Sobhy[1], Samar Mowafy[1], Deena S Lasheen[2] and Khaled A M Abouzid[2]

[1]Misr International University, Egypt
[2]Ain Shams University, Egypt

A novel series of 6,7-dihydro-5H-cyclopenta[d]pyrimidine derivatives was successfully designed, synthesized and evaluated as new chemical scaffold with vascular endothelial growth factor receptor VEGFR 2 inhibitory activity. Compounds 6c and 6b showed enzyme inhibition of 97% and 87% respectively and they also exhibited potent dose related VEGFR 2 inhibition with IC50 value of 0.85 µM and 2.26 µM respectively. The design of the 6,7-dihydro-5H-cyclopenta[d]pyrimidine scaffold was implemented via consecutive protocols of molecular modelling, prior to their synthesis and biological evaluation. First, Sorafenib was docked in the binding site of VEGFR 2 to study its binding orientation and affinity, followed by generation of valid 3D QSAR pharmacophore model to be implemented in virtual screening of 3D databases. Structures with promising results of pharmacophore based virtual screening were refined using molecular docking studies into the binding site of VEGFR 2. Design of the novel scaffold was accomplished adopting the results of pharmacophore model generation and molecular docking studies. Different derivatives with the novel scaffold were validated using docking studies and pharmacophore mapping where they exhibited promising results as VEGFR 2 inhibitors to be synthesised and biologically evaluated.6,7-dihydro-5H-cyclopenta[d]pyrimidine is a new scaffold that can be further optimized for synthesis of promising VEGFR 2 inhibitors.



Biography

Nahla A H Farag is a Professor of Pharmaceutical Medicinal Chemistry, Head of department, Faculty of Pharmacy at Misr International University (MIU), Cairo, Egypt since 2015. She has completed PhD in Pharmaceutical Medicinal Chemistry from Faculty of Pharmacy, Cairo University, Cairo, Egypt in 2001. She has established a new course in computer aided drug design for senior undergraduate students in MIU since 2013 till now. She has also established a Drug Design Center with highly advanced computer labs and high trained teaching assistant team for post graduate and undergraduate teaching course and workshops for advanced researches in molecular modeling techniques.

nahla.farag@miuegypt.edu.eg