Journal of Molecular Structure 1217 (2020) 128442

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc

QSAR modeling, docking, ADME and reactivity of indazole derivatives as antagonizes of estrogen receptor alpha (ER-α) positive in breast cancer

Afaf Zekri [a, *], Dalal Harkati [a, **], Samir Kenouche [b], Basil A. Saleh [c]

[a] Group of Computational and Pharmaceutical Chemistry, LMCE Laboratory, University of Biskra, BP 145, Biskra, 07000, Algeria
[b] Department of Matter Sciences, Faculty of Exact and Natural Sciences, University of Biskra, BP 145, Biskra, 07000, Algeria
[c] Department of Chemistry, College of Science, University of Basrah, Basrah, Iraq

ARTICLE INFO

Article history:
Received 10 April 2020
Received in revised form
8 May 2020
Accepted 12 May 2020
Available online 16 May 2020

Keywords:
ADME
Estrogen receptor
Indazole
Molecular docking
QSAR Analysis
Reactivity

ABSTRACT

To establish a quantitative structure-activity relationship, 54 indazole derivatives were analyzed by multiple linear regression MLR. The DFT-B3LYP method, with the basis set 6-311G, was performed to define the structure, chemical reactivity and properties of the compounds. This study was accompanied by molecular docking, global reactivity descriptors, absorption, distribution, metabolism and elimination (ADME) properties on a series of 21 compounds of selective estrogen receptor degraders (SERDs) that present the most active compounds from the dataset. The MLR regression equation displayed a good agreement between fitted and observed biological activities. A high average R^2_{Boots} greater than 0.5 indicates that the obtained model has good predictive power and robustness. In addition, an average value of R^2_{pred} (0.57) approximately equal to 0.6 may be taken as an indicator of good external predictability. The interactions between the most active compounds from the indazole series and ERα targets were explored through a molecular docking to elucidate the binding mode between the studied compounds and corresponding protein. Based on this study compounds **14**, **43**, **8** and **45** have no violated Lipinski's rule of five and Veber's rule, suggesting that these compounds would not have problems with oral bioavailability. Most of global reactivity results have an agreement with those obtained in this docking study.