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QUINAZOLINE BASED EGFR INHIBITORS: PHARMACOPHORE MODELING, 3D-QSAR, DOCKING AND DRUG LIKELINESS PREDICTION

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Pharmacophore modeling, molecular docking and *in silico* ADME prediction of a series of quinazoline based EGFR inhibitors [1,2,3] was performed using Schrodinger software. The study was performed inorder to identify the binding pattern and drug likeliness nature of these EGFR inhibitors. A five point pharmacophore model (AAARR.7) was generated for these compounds. The model came out to be statistically significant with a good correlation coefficient (R^2) of 0.9433, which was considerably towards higher side, a cross validation coefficient (Q^2) of 0.8493 and F value of 97.10 at 6 component PLS factor. Results of external validation were also indicative of high predictive power (R^2 =0.86). The model also passed Tropsha's test for predictive ability and Y-randomization test. The Domain of Applicability (APD) of the model was also successfully defined to ascertain whether the given prediction can be considered reliable or not. Further, to determine the effectiveness of docking protocol, co-crystallized ligand was extracted from the ligand binding domain of the protein and was re-docked into the same position. The conformer obtained on re-docking and the cocrystallized ligand were superimposed. Root mean square deviation (RMSD) between the two was found to be 1.005 A°, justifying the efficacy of performed docking. Outcomes of this work provide an insight for the development of novel potential EGFR inhibitors.

1. Qin X. et al. *Bioorganic & Medicinal Chem*istry, 2016, **24**: 2871-2881.
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The authors would like to acknowledge Jamia Hamdard, New Delhi, India-110062.