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P38α MAP KINASE INHIBITORS: PHARMACOPHORE MODELING, 3D-QSAR, DOCKING AND DRUG LIKELINESS PREDICTION

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A set of dibenzepinones, dibenzoxepines, and benzosuberones based p38α MAP kinase inhibitors [1] was subjected to pharmacophore modeling, molecular docking and *in silico* ADME prediction. This study has been performed to identify the binding pattern and drug likeliness nature of these p38α MAP kinase inhibitors. For these compounds, a five point pharmacophore model (DDHRR.8) was generated. This model came out to be statistically significant as it had a correlation coefficient (R^2) of 0.98, which was considerably towards higher side, a cross validation coefficient (Q^2) of 0.95 and F value of 330 at 6 component PLS factor. Results of external validation were also indicative of high predictive power (R^2 =0.90). This 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 0.548 A°, justifying the efficacy of performed docking. Outcomes of this work provide an insight for the development of novel p38α MAP kinase inhibitors.

1. Martz K.E. et al. *Journal of Medicinal Chem*istry, 2012, **55**: 7862-7874.

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