World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:16, No:04, 2022

Application of Computational Chemistry for Searching Anticancer Derivatives of 2-Phenazinamines as Bcr-Abl Tyrosine Kinase Inhibitors

Authors : Gajanan M. Sonwane

Abstract : The computational studies on 2-phenazinamines with their protein targets have been carried out to design compounds with potential anticancer activity. This strategy of designing compounds possessing selectivity over specific tyrosine kinase has been achieved through G-QSAR and molecular docking studies. The objective of this research has been to design newer 2-phenazinamine derivatives as Bcr-Abl tyrosine kinase inhibitors by G-QSAR, molecular docking studies followed by wet-lab studies along with evaluation of their anticancer potential. Computational chemistry was done by using VLife MDS 4.3 and Autodock 4.2 followed by wet-lab experiments for synthesizing 2-phenazinamine derivatives. The chemical structures of ligands in 2D were drawn by employing Chemdraw 2D Ultra 8.0 and were converted into 3D. These were optimized by using a semi-empirical method called MOPAC. The protein structure was retrieved from RCSC protein data bank as a PDB file. The binding interactions of protein and ligands were done by using PYMOL. The molecular properties of the designed compounds were predicted in silico by using Osiris property explorer. The parent compound 2-phenazinamine was synthesized by reduction of 2, 4-dinitro-N-phenyl-benzenamine in the presence of tin chloride followed by cyclization in the presence of nitrobenzene and magnesium sulfate. The derivatization at the amino function of 2-phenazinamine was performed by treating parent compound with various aldehydes in the presence of dicyclohexylcarbodiimide (DCC) and urea to afford 2-(2-chlorophenyl)-3-(phenazine-2-yl) thiazolidine-4-one. Synthesized 39 novel derivatives of 2-phenazinamine and performed antioxidant activity, anti antiproliferative on the bulb of onion and anticancer activity on cell line showing significant competition with marked blockbuster drug imatinib.

Keywords : computer-aided drug design, tyrosin kinases, anticancer, docking
Conference Title : ICADDSBDD 2022 : International Conference on Anticancer Drug Development and Structure-Based Drug Design
Conference Location : Cape Town, South Africa
Conference Dates : April 14-15, 2022