World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:16, No:05, 2022

# Design, Synthesis and Pharmacological Investigation of Novel 2-Phenazinamine Derivatives as a Mutant BCR-ABL (T315I) Inhibitor

**Authors :** Gajanan M. Sonwane

**Abstract :** Nowadays, the entire pharmaceutical industry is facing the challenge of increasing efficiency and innovation. The major hurdles are the growing cost of research and development and a concurrent stagnating number of new chemical entities (NCEs). Hence, the challenge is to select the most druggable targets and to search the equivalent drug-like compounds, which also possess specific pharmacokinetic and toxicological properties that allow them to be developed as drugs. The present research work includes the studies of developing new anticancer heterocycles by using molecular modeling techniques. The heterocycles synthesized through such methodology are much effective as various physicochemical parameters have been already studied and the structure has been optimized for its best fit in the receptor. Hence, on the basis of the literature survey and considering the need to develop newer anticancer agents, new phenazinamine derivatives were designed by subjecting the nucleus to molecular modeling, viz., GQSAR analysis and docking studies. Simultaneously, these designed derivatives were subjected to in silico prediction of biological activity through PASS studies and then in silico toxicity risk assessment studies. In PASS studies, it was found that all the derivatives exhibited a good spectrum of biological activities confirming its anticancer potential. The toxicity risk assessment studies revealed that all the derivatives obey Lipinski's rule. Amongst these series, compounds 4c, 5b and 6c were found to possess logP and drug-likeness values comparable with the standard Imatinib (used for anticancer activity studies) and also with the standard drug methotrexate (used for antimitotic activity studies). One of the most notable mutations is the threonine to isoleucine mutation at codon 315 (T315I), which is known to be resistant to all currently available TKI. Enzyme assay planned for confirmation of target selective activity.

**Keywords :** drug design, tyrosine kinases, anticancer, Phenazinamine
**Conference Title :** ICCDDMT 2022 : International Conference on Computational Drug Discovery and Medical Technologies
**Conference Location :** Amsterdam, Netherlands
**Conference Dates :** May 16-17, 2022