# Pharmaco-Informatics Profiling of Small Molecules Targeting c-Kit Protein

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## Abstract

The proto-oncogenic c-Kit is essential for the intracellular signaling mechanism and its mutations were associated with various types of cancers. Protein c-Kit belongs to RTKs family; activated by its SCF, induces several signaling pathways RAS, PI3K and JAK/STAT in CRC. Herein, the SAR based approaches focuses on developing potent c-Kit inhibitors with high kinase selectivity for CRC. Pharmacophore modeling was carried using Phase module of Schrodinger for FDA approved C-Kit drugs. The five point pharmacophore model of ADHRR was explored as a template to screen compounds from databases using ligand-based virtual screening. The top hits from the screened COCONUT database, were identified as potential inhibitors with high insilico predicted activity and strong key binding interactions with the c-Kit receptor. The MD analysis confirms that the chosen compounds with the drug target maintain a stable conformation throughout the simulation run. The amino acid interaction profiling for the binding patterns were discussed to facilitate future development of more potent and pharmacokinetically stable small-molecule c-Kit inhibitors. Overall the obtained pharmacophore model reliably used to identify new c-Kit inhibitors, and can provide useful information when designing new inhibitors for CRC. Thus, the inhibition of c-Kit has emerged as a promising therapeutic target for CRC.

**Keywords**: Colorectal cancer, c-Kit, pharmacophore, Virtual screening, Molecular dynamics.