2013-14

Rajnibhai V. Patel
PharmInnova Award
Best M. Pharm Thesis

WINNER

Runner-Up

Mr. Pankaj Bari

Research Guide

Dr. P S Jain

Subject:
Pharmaceutical Chemistry

Thesis Title :
Design and Synthesis of VEGFR-2 Tyrosine Kinase Inhibitors as potential Anti-Cancer agents by virtual based screening

College:
R C Patel Institute of Pharma. Edu & Res (RCIPER), Shirpur, MH

Cheaper substitute of anticancer drug - Gefitinib

Outcome of Research:

Gefitinib (anti-cancer drug) slows the growth and spread of the cancer by blocking an essential cell signaling pathway involved in uncontrolled cell division. Gefitinib is currently available as 250 mg. film coated tablet and is extremely expensive. Hence, this study screened for more economic and safer, structurally similar analogues of Gefitinib. Out of the eighty compounds screened based on structure and physicochemical properties, five compounds showed potent anti-cancer activity. One of the compounds (compound 50) showed highest anticancer activity against non-small cell lung HOP-92 cancer cell line.

Thesis Title: Design and Synthesis of Small Molecule VEGFR Tyrosine Kinase Inhibitor as a Potential Anti-cancer Agent by Virtual screening Based Approach

---

ABSTRACT

Vascular epidermal growth factor receptor (VEGFR) protein tyrosine kinases (PTKs) are known for its role in cancer. In the present study virtual screening based approach has been used for the designing of VEGFR-2 inhibitors. Pharmacophore based 3D-QSAR study, docking study, Lipinski's rule of five and ADME prediction; these are the different filters used for virtual screening. In the beginning; a series of quinazoline derivatives with VEGFR-2 tyrosine kinase inhibitory activity was subjected to a 3D-QSAR study. Based upon pharmacophore 3D-QSAR and literature survey of VEGFR-2 inhibitors, we designed the library of 75 compounds. This library is passed through the developed 3D-QSAR model and those compounds which are showing good fitness and predicted activity are further selected for docking study. Compounds having good docking score were passed through filter 3 i.e. Lipinski's rule; also in silico ADME properties were analysed. Finally virtually screened 24 compounds were screened at NCI for the in vitro anti-cancer activity. Among the tested compounds 06 compounds were showing the significant cancer growth inhibition and further selected for the five dose study. Among the tested compounds, Compounds 50 shows highest anticancer activity against Non-Small Cell Lung HOP-92 Cancer cell line with GI50 value of 0.36 μM