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RESEARCH PAPER

QSAR STUDIES INVOLVING 2D, 3D QSAR AND PHARMACOPHORE MAPPING STUDIES ON ARYLSULFONYL IMIDAZOLIDINONE DERIVATIVES AS ANTICANCER AGENTS

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QSAR analysis including 2D QSAR, 3D QSAR and pharmacophore mapping studies have been performed on a series of arylsulfonylimidazolidinone derivatives to explore the physico-chemical properties and basic pharmacophore responsible for anti-cancer activity. The 2D-QSAR studies were carried out using the partial least squares (PLS) method coupled with stepwise variable selection, with $r^2 = 0.7106$ and $q^2 = 0.5176$; the 3D-QSAR studies were performed using stepwise variable selection k-nearest-neighbor molecular field analysis (kNNMF) approach; with cross-validated correlation coefficient (q^2) of 0.5909. Pharmacophore mapping resulted in highly predictive pharmacophore based 3D-QSAR model with five point hypotheses (AADHR.18) with two acceptor atom, one donor group, one hydrophobic group and one aromatic ring as pharmacophore features. This is denoted as A2A3D5R10H7. Research indicated that alignment-independent descriptors, steric field and electrostatic field descriptors were significantly correlating with anticancer activity of arylsulfonylimidazolidinone derivatives.

Key words: QSAR, Pharmacophore mapping, Arylsulfonylimidazolidinone, Anticancer activity, kNNMF.

INTRODUCTION

Much of the general public sees cancer as a modern day plague that results in high morbidity (Green and Evan, 2002). Cancer cells rapidly acquire resistance against numerous cytotoxic drugs or are even intrinsically resistant. Despite over 50 years of research, it is still debated, how cancer cells generate complex resistance phenotypes against a multitude of drugs much more rapidly than predicted by conventional mutation, and how cancer cells generate such resistance with the very same genes they just inherited from normal, drug sensitive precursor cells (Duesberg *et al* 2007). The occurrence of localized changes in chromatin structure at transcriptional start sites has been well appreciated; however, it is now emerging that the alterations are genome wide.