



RESEARCH PAPER

EXPLORING 2D AND 3D QSAR STUDIES OF INDOLE/ BENZOXIMIDAZOLE-5-CARBOXIMIDINE DERIVATIVES AS ANTICANCER AGENTS FOR THE DEVELOPMENT OF PREDICTIVE MODEL

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2D QSAR and 3D QSAR studies of indole/benzoximidazole-5-carboximidine derivatives as anti-cancer agents by Vlife Sciences MDS molecular modelling package has been performed to explore the physico-chemical properties and spatial disposition of the chemical groups towards the biological activity. The 2D-QSAR studies were carried out using the partial least squares (PLS) method coupled with stepwise variable selection, with $r^2 = 0.5960$ and $q^2 = 0.4062$ and the 3D-QSAR studies were performed using stepwise variable selection k-nearest-neighbour molecular field analysis (kNNMF) approach; with cross-validated correlation coefficient (q^2) of 0.6453 and a predicted r^2 for the external test ($pred_r^2$) of 0.7316.

Key words: QSAR, kNNMFA, PLS, Indole/benzoximidazole-5-carboximidine, Anticancer agents.

INTRODUCTION

Cancer is the second leading cause of death in the developed world. Cancer accounted 7.9 million deaths (around 13% of all deaths) in 2008 (Zali *et al* 2011). Regular use of some established screening tests can prevent the development of cancer through identification and removal or treatment of premalignant abnormalities (American Cancer Society, 2013). Currently, inspite of intensive research and some major advances in treatment, cancer claims the life of nearly one out of four. It is second to heart diseases responsible for 35% of deaths in United States (Copper, 1992). The failure of the curative

treatment of cancer patients often occurs as a result of intrinsic or acquired drug resistance of the tumor to chemotherapeutic agents. The resistance of tumors occurs not only to a single cytotoxic drug used, but also occurs as a cross-resistance to a whole range of drugs with different structures and cellular targets (Ozben, 2006). There are more than 100 distinct types of cancer and subtypes of tumors can be found within specific organs (Hanahan and Weinberg, 2000). The urokinase (uPA) pathway of plasminogen activation plays a key role in tissue remodelling, cancer cell invasion and in metastasis. uPA is one of the serine proteases