CoMFA 3D-QSAR STUDIES ON BENZAZOLE DERIVATIVES AS EUKARYOTIC TOPOISOMERASE II INHIBITORS

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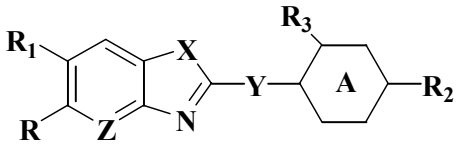
Since the activity of topoisomerases is essential for several cellular processes such as replication, transcription, and chromosome condensation, investigation of the inhibitory activities of eukaryotic topoisomerases is widely used in anticancer drug development. Topo II is the target for some of the most active anticancer drugs such as etoposide, teniposide, and doxorubicin used in the treatment of human malignancies [1-3]. Therefore selective Topoisomerase II inhibitors have attracted much attention in recent times in the design of new antitumor compounds.

Many pharmacological studies have resolved receptor active/binding sites using numerous computational 3D-quantitative structure-activity relationship (3D-QSAR) techniques [4].

In this study, 3D-QSAR studies have been performed on a series of benzazoles (**Figure**) that act as eukaryotic topoisomerase II inhibitors [5], using C*o*mparative Molecular Field Analysis (CoMFA) [6] with partial least squares (PLS) fit. The analysis was carried out on 23 analogues of which 16 were used in the trainig set and the rest considered for the test set. These studies produced reasonably good predictive models with high cross-validated and conventional r^2 values in all the three cases.



X|= O, NH, S; **Y** = –, CH_2, CH_2O, CH_2S, C_2H_4;
Z = CH, N; **A**= Phenyl, Cyclohexyl, Cyclopenthyl;
R = H, NH_2, NO_2, CH_3, Cl, $COOCH_3$; $\mathbf{R_1}$ = H, NO_2;
$\mathbf{R_2}$ = H, Cl, CH_3, C_2H_5, NH_2, $NHCH_3$, OCH_3, OC_2H_5;
$\mathbf{R_3}$ = H, CH_3, OCH_3

Figure

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