3D-QSAR AND PHARMACOPHORE MODELING OF NAPHTHOQUINONE DERIVATIVES WITH CYTOTOXIC ACTIVITY IN HL60 CELL LINES.

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Catalyst HypoGen pharmacophore modeling approach and 3D-QSAR comparative molecular similarity indices analysis (CoMSIA), were employed on a set of 51 naphthoquinones tested in HL-60 leukaemia cell lines. The aim was to identify pharmacophores and to outline structural requirements of these naphthoquinones as antitumoral agents. Quantitative chemical functions based on pharmacophore models were generated using the HypoGen algorithm, which is implemented in the CATALYST program. The best output hypothesis consists of three features: two hydrogen bond acceptor (HBA) and one hydrophobic (Hy). The 3D-QSAR modeling afforded predictive models with consistently high values of both leave-one-out cross-validated R2(0.967) for the training set and predictive R2(0.999) for the test set. The results of both modeling approaches were sensitive to the selection of the training and test sets used for model development and validation.