Design, synthesis, in vitro antiproliferative effect and in situ molecular docking studies of a series of new benzoquinoline derivatives

ABSTRACT

Quinoline derivatives have been reported to possess multi-therapeutic potential owing to the manifestations of different pharmacological effects. The current research work describes about the design and synthesis of a series of novel benzoquinoline analogues with an objective to evaluate their antiproliferative structure–activity relationship against colon, breast and hepatocellular cancers. Upon synthesis, all derivatives' chemical structures were elucidated through FTIR, 1HNMR and 13CNMR spectroscopic analysis. All derivatives were investigated for their in vitro anti-proliferative property against three different cancer cell lines (viz., colon carcinoma HT29, Caucasian breast adenocarcinoma MCF7, hepatocellular carcinoma HepG2) and a normal non-transformed human foreskin fibroblast Hs27 cell line. All derivatives demonstrated varied degrees of strong anticancer effect against all of the cell lines with the 2-Amino-4-(4-nitrophenyl)-5,6-dihydrobenzo[h]quinoline-3-carbonitrile (CNMP, 2) exhibited the most potent antiproliferative effect viz. LC50 21.23 lM for breast, 8.24 lM for colon, and 26.15 lM for the hepatocellular, respectively. Molecular docking studies against all the the target crystal structures of cancer proteins (1HK7, 3EQM, 3IG7 and 4FM9) revealed significant binding affinities via hydrophobic and H-bonding interactions with all the compounds in conformity with the wet lab results. CNMP showed the highest binding energy of □ 7.55 in the HT29, □ 6.9 (both in MCF7 HepG2) kcal/mol. Based on the results obtained from wet lab and dry lab experiments, it can be proposed that CNMP might prove to be a potential lead structure for the design and synthesis of more potent anticancer candidates.