

Synthesis, antitumor testing and molecular modeling study of some new 6-substituted amido, azo or thioureido-quinazolin-4(3H)-ones

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Abstract

A new series of 6-substituted amido, azo or thioureido-quinazolin-4(3H)-one was synthesized and tested for their in-vitro antitumor activity. Compounds 21, 53 and 60 showed broad spectrum antitumor activity with average IC₅₀ values of 6.7, 7.6 and 7.8 μM, respectively. As an attempt to reveal the mechanism of the antitumor potency, cell cycle analysis and DHFR inhibition were performed. Compounds 59 and 61 induced their cytotoxicity in HCT116 and H1299 cell lines, respectively through Pre-G1 apoptosis, inhibiting cell growth at G2-M phase. Compounds 29, 55 and 61 showed high affinity binding toward the amino acid residues Thr56, Ser59 and Ser118. The active compounds obeyed Lipinski's rule of five and could be used as template model for further optimization.

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