Non Classical Antifolates, Part 3: Synthesis, Biological Evaluation and Molecular Modeling Study of Some New 2-Heteroarylthio-Quinazolin-4-Ones

Hussein Ibrahim Ismail El Subbagh

Professor

Abstract

A new series of 2-heteroarylthio-6-substituted-quinazolin-4-one analogs was designed, synthesized and evaluated for their in vitro DHFR inhibition, antimicrobial, and antitumor activities. Compounds 21,25 and 39 proved to be active DHFR inhibitors with IC50 range of 0.3-0.8 M. Compounds 25, 28,33,35 and 36 showed broad spectrum antimicrobial activity comparable to the known antibiotic gentamicin. Compound 29 showed broad spectrum antitumor activity toward several tumor cell lines with GI values range of 25.8-41.2%. Molecular modeling studies concluded that recognition with key amino acid Arg38 and Lys31 are essential for binding and biological activities. Flexible alignment, electrostatic and hydrophobic mappings revealed that the obtained model could be useful for the development of new DHFR inhibitors.

European Journal For Medicinal 2013 - 2013, January