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Research article

Synthesis, molecular modeling and bioevaluation of new benzimidazole derivatives as dual KSP (Kinesin Spindle Protein) and Aurora A Kinase inhibitors for antitumor activity

Asmaa A. Magd El-Din*[1], Weam. S. El-serwy[1], Amira S. Abd El-All[1], N.M.A .El-Ebrashi[1], Mohamed M. Abdalla[2], Ahmed A. El-Rashedy[1]

[1]*Department of Natural and Microbial Product, Research Division of Pharmaceutical and Drug Industries, National Research Centre, Giza, Egypt.*
[2]*Research Unit, Saco Pharm. Co. 6 October city 11632, Egypt.*

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***Corresponding Author: Asmaa A. Magd El-Din,** Department of Natural and Microbial Product, Research Division of Pharmaceutical and Drug Industries, National Research Centre, Dokki, Giza 12622.

Abstract

A series of dioxopyrimido[2,1-b][1,3]thiazine derivatives (3a-f,6a-e) has been synthesized and their biological activities were also evaluated as potential dual KSP and Aurora A Kinase inhibitors. Bioassay tests demonstrated that most of the compounds exhibited substantial broad-spectrum antitumor activity against the seven cancer cell lines (HepG2, SNB19, HT29, K562, A549-ATCC, MDA-MB-435 and SKOV3). Moreover, all the title compounds were assayed for as dual KSP and Aurora A kinase inhibition using the MT-activated ATPase assay. Compound (6b) displayed the most potent anticancer activities, which was comparable to the positive control and Molecular modeling has been done for this compound. The results may be used for developing a new class of inhibitors having a dual roles, KSP inhibition and Aurora-A kinase inhibition for the treatment of cancer.