Anticancer profile of newly synthesized B-RAF inhibitors possess 5(pyrimidin-4-yl)imidazo[2,1-b]oxazole scaffold

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In the present work, a novel series of B-RAF inhibitors having imidazo[2,1-b]oxazole scaffold was designed and synthesized based on the structures of the well-known BRAF inhibitors and on our previous work. The final compounds were tested over A375 and SKMEL28 cell lines to determine the primary cytotoxic activity of these compounds using sorafenib as standard. Compounds **11r, 11q, 11u, 11o, 11e** and **11c** exhibited higher cellular activity compared to sorafenib. In addition, the final target compounds were screened for their anticancer activity by the National Cancer Institute 60 cell lines assay. Compounds 11v and 11u were the most potent compounds with percent inhibition reached 95.99% for **11v** and 87.03% for **11u** over K562 cell line. Compound **11v** was selected for 5 doses test mode. The RAF inhibitory activities of **11a, 11c, 11e, 11i, 11o, 11q, 11r, 11u** and **11v** were determined. Moreover, the molecular docking simulation of the synthesized compounds was performed with the B-RAF protein kinase domain (PDB code: 4FK3) in order to investigate the binding modes of the tested compounds with the target enzyme active site.

Biography

Usama Ammar was graduated from two faculties, Faculty of Science (Zagazig University, Egypt, 2005) and Faculty of Pharmacy (Ahram Canadian University, Egypt, 2010). He got his Master degree in Pharmaceutical Chemistry (Faculty of Pharmacy, Cairo University, Egypt, 2016). He is studying PhD program in Bio-Med (University of Science & Technology, South Korea). He is interested in synthesis of small chemical molecules in order to inhibit a number of enzymes involved in cancer disease. Moreover, He is involved in a number of projects focusing on optimization of synthetic pathways of target compounds to be suited in industrial large scale.