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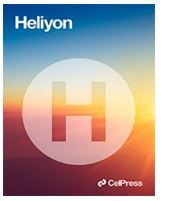

Design, synthesis, anticancer activity and docking studies of novel quinazoline-based thiazole derivatives as EGFR kinase inhibitors

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ABSTRACT

The *in vitro* anticancer efficacy of a new series of quinazoline-based thiazole derivatives was explored. Three cancer cell lines, MCF-7, HepG2, and A548, as well as the normal Vero cell lines, were tested employing the synthesized quinazoline-based thiazole compounds (4a-j). All of these compounds showed a moderate to significant cytotoxic impact that would have been noticeable and, in some cases, much more pronounced than the widely used drug erlotinib. For the MCF-7, HepG2, and A549 cell lines, respectively, the IC_{50} values of compound 4i were 2.86, 5.91, and 14.79 μM while those of compound 4j were 3.09, 6.87, and 17.92 μM. For their *in vitro* inhibitory effects against different EGFR kinases, such as the wild-type, L858R/T790 M, and L858R/T790 M/C797S, all the synthesized compounds were tested. The IC_{50} values for compound 4f against the wild-type, L858R/T790 M, and L858R/T790 M/C797S mutant EGFR kinases were 2.17, 2.81, and 3.62 nM, respectively. Investigations on the molecular docking of significant molecules indicated potential mechanisms of binding into the EGFR kinase active sites. By using in-silico simulations, compounds' putative drug-like qualities were verified. Finally, it has been shown that the newly synthesized compounds 4i and 4j are good candidates and beneficial for future design, optimization, and research to build more potent and selective EGFR kinase inhibitors with higher anticancer activity.

1. Introduction

The majority of fatalities worldwide are linked to cancer; hence, it is crucial to continue developing new antitumor drugs with high efficacy [1]. It is generally recognized that receptor tyrosine kinases are important protein signalling regulators for a variety of cellular activities, including those connected to cancer. Tyrosine kinase inhibitors (TKI) are currently widely used in the treatment of cancer

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