Synthesis of New Thiazole-Pyridine Hybrids and Their Anticancer Activity

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Abstract—A series of new thiazole incorporated pyridine derivatives containing the phenoxyacetamide moiety as a linking bridge has been synthesized. The synthetic strategy involves condensation of 2-(4-formylphenoxy)-*N*-(thiazol-2-yl)acetamide with cyanoacetic hydrazide followed by heterocyclization with acetylacetone, treatment of the produced acrylamides with malononitrile and substituted acetophenones, then heating the generated chalcones with mononitrile in acetic acid and ammonium acetate. In vitro anticancer activity of the newly synthesized thiazole-pyridine hybrids has been evaluated against prostate (PC3), liver (HepG2), laryngeal (Hep-2), and breast (MCF-7) cancer cell lines. One of thiazole-pyridine compounds **8c** demonstrates higher activity (IC_{50} 5.71 μM) against breast cancer than 5-fluorouracil used as a reference (IC_{50} 6.14 μM). Molecular docking procedure has provided valuable information on the binding sites of the synthesized compounds with rho-associated protein kinase 1 (ROCK-1).

Keywords: thiazole, 2-cyanoacetanilide, malononitrile, pyridone, cytotoxicity, molecular docking

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