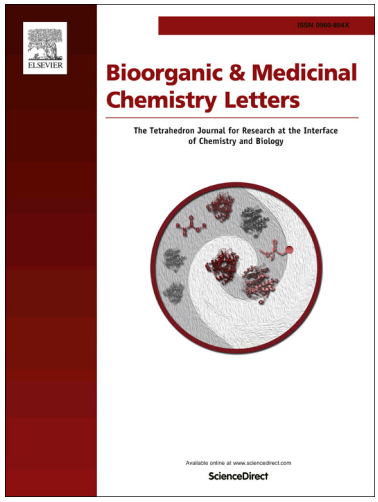

Design and synthesis of novel 1,2,3-triazole-pyrimidine-urea hybrids as potential anticancer agents

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Abstract: A series of novel 1,2,3-triazole-pyrimidine-urea hybrids were designed, synthesized and evaluated for anticancer activity against four selected cancer cell lines(MGC-803, EC-109, MCF-7 and B16-F10). Majority of the synthesized compounds exhibited moderate to potent activity against all the cancer cell lines assayed. Particularly, compounds **26**, **30** and **38** exhibited excellent growth inhibition against B16-F10 with IC_{50} values of 32nM、35nM and 42nM, respectively. Flow cytometry analysis demonstrated that compound **26** induced the cellular apoptosis in a concentration-dependent manner.

Keywords: Pyrimidine; urea; triazole; anticancer; apoptosis.

Cancer, being one of the leading causes of death globally, poses a major socioeconomic hazard to humanity at large. Although there have been progresses in the development of treatment and prevention of cancer, the successful treatment of cancer remains a challenge. Still, there is a need to search for newer and safer anticancer agents that have excellent cytotoxicity to cancer cells.[1] Molecular hybridization which covalently combines two or more drug pharmacophores into a single molecule is an effective tool to design highly active novel entities.[2, 3] In particular, the hybrids may also minimize unwanted side effects and allow for synergic action.[4]

The pyrimidine skeleton is a constituent of a large number of biologically active compounds represents a class of heterocyclic compounds with significant pharmacological efficiency, including anti-viral, anti-HIV, anti-bacterial, especially anticancer.[5-20] For example, Hoff et al. reported that thienopyrimidine (**Fig. 1A**) was identified as a novel and proprietary small molecule scaffold for potential antitumor agents as EGFR inhibitor.[21] On the other hand, urea-based compounds are considered privileged scaffolds in drug discovery with a wide array of biological activities. In particular, their applications in the treatment of cancer have been explored.[22-25]

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