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Extended Abstract

Novel Dipyridothiazines with 1,2,3-Triazole Substituents—Synthesis and Anticancer Activities †

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Cancer has now become a global problem and been ranked as the top leading cause of death worldwide after cardiovascular disease, tuberculosis, and malaria combined. Chemotherapy has still been improved in cancer therapy, and the survival has been greatly increased, but there is need to discover and develop new, more potent antitumor agents with better selectivity and reduced side effects. In recent years, a lot of effort has been applied to the synthesis of potential anticancer drugs with better selectivity and minor or no side effects [1]. Phenothiazines are an important class of heterocyclic compounds with a wide spectrum of biological properties. Recent reports have shown promising anticancer, antiplasmid, antibacterial, anti-inflammatory, and immunosuppressive activities of classical and new phenothiazines [2]. Previously synthesized dipyridothiazine derivatives (1,6-, 1,8-, 2,7-, and 3,6-diazaphenothiazines) were shown to possess interesting antiproliferative, anticancer, antioxidant, and immunosuppressive activity [2–4]. In continuation of our search, we obtained new derivatives of dipyridothiazines with various 1,2,3-triazole substituents in the "click chemistry" 1,3-dipolar cycloaddition. For those compounds, the anticancer action on selected tumor lines (SNB-19, Caco-2, A549, MDA-MB231) was investigated. The compounds exhibited differential inhibitory activities, but some compounds were more active (IC_{50} = 0.02 μg/mL) than reference compound cisplatin. For the most active compounds, the expression of *H3*, *TP53*, *CDKN1A*, *BCL-2*, and *BAX* genes was detected using the RT-QPCR method.

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