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Design, synthesis, biological assessment and molecular docking studies of new 2-aminoimidazole-quinoxaline hybrids as potential anticancer agents

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Abstract

In a search for novel antiproliferative agents, a series of quinoxaline derivatives containing 2-aminoimidazole (**8a-8x**) were designed and synthesized. The structures of synthesized compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR, Mass Spectroscopy and analyzed using HSQC, COSY, ROESY, HMBC techniques. The anticancer activity of all derivatives were evaluated for colon cancer and breast cancer cell lines by the MTT assay and acridine orange/ethidium bromide double staining method. The anti-cancer effect in human colon cancer (HCT-116) and breast cancer (MCF-7) cell lines exhibited that compounds **8a**, **8s**, **8t**, **8w**, **8x** appeared as potent antiproliferative agents and especially inhibited the human colon cancer cell proliferation with percentage of inhibition by over 50%. The most active compound was (*E*)-4-phenyl-1-((quinoxalin-2-ylmethylene)amino)-1H-imidazol-2-amine (**8a**) with the highest inhibition for MCF-7 (83.3%) and HCT-116 (70%) cell lines after 48 and 24 hours, respectively. Molecular docking studies of these derivatives within c-kit active site as a validated target might be suggested them as appropriate candidates for further efforts toward more potent anticancer compounds.

Keywords

Quinoxaline; 2-Aminoimidazole; Molecular modeling; Antiproliferative agent; 2D NMR

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