البحث الثامن
رقم البحث فى قائمة الابحاث الكلية (30)

عنوان البحث باللغة الإنجليزية:

Title:

Synthesis of Bis-Pyrimidothiazine and Bis-Pyrimidothiadiazinone Derivatives as VEGFR2/KDR Inhibitors via Michael and Mannich Reactions

اسم المجلة المنشور بها البحث وسنة النشر

Molecular Structure, 1344 ,2025, 142968

Abstract:

In this study, a simple and readily available bifunctional compound, terephthalaldehyde, was employed to synthesize the bis-pyrimidinthione derivative **4**. The thiocarbonyl group and adjacent NH functionalities underwent Michael-type additions with activated unsaturated compounds—namely arylidenemalonitrile and DMAD—yielding bis-thiazine derivatives **6a–f** and bis-thiazole **8**, respectively. Additionally, reaction of derivative **4** with various aromatic amines and formaldehyde under Mannich conditions afforded bis-thiadiazines **10**. All synthesized compounds were characterized using NMR and MS techniques. Molecular docking studies targeting the VEGFR2/KDR receptor (PDB ID: 3CPC) revealed high binding affinity, particularly for compound **10i**. ADMET analysis further indicated favorable drug-like properties for selected compounds. In vitro cytotoxicity against the MCF-7 human breast cancer cell line showed that compound **10i** had the strongest activity (IC_{50} = 2.60 ± 1.41 μM), followed by **10g** (3.75 ± 2.52 μM) and **6f** (3.97 ± 1.85 μM), all comparable to or exceeding the activity of

sorafenib (3.51 ± 1.43 μM). VEGFR-2 enzyme inhibition assays for compounds **10g** and **10i** yielded IC_{50} values of 8.06 ± 3.32 μM and 5.15 ± 2.89 μM, respectively, relative to sorafenib (3.12 ± 1.79 μM). These findings position compound **10i** as a promising candidate for VEGFR-2-targeted anticancer therapy.

اسماء المشاركون:

Mohamed G. Badrey , Magdi E. A. Zaki, Basant Farag , Sobhi M. Gomha