In Silico Study of 1,2,4-Triazole Derivatives as Anti-Metastatic Candidates for Lung Cancer

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ABSTRACT

Lung cancer causes the highest mortality in the world, which is dominated by lung cancer metastases to other tissues. Lung cancer metastasis is related to the chemokine CXCR4/CXCL12 axis. This axis is a potential target for discovering new anti-metastatic drugs for lung cancer. Anti-proliferative efficacy of 1,2,4-triazole derivatives in lung cancer has been reported. These molecules were discovered to have anti-metastatic effects in pancreatic cancer. Therefore, 1,2,4-triazole derivatives can be promising compounds to be developed as novel anti-metastatic lung cancer. In the present study, 79 of 1,2,4-triazole derivatives were investigated. Ligand-based pharmacophore modeling was carried out with LigandScout Essential 4.4.9. and molecular docking study was performed using AutoDock 4.2.6. There are 16 derivatives conform to the pharmacophore model with CXCR4 and CXCL12 targets, including D41, D42, D43, D44, D45, D46, D47, D48, D49, D50, D51, D53, D54, D55, D56, and D57. Molecular docking studies of these compounds against CXCR4 and CXCL12 targets yielded two compounds that had better affinity than the reference compounds mavorixafor (CXCR4 inhibitor) and LIT-927 (CXCL12 inhibitor). These compounds are D54 (*2-((5-Amino-1-((2-chlorophenyl)sulfonyl)-1H-1,2,4-triazol-3-yl)thio)-6-isopropyl-4,4-dimethyl-3,4-dihydronaphthalen-1(2H)-one*) and D57 (*2-((5-amino-1-((4-bitriphenyl)sulfonyl)-1h-1,2,4-triazol-3-yl)thio)-6-isopropyl-4,4-dimethyl-3,4-dihydronaphthalen-1(2H)-one*).

Keywords: 1,2,4-triazole, anti-metastatic, CXCR4, CXCL12, lung cancer