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Searching for Novel Scaffolds of Triazole Non-Nucleoside Inhibitors of HIV-1 Reverse Transcriptase

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Abstract : Azoles are a promising class of the new generation of HIV-1 nonnucleoside reverse transcriptase inhibitors (NNRTIs). From thousands of reported compounds, many possess the same basic structure of an aryl substituted azole ring linked by a thioglycolamide chain with another aromatic ring. To find novel extensions for this primary scaffold, we explored the 5-position substitution of triazole NNRTIs using molecular docking followed by synthesis of selected compounds. We discovered that heterocyclic substituents in 5-position of the triazole ring are detrimental to the inhibitory activity of compounds with 4-membered thioglycolamide linker. This substitution seems to be viable only for compounds with a shorter 2-membered linker such as in derivatives of 4-benzyl-3-(benzyl-sulfanyl)-5-(thiophen-2-yl)-4H-1,2,4-triazole reported earlier. A new scaffold of 2-[(4-benzyl-5-methyl-4H-1,2,4-triazol-3-yl)sulfanyl]-N-phenylacetamide has been identified in this study.

Keywords : docking, molecular modeling, drug design, novel scaffolds
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