Biological activity, Molecular Docking Studies and Molecular Dynamics Simulations of 2,3,4,5-Tetrahydro-1\(H\)-pyrido[4,3-b] indoles as c-Met inhibitors

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SUMMARY. c-Met has been deregulated in many cancers and become one of the leading molecular targets in cancer. In our previous research, we designed and synthesized six novel 2,3,4,5-tetrahydro-1\(H\)-pyrido[4,3-b] indoles as c-Met inhibitors. In this study, we evaluated their biological activity at cellular and molecular level. The results showed that the majority of the compounds exhibited significant inhibitory effect on c-Met with IC\(_{50}\) values of 0.0145-0.5 \(\mu\)M in TR-FRET-based assay and IC\(_{50}\) values of 1.34-34 \(\mu\)M in cell-based assay. Furthermore, our docking experiments analyzed the results and explained the molecular mechanism of eminent activities to c-Met; and molecular dynamics simulations method was then applied to perform further evaluation of the binding stabilities between the compounds 4\(a\), 5\(a\) and their receptor 3dkf.

KEYWORDS: biological activity, c-Met inhibitors, molecular docking, molecular dynamics simulations, molecular mechanism, 2,3,4,5-tetrahydro-1\(H\)-pyrido[4,3-b] indoles.

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