Discovery of a more potent anticancer agent than C4-benzazole 1,8-naphthalimide derivatives against murine melanoma
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Abstract

Three novel naphthalimide-based derivatives were synthesized and tested in vitro as anti-cancer agents. Our previous report of the C4-benzazole 1,8-naphthalimide derivatives showed good inhibition against murine melanoma. We aimed to synthesize more potent agents and found that compound 5 reported in this article behaved 5- to 10-fold potency than our previous best results. The unique compound 5 consisted of a naphthalimide framework in which C4 position was linked with an ethylenediamine group where the amino group was coupled with a 2-piconic acid moiety. Compound 5 exhibited not only the lowest IC50 value, 2.6 ± 0.1, against murine B16F10 melanoma cells, but also the most potent inhibitory activity toward human DNA topoisomerase II proteins among the three compounds synthesized in this study. In accordance with this finding, the results of molecular docking also revealed that compound 5 has the highest affinity with human DNA topoisomerase II among the selected compounds. Compound 5, therefore, has high potential for becoming a lead compound.

Keyword: B16F10 cells; Melanoma; Naphthalimide; Topoisomerase II; WST assay