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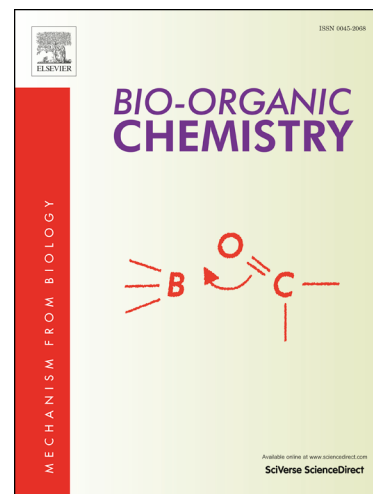
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Synthesis of Imidazo-thiadiazole linked Indolinone Conjugates and evaluated their Microtubule network disrupting and Apoptosis Inducing ability

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Abstract

A series of imidazo[2,1-*b*][1,3,4]thiadiazole linked indolinone conjugates were synthesized and investigated for antiproliferative activity in different human cancer cell lines by changing various substitutions at indolinone and phenyl ring systems. Among them conjugates **7**, **14** and **15** were exhibited potent antiproliferative activity with GI₅₀ values from 0.13-3.8 μ M and evaluated for cell cycle analysis, tubulin polymerization assay and apoptosis. Treatment with **7**, **14** and **15** were resulted in accumulation of cells in G2/M phase, inhibition of tubulin assembly, disruption of microtubule network. Inhibition of tubulin polymerization was further supported by Western blot analysis. In addition, the conjugates (**7**, **14** and **15**) also showed apoptosis in HeLa cell line, detailed biological studies such as Hoechst 33258 staining, DNA fragmentation and caspase-3 assays suggested that these compounds induce cell death by apoptosis. Docking studies revealed that these compounds (**7**, **14** and **15**) bind with α Asn101, α Thr179, α Ser178, β Cys241, β Lys254 and β Lys352 in the colchicine-binding site of the tubulin.

Keywords: Imidazothiadiazoles, cell cycle, cytotoxicity, tubulin polymerization, apoptosis.

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