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Design, synthesis and biological evaluation of a novel library of antimitotic C_2-aroyl/arylimino tryptamine derivatives that are also potent inhibitors of indoleamine-2, 3-dioxygenase (IDO)

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Abstract

A novel library of C_2-substituted tryptamines (based on diverse C_2-aroyl/arylimino indoles and indole-diketopiperazine hybrids) possessing antimitotic properties were designed, synthesized and screened for their inhibitory activity against tubulin polymerization, and against proliferation of A549 lung cancer, HeLa cervical cancer, MCF7 breast cancer and HePG2 liver cancer cell lines. The design of molecules were inspired from known antimitotic compounds and natural products. The molecular docking of the designed compounds indicated that they bind to the colchicin binding site of tubulin. They were synthesized by a unique iodine catalysed oxidative ring opening reaction of 1-aryltetrahydro-β-carbolines. Among the compounds synthesized quite a few compounds induced cytotoxicity on the cancer cells by disrupting the tubulin polymerization. They were found to be non-toxic for healthy cells. Immuno Fluorescence study for the most active molecules (between ~6 μM concentration) against A549 and HeLa cells demonstrated complete disruption and shrinkage of the