

Newly Designed and Synthesized Curcumin Analogs with *in vitro* Cytotoxicity and Tubulin Polymerization Activity

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Abstract

Novel curcumin analogs with 4-piperidone ring were designed, synthesized, and evaluated for their cytotoxic activities against five different cancer cell lines. 3,5-bis(4-Hydroxy-3-methoxybenzylidene)-4-oxo-N-phenylpiperidine-1-carbothioamide (XIIe) exhibited considerable cytotoxic activity with IC₅₀ values in 1–2.5 μm range. *In silico* and *in vitro*, studies were also performed to predict the binding affinity of the target compounds to the β-chain of tubulin receptor (PDB code 1SA1) and their abilities to affect microtubules polymerization cycle. 3,5-bis(3-Iodo-5-methoxy-4-propoxybenzylidene)-N-acetylpiperidin-4-one (VIIa) was found to exert 93.3% inhibition of tubulin and destabilization of microtubules *in vitro* compared to vincristine while, 3,5-bis(3,4,5-trimethoxybenzylidene)-N-benzoylpiperidin-4-one (XIIc) showed high potency in a different way where it exerted 94.8% stabilization of microtubules *in vitro* compared to positive control paclitaxel.

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