Newly Designed and Synthesized Curcumin Analogs with in vitro Cytotoxicity and Tubulin Polymerization Activity Iten M. Fawzy, Khairia M. Youssef, Nasser S.M. Ismail, J.Gulbo, Khaled A.M. Abouzid

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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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