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Epothilone B and D Arrest Cell Growth via Inhibition of NF-κB Signaling Pathway in SW620 Human Colon Cancer Cell

Seung Ho Lee, Dong Ju Son, Mi Hee Park, Sukgil Song, Hwan Soo Yoo, Ki Wan Oh, Jae Chul Jung*, Mitchell A. Avery* and Jin Tae Hong

*College of Pharmacy, Chungbuk National University, Cheongju, Korea. *School of Pharmacy, University of Mississippi, Mississippi, USA.*

Epothilones are novel nontaxane microtubule-stabilizing agents with proven efficacy in various cancer cells. Similar to paclitacel (taxol), epothilones bind to β-tubulin in the microtubule polymer, and stabilize microtubules promoting cancer cell growth arrest. Activation of the NF-κB transcription factor has influenced to the microtubule network. Taxol has been known to block phorbol ester (TPA)-induced NF-κB activation in its action on cancer cell growth arrest. However, it has not been apparent whether epothilones blocks NF-κB activation. In this study, we therefore explored the mechanisms underlying epothilone B and D (EpoB and D) mediated cell gowth inhibition, and this effect could be related with NF-κB activation in SW620 human colon cancer cells. Nanomolar concentration of epothilone B and D (100 nM) exerted cell cycle arrest at the G2-M transition in a time-dependent manner. Treatment of several concentrations (0.001-1000 nM) for various periods (0-72 hr) inhibited cell proliferation in a dose-, and time-dependent manner. Epothilone B was observed more potent effect than epothilone D in the inhibitory effect of cell proliferation. Pretreatment of epothilone B and D resulted in inhibition of TPA-induced NF-κB activation and reduced NF-κB dependent reporter gene activity. All of these results suggest that NF-κB signaling pathway may contribute to the inhibiting effect of epothilones on cell growth in SW620 human colon cancer.

Keyword: NF-κB, Epothilones, microtubule, cancer