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Krishan Parashar

Siddhartha Sood

Ali Mehaidli

Colin Curran

Caleb Vegh

See next page for additional authors

Authors
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Krishan Parashar [1], Siddhartha Sood [1], Ali Mehaidli [1], Colin Curran [1], Caleb Vegh[1], Christopher Nguyen [1], Christopher Pignanelli [1], Jianzhang Wu [2], Guang Liang [2], Yi Wang [2] and Siyaram Pandey [1]*

[1] Affiliation 1; Department of Chemistry and Biochemistry, University of Windsor, 401 Sunset Avenue, Windsor, Ontario, N9B 3P4, Canada.
[2] Affiliation 2; Chemical Biology Research Center, School of Pharmaceutical Sciences, Whenzhou Medical University, University Town, Chashan, Wenzhou, Zhejiang, 325035, P.R. China.
* Correspondence: spandey@uwindsor.ca; Tel.: 519-253-3000 Ext. 3701

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Abstract: Melanoma is the leading cause of skin-cancer related deaths in North America. Metastatic melanoma is difficult to treat and chemotherapies have limited success. Furthermore, chemotherapies lead to toxic side effects due to nonselective targeting of normal cells. Curcumin is a natural product of *Curcuma longa* (turmeric) and has been shown to possess anti-cancer activity. However, due to its poor bioavailability and stability, natural curcumin is not an effective cancer treatment. We tested synthetic analogs of curcumin that are more stable. One of these derivatives, Compound A, has shown significant anti-cancer efficacy in colon, leukemia, and triple-negative inflammatory breast cancer cells. However, the effects of Compound A against melanoma cells have not been studied before. In this study, for the first time, we demonstrated the efficacy of Compound A for the selective induction of apoptosis in melanoma cells and its interaction with tamoxifen, taxol, and cisplatin. We found that Compound A induced apoptosis selectively in human melanoma cells by increasing oxidative stress. The anti-cancer activity of Compound A was enhanced when combined with tamoxifen and the combination treatment did not result in significant toxicity to noncancerous cells. Additionally, Compound A did not interact negatively with the anti-cancer activity of taxol and cisplatin. These results indicate that Compound A could be developed as a selective and effective melanoma treatment either alone or in combination with other non-toxic agents like tamoxifen.

Keywords: melanoma; curcumin analog; apoptosis; oxidative stress; drug–drug interaction; tamoxifen; taxol; cisplatin