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Cupressus sempervirens extract inhibited human basal cell carcinoma tumorigenesis, local invasion and angiogenic property

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Background: Basal cell carcinoma (BCC), a non-invasive and rarely metastatic tumor, with clinical and histological involvement of basal epithelial cells occurr due to dysregulation of hedgehog-patched1 signaling pathway.

Objective: The current study was conducted to evaluate the *in vitro* cytotoxic effects of *Cupressus sempervirens* methanolic extract against primary basal cell carcinoma cells, over a period of 48 hours.

Methods: We measured the increased levels of Annexin-V as well as lactate dehydrogenase leakage in cells being-exposed to 420 μM extract. In addition to transcript levels of *PTCH-1* of hedgehog-patched1 signaling pathway, angiogenic activity of vascular endothelial growth factor and angiopoietin-2 and metastatic levels of matrix metalloproteinase 2 and 9.

Results: The cytotoxicity test results showed that BCC cells survival decreased dose-dependently through 48 hours. The expression of Annexin-V was induced ($p<0.05$) in treated cells which coincided with raised levels of lactate dehydrogenase leakage in supernatant media ($p<0.05$). Noticeably, the expression of *PTCH-1*, vascular endothelial growth factor, angiopoietin-2 and matrix metalloproteinase 2 and 9 were robustly decreased. Interestingly, six-month clinical trial follow-up of *Cupressus sempervirens* extract 5% ointment showed antitumor activity against cutaneous basal cell carcinoma by the reduction of tumor and inflammatory cells replaced with development of fibrotic stroma.

Conclusions: The data of present experiment may suggest that the methanolic extracts of *Cupressus sempervirens* possess oncostatic and cytotoxic properties, and therefore, can be prescribed as natural protective and therapeutic ingredients for basal cell associated cutaneous tumor.

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