Effect of Curcumin in Comparison With Trichostatin A on the Reactivation of Estrogen Receptor Alpha Gene Expression, Cell Growth Inhibition and Apoptosis Induction in Hepatocellular Carcinoma Hepa 1-6 Cell lLine

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Abstract

Background: A multistep process with an accumulation of epigenetic alterations of tumor suppressor genes (TSGs) can induce cancer. Abnormal regional hypermethylation and histone deacetylation of several TSGs has been observed in hepatocellular carcinoma (HCC). Acetylation and deacetylation of histone are carried out by histone acetyltransferase (HAT) and histone deacetylase (HDAC) respectively. Besides, DNA methylation is carried out by DNA methyltransferases (DNMTs). Previously, we evaluated the effect of DNA demethylating agents and histone deacetylase inhibitors on HCC and colon cancer. This study aimed to evaluate the effect of curcumin (CUR) in comparison with trichostatin A (TSA) on estrogen receptor alpha (ERα) reactivation, apoptotic induction, and cell growth inhibition in HCC.

Methods: the cells were cultured and treated with various concentrations of CUR and TSA and the MTT assay, flow cytometry assay and Real-Time RT-PCR were achieved to determine cell viability, cell apoptosis, and ERα gene expression respectively.

Results: CUR indicated dose and time-dependent antiproliferative effects ($P < 0.035$). A similar antiproliferative effect was observed by TSA ($P < 0.001$). Both compounds indicated significant apoptotic effects in all different periods ($P < 0.001$), CUR indicated a more significant apoptotic effect than TSA ($P < 0.001$). The ERα gene expression quantity was increased significantly by treatment with CUR and TSA ($P <0.012$).

Conclusion: CUR and TSA play important roles in restoring the ERα resulting in cell growth inhibition and apoptosis induction. Therefore, ERα may be a potential target for therapeutic intervention in the treatment of HCC.

Keywords: Estrogen receptor alpha; Hepatocellular carcinoma; Trichostatin A; curcumin.