

# **Effect of Zebularine in Comparison to Trichostatin A on the Intrinsic and Extrinsic Apoptotic Pathway, Cell Viability, and Apoptosis in Hepatocellular Carcinoma SK-Hep 1, Human Colorectal Cancer SW620, and Human Pancreatic Cancer PaCa-44 Cell Lines**

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## **Abstract:**

Aberrant histone modifications or promoter region hypermethylation of tumor suppressor genes (TSGs) have been recognized as the important epigenetic molecular mechanism in cancer induction. The potential anticancer activities of histone deacetylase inhibitors (HDACIs) and DNA methyltransferase inhibitors (DNMTIs) have been investigated in recent years. The current study was assigned to investigate the effect of trichostatin A (HDACI) in comparison to zebularine (DNMTI) on the intrinsic pro-apoptotic (Bax, Bim, and Bak) and anti-apoptotic (Bcl-2, Mcl-1, and Bcl-xL) genes and extrinsic (DR4, DR5, FAS, FAS-L, and TRAIL genes) pathways, DNA methyltransferase 1, 3a, and 3b, histone deacetylase inhibitors 1, 2, and 3, cell viability, and apoptosis in hepatocellular carcinoma (HCC) SK-Hep 1, colorectal cancer SW620, and pancreatic cancer PaCa-44 cell lines. The SK-Hep 1, SW620, and PaCa-44 cells were cultured and treated with TSA and zebularine. To determine cell apoptosis, cell viability, and the relative gene expression level, flow cytometry assay, MTT assay, and qRT-PCR were done respectively. The result indicated that zebularine and TSA changed the expression level of the Bax, Bak, Bim Bcl-2, Bcl-xL, Mcl-1, DR4, DR5, FAS, FAS-L, TRAIL, DNA methyltransferase 1, 3a, and 3b, histone deacetylase inhibitors 1, 2, and 3 by which induced cell apoptosis and inhibit cell growth in all three cell lines. Concluding, TSA induced its role through both extrinsic and intrinsic apoptotic pathways in three cell lines, whereas, zebularine played its role via both pathways in the SK-Hep 1 cell line, it had no significant effect on Bcl-2, Bcl-xL, and Mcl-1 gene expression in SW620 and PaCa-44 cell lines.

**Keywords:** Zebularine, Trichostatin A, Extrinsic, Intrinsic, Pathway