Effect of 5'-fluoro-2'-deoxycytidine and sodium butyrate on the gene expression of the intrinsic apoptotic pathway, p21, p27, and p53 genes expression, cell viability, and apoptosis in human hepatocellular carcinoma cell lines

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Abstract

Background: Epigenetic mechanisms play an important role in the regulation of gene expression and genetic information. DNA methyltransferases are a family of enzymes that methylate DNA at the promoter region of the gene which can significantly contribute to gene silencing and carcinogenesis. In addition, histone deacetylation leads to gene silencing and tumorigenesis. Our previous work indicated that histone deacetylase (HDAC) inhibitors can induce its apoptotic role through down-regulation of HDACs. This study aimed to investigate the effect of 5'-fluoro-2'-deoxycytidine (FdCyd) and sodium butyrate on the genes of intrinsic apoptotic pathway (BAX, BAK and APAF1, Bcl-2, and Bcl-xL), p21, p27, and p53 gene expression, cell viability, and apoptosis in human hepatocellular carcinoma Hep3B, SMMC-7721, and HA22T/VGH cell lines

Materials and Methods: The Hep3B, SMMC-7721, and HA22T/VGH cells were cultured and treated with FdCyd and sodium butyrate. To determine cell viability, cell apoptosis, and the relative gene expression level, MTT assay, flow cytometry assay, and quantitative real-time polymerase chain reaction were done, respectively.

Results: Both compounds induced significant cell growth inhibition and cell apoptosis significantly ($P < 0.0001$). Sodium butyrate up-regulated the BAX, BAK, APAF1, p21, p27, and p53 and down-regulated Bcl-2, and Bcl-xL significantly in all three cell lines. Similar results were observed in the Hep3B, and SMMC-7721 cell lines treated with FdCyd. It has no significant effect on p53 gene expression in HA22T/VGH. The expression of the other genes in this cell line was similar to other cell lines.

Conclusion: Both compounds induced their roles through the intrinsic apoptotic pathway to induce cell apoptosis.

Keywords: *Acetylation, carcinoma, hepatocellular, methylation*