Genistein and Trichostatin A Induction of Estrogen Receptor Alpha Gene Expression, Apoptosis and Cell Growth Inhibition in Hepatocellular Carcinoma HepG 2 Cells

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Abstract

Epigenetic changes such as DNA methylation and histone acetylation play important roles in determining gene expression. Hypermethylation of CpG islands of the promoter region of tumor suppressor genes can greatly influence carcinogenesis through transcriptional silencing. Acetylation of lysine in histone tails causes relaxation of chromatin, which facilitates gene transcription, while deacetylation is associated with condensed chromatin resulting in gene silencing. DNA demethylating agents such as genistein (GE) and histone deacetylase inhibitors (HDACIs) such as trichostatin A (TSA) may strongly reactivate silenced genes and exposure to these two agents in combination is reported to enhance estrogen receptor alpha (ERα) reactivation and induction of apoptosis. The present study was designed to evaluate the effect of these compounds on ERα gene expression, cell viability and apoptosis in hepatocellular carcinoma (HCC) Hep G2 cells. GE exerted biphasic effects; it stimulated cell growth at a low concentration (1 μM) but inhibitory influence was noted with high concentrations (10, 20 and 40 μM). In contrast, TSA demonstrated inhibitory effects on growth at all of concentrations tested. Furthermore, GE and GE/TSA significantly induced apoptosis at all concentrations, but TSA only after 72 h. GE induced ERα re-expression and this was maximal in combined treatment groups treated with GE/TSA for 72 h.

DISCUSSION:

Our finding clearly indicates that GE and TSA have an inhibitory cell growth, induce apoptosis and reactivate the ERα gene expression.

CONCLUSION:

GE and TSA can significantly inhibit the growth of HCC cells and play a significant role in apoptosis and reactivation of ERα gene.

KEYWORDS:

Genistein; trichostatin A; hepatocellular carcinoma