Resveratrol inhibits genistein-induced multi-drug resistance protein 2 (MRP2) expression in HepG2 cells.

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Source

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Abstract

The interactions between various dietary cancer chemopreventive phytochemicals in drug transporter functions are not well studied. In this study, the effects of genistein and resveratrol on the multidrug resistance protein 2 (MRP2) expression and the underlying molecular mechanisms were investigated using HepG2-C3 cells that are stably transfected with a construct containing human MRP2 promoter region conjugated with luciferase reporter gene. A 3-fold induction of MRP2 luciferase activity was observed after genistein (50μM) treatment to HepG2-C3 cells, but was diminished by the resveratrol (50μM) cotreatment. This observation was further validated by Western blot analysis and RT-PCR analysis as resveratrol also inhibited genistein-induced MRP2 protein synthesis and mRNA expression. Immunofluorescence study revealed that genistein-induced formation of MRP2 vacuoles was dramatically reduced by resveratrol. The binding affinity between retinoid X receptor alpha (RXRα) and MRP2 promoter was examined by DNA-protein pull-down assay. The results showed that resveratrol inhibited the genistein-induced binding of RXRα to the promoter sequence of MRP2 gene, and this mechanism could potentially contribute to the inhibition of genistein-induced MRP2 expression by resveratrol. Taken together, our present study suggests that naturally occurring phytochemicals can potentially interfere with
each other's regulatory function on the cancer chemoprevention-related genes through a competitive mechanism.

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