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Induction of Phase 2 Detoxifying Enzymes by Dehydroglyasperin C Isolated from Licorice

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Objectives

This study has been performed to confirm the potential of dehydroglyasperin C isolated from licorice to induce phase 2 detoxifying (antioxidant) enzymes using cultured cell and mouse model systems.

Materials and Methods

Materials

Dehydroglyasperin C was purified from licorice by bioassay-guided fractionation and its structure was identified by NMR (Lim, Soon Sung from Hallym University). Mouse hepatoma cells hepa1c1c7 and its mutant cell line BPRc1, and HepG2-C8, which is a human hepatoma transfectant carrying vector constructed with antioxidant response element (ARE) linked to reporter gene (luciferase), were used.

Methods

NAD(P)H:quinone oxidoreductase 1 (NQO1, QR) was assyed according to Benson's method using 2,6-dichlorophenolindophenol as a substrate (Benson et al., 1980). Intracellular level of QR, a anticarcinogenic marker enzyme, was measured by Western blot. Involvement of ARE in promoter regions of relevant genes in the induction of phase 2 detoxifying (antioxidant) enzymes was tested by assaying leciferase activity of cells before and after treatment of HepG2-C8 cells with dehydroglyasperin C at various levels. Nuclear translocation of Nrf2 by dehydroglyasperin C was also evaluated by immunocytochemistry using anti-Nrf2 antibody. The QR-inducing potential of dehydroglyasperin C in mouse was also evaluated by assaying QR activities in liver, kidney and large intestine collected from the animals injected with the compound three times for one week.

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Results

Dehydroglyasperin C caused a dose-dependent induction of QR enzyme activity in hepa1c1c7 mouse hepatoma cells and its mutant BPRc1 cells. The compound increased the luciferase activity of HepG2-C8 cells, transfectants carrying antioxidant response element (ARE)-luciferase gene, in a dose-dependent manner, suggesting ARE-mediated transcriptional activation of antioxidant enzymes. Dehydroglyasperin C also stimulated nuclear accumulation of Nrf2 as evaluated by immunocytochemistry. Furthermore, the compound resulted in a significant induction of QR activity of kidney large intestine in mice when injected at the dose of 5 mg/kg b.w. three times for one week, suggesting that dehydroglyasperin C might have the anticarcinogenic potential in whole body system.

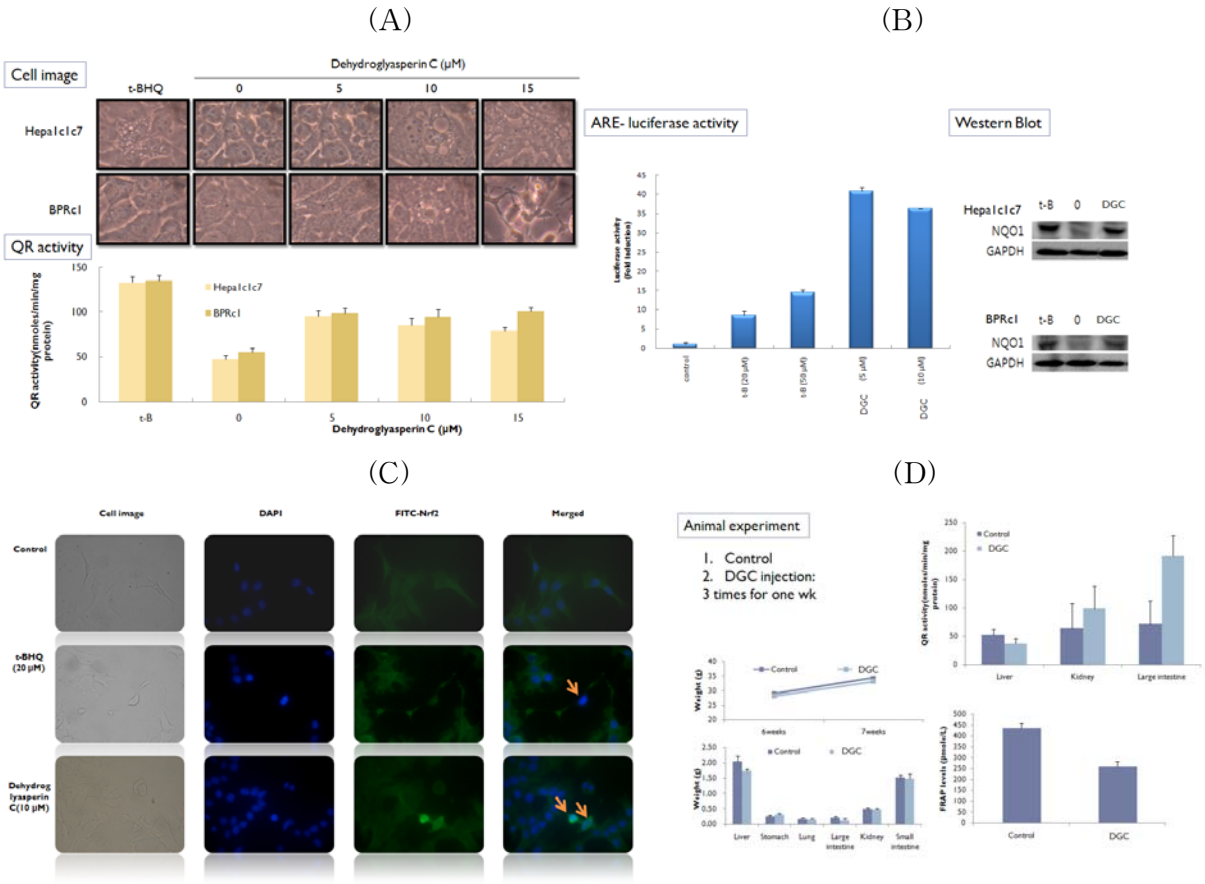

Figure 1. Induction of QR by dehydroglyasperin C(DGC) in mouse hepatoma cells (A, B) and organs from mice (D), and nuclear translocation of Nrf2 by DGC (C).