Induction of cytochrome P450 1A1 and 1B1 by emodin in human lung adenocarcinoma cell line CL5

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摘要

Abstract

Emodin (3-methyl-1,6,8-trihydroxyanthraquinone) is an active compound of many laxative herbal drugs. The present study aimed to determine the effects of emodin on cytochrome P450 (P450)-dependent monooxygenases of human lung adenocarcinoma CL5 cells. Treatment of CL5 cells with 100 microM emodin for 24 h induced benzo[a]pyrene hydroxylation, 7-ethoxyresorufin O-deethylation, and 7-ethoxycoumarin O-deethylation activities of S9 fractions. Immunoblot analysis of CL5 S9 proteins revealed that emodin induced proteins immunorelated to P450s 1A1 and 1B1. Northern blot analysis of total cellular RNA showed that emodin induced P450s 1A1 and 1B1 mRNA levels in CL5 cells. These inductive effects on P450 monooxygenase activity, protein, and mRNA were concentration- and time-dependent. Addition of emodin to CL5 cell microM S9 inhibited its 7-ethoxycoumarin O-deethylation activity. Treatment of CL5 cells with 10 microM 3-methylcholanthrene for 24 h induced monooxygenase activity and P450s 1A1 and 1B1 proteins and mRNA levels. Treatment of the lung cells with 100 microM emodin or purpurin (1,2,4-trihydroxyanthraquinone) for 24 h produced greater induction of P450s 1A1 and 1B1 mRNA than did anthraflavic acid (2,6-dihydroxyanthraquinone) or anthraquinone. The emodin treatment induced P450s 1A1 and 1B1 mRNA in human lung carcinoma NCI-H322 and breast cancer MCF-7 cells. Emodin induced P450 1A1, but not 1B1, mRNA in human hepatoma HepG2 cells. The present study demonstrates that emodin is an inducer of P450s 1A1 and 1B1 protein and mRNA in human lung adenocarcinoma CL5 cells. Modulation of P450 by emodin may be an important factor affecting metabolism and toxicity of the hydroxyanthraquinone in humans.