

Induction of NAD(P)H:quinone oxidoreductase 1 expression through the p38/Nrf2 signaling pathway by carnosic acid

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The anticarcinogenic effect of rosemary has been partly attributed to the modulation of the activity and expression of phase II detoxification enzymes. We compared the effects of phenolic diterpenes from rosemary on the expression of NAD(P)H:quinone oxidoreductase 1 (NQO1) in rat Clone 9 liver cells. Both CA and CS dose-dependently increased NQO1 enzyme activity, mRNA and protein expression, and the induction potency of CA was stronger than that of CS for 24 h. Furthermore, CA dose-dependently induced transcription of Nrf2 and antioxidant response element (ARE)-luciferase reporter activity. Moreover, the phosphorylation of p38 was mainly stimulated in the presence of CA. Pretreatment with SB203580 or silencing of Nrf2 or p38 expression alleviated the activation of NQO1 protein expression by CA. These results suggest that induction of NQO1 by CA involved the p38-Nrf2 pathway and help to clarify the possible molecular mechanism of action of rosemary in drug metabolism and cancer prevention.

Keywords: Carnosic acid, carnosol, NAD(P)H:quinone oxidoreductase 1, p38, Nrf2, rat Clone 9 liver cells