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Butylhydroxytoluene (BHT) increases susceptibility of transgenic rasH2 mice to lung carcinogenesis.

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PURPOSE: Transgenic mice carrying the human prototype c-Ha-ras gene (rasH2 mice) are highly susceptible to lung carcinogens. In order to investigate the possibility of developing a rapid in vivo assay for lung carcinogens, we examined whether the tumor-promoting activity of butylhydroxytoluene (BHT) is efficacious in rasH2 mice. METHODS: rasH2 mice and wild littermates of both genders were pre-treated with carcinogens [urethane (UR), 4-nitroquinoline 1-oxide (4NQO) or diethylnitrosamine (DEN)], and, one day later, given a 400 mg/kg dose of BHT. RESULTS: Six weeks after the initiation treatment, evidence of carcinogenicity could be detected in male and female rasH2 mice that had received UR doses of > or = 250 mg/kg and > or = 125 mg/kg, respectively, prior to exposure to BHT, whereas only 500 mg/kg of UR was sufficient to induce tumors in female rasH2 mice given the carcinogen alone. The carcinogenicity of 15 mg/kg of 4NQO could be detected after 9 weeks in male rasH2 mice given the carcinogen followed by BHT. Similarly, the carcinogenicity of 60 mg/kg of DEN could be detected after 9 weeks and 6 weeks, respectively, in male and female rasH2 mice given the carcinogen followed by BHT. No carcinogenicity could be demonstrated through the experimental period with doses of 4NQO or DEN given alone. CONCLUSIONS: These results indicate that BHT administration increases the susceptibility of rasH2 mice to lung carcinogens, and suggest that the use of BHT in rasH2 mice might lead to the establishment of a rapid in vivo assay for lung carcinogens.

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