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## MUTAGENICITY AND ANTIMUTAGENICITY OF CATECHIN AND TANNINS FROM THE BARK OF *HAMAMELIS VIRGINIANA* L. IN HUMAN Hep G2 CELLS

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The mutagenic and antimutagenic activities of catechin, hamamelitannin and two proanthocyanidin fractions prepared from the bark of *Hamamelis virginica* L. - a commonly used medicinal herb - were investigated in a human derived hepatoma (Hep G2) cell line using the single cell gel electrophoresis (SCGE, syn. Comet assay) for the detection of DNA-migration. The cells possess different phase I and phase II enzymes involved in the biotransformation of xenobiotics. As a measurement for DNA-migration caused by DNA single strand breaks we calculated the Olive tail moment (OTM).

Catechin and the proanthocyanidin fraction with lower molecular weight did not exhibit any increases of OTM in Hep G2 cells whereas hamamelitannin and the proanthocyanidin fraction with higher molecular weight caused slight and dose-independent, not significant increases of OTM at all concentrations tested (2, 6, 18  $\mu\text{g/ml}$ ). Treatment of the Hep G2 cells with low doses of catechin, hamamelitannin and the two proanthocyanidin fractions (2-18  $\mu\text{g/ml}$ ) prior to the exposure to benzo[a]pyrene (B(a)P) led to a reduction of chemically induced DNA migration which was dose-dependent for all test compounds except for hamamelitannin. The inhibitory effect of the proanthocyanidin fractions on OTM was stronger than that of catechin and hamamelitannin, the lowest effective concentration was about 2  $\mu\text{g/ml}$ . Measurements of activities of enzymes involved in the biotransformation of B(a)P showed that neither the inhibition of activation by cytochrome P450 dependent oxygenases (CYP1A1) nor the induction of detoxification by glutathion-S-transferases (GST)

were responsible for the antimutagenic properties of the *Hamamelis virginiana* fractions. Additional experiments were performed with the reactive metabolite of B(a)P, ( $\pm$ )-anti-benzo[a]-pyrene-7,8-dihydrodiol-9,10-epoxide (BPDE). Combination experiments with catechin, hamamelitannin and with the two proanthocyanidin fractions showed that the observed DNA-protective effects were probably caused by scavenging of the ultimate mutagen. Exposure of Hep G2 cells to the test compounds after B(a)P treatment did not influence the B(a)p induced mutagenicity, indicating that repair mechanisms were not affected by the flavanol catechin and the tannins. The studies were supported by the EC grant QLK1-CT-1999-0810