P-6

STUDIES ON THE ANTIMUTAGENICITY OF VITAMINS AND NAPHTHOFLAVONES TOWARDS HETEROCYCLIC AMINES

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Former studies dealing with combined effects caused by chemical compounds in the metabolically competent hepatoma cell line Hep G2 indicated that Hep G2 cells are useful and sensitive indicators for the identification of synergisms of promutagens, comutagens and antimutagens which are relevant in eukryontic (human) cells. In the present study we examined the modulation of DNA damages by the suspected antimutagens ascorbic acid, beta-carotene, alpha-naphthoflavone and beta-naphthoflavone in Hep G2 cells. Vitamins and flavonoids are present in dietary and medicinal plants in partly high concentrations. They have been reported to exhibit a wide variety of biological effects, including antimutagenicity and anticarcinogenicity. As biological endpoint we examined DNA single strand breaks using the single cel gel electrophoresis (SCGE, syn: Comet assay). For that Hep G2 cells were incubated with the suspected antimutagens prior to the application of well-known promutagens. As promutagens the heterocyclic amines 2-amino-1-methyl-6-phenylimidazol[4,5-b]pyridine (PhIP) and 2-amino-3-methylimidazol [4,5-f]quinoline (IQ) (cooked food mutagens) were used. As a parameter for mutagenicity we calculated the cumulative Olive Tail Moment (OTM_{cum}). In all experiments the pretreatment of PhIP and IQ exposed Hep G2 cells with ascorbic acid, beta-carotene, alpha- and beta-naphthoflavone over a period of 24 h led to significant and dose-dependent antimutagenic effects. Whereas the cumulative Olive tail moment (OTM_{cum}) of 100 IQ and PhIP treated Hep G2 cells which were pretreated only with dilution buffer or DMSO was about 1,100 the IQ and PhIP induced mutagenicity after pretreatment with ascorbic acid, beta-carotene, alpha- and beta-naphthoflavone

decreased to a minimum OTM_{cum} of 200 to 300 (OTM_{cum} of negative control: 180). As a result, Hep G2 cells were able to detect the antimutagenic potential of vitamins and naphthoflavones. With respect to former studies dealing with the identification of comutagenic and antimutagenic effects using Hep G2 cells and under consideration of the fact that the use of prokaryontic and animal models imply numerous questions and problems (application to human pathomechanisms, metabolism, ethical problems, finances) human, metabolically competent Hep G2 hepatoma cells seem to be a very useful instrument for the screening and detection of antimutagens and anticarcinogens significant in human nutrition. The studies were supported by the EC grant QLK1-CT-1999-0810