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[Lab. of Biochemistry]

Chemoprevention of 4-Nitroquinoline 1-Oxide-induced Oral Carcinogenesis in Rats by Flavonoids Diosmin and Hesperidin, Each Alone and in Combination.

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The modifying effects of the two flavonoids diosmin and hesperidin given during the initiation and postinitiation phases of oral carcinogenesis initiated with 4-nitroquinoline 1-oxide (4-NQO) were investigated in male F344 rats. The compounds were tested alone and in combination. Dietary administration of these compounds significantly decreased the expression of cell proliferation biomarkers (5-bromodeoxyuridine-labeling index and AgNORs) of the nonlesional tongue squamous epithelium, and caused a significant reduction in the frequency of the tongue carcinoma. These findings suggest that diosmin and hesperidin supplementation is effective in inhibiting the development of oral carcinogenesis initiated with 4-NQO.

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[Lab. of Biochemistry]

Involvement of Two Basic Residues (Lys-270 and Arg-276) of Human Liver 3 α -Hydroxysteroid Dehydrogenase in NADP(H) Binding and Activation by Sulphobromophthalein: Site-directed Mutagenesis and Kinetic Analysis.

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A human liver 3 α -hydroxysteroid dehydrogenase isoenzyme, a member of the aldo-keto reductase family, shows a marked preference for NADP(H) over NAD(H), and is activated by sulphobromophthalein. The mutated enzymes, K270M and R276M, showed increases in the K_m for NADP⁺ of 22- and 290-fold respectively, and attenuated activation by sulphobromophthalein. The results suggest that the two basic residues in the 3 α -hydroxysteroid dehydrogenase isoenzyme play crucial roles in binding both the negatively charged 2'-phosphate group of NADP⁺ and the sulphonic groups of sulphobromophthalein.

[*YAKUGAKU ZASSHI*, 117, 167-177 (1997)]

[Lab. of Biochemistry]

A Sensitive Fluorometric Assay for Dihydrodiol Dehydrogenase.

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Dihydrodiol dehydrogenase (DD) oxidizes naphthalene dihydrodiol to 1,2-dihydronaphthalene, which is immediately autoxidized to 1,2-naphthoquinone. Here we established a fluorometric assay for the enzyme, which is based on the conversion of 1,2-naphthoquinone to fluorescent compounds by reacting with ethylenediamine. The formed fluorescent compounds were synthetically identified as 6-(2-aminoethylamino)benzo[f]quinoxaline and 2,6- or 3,6-bis(2-aminoethylamino)benzo[f]quinoxaline, which showed the same fluorescence at 550 nm at an excitation wavelength of 420 nm. The method provides a 9000-fold increase in sensitivity over a currently available assay which measures the change in the absorbance of a cofactor, NADPH. Since this method allowed many samples to be assayed simultaneously, we applied it to the analysis of multiple forms of DD, separated by an anion-exchange chromatography, from six human liver specimens.

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[Lab. of Biochemistry]

Modulation of N-Methyl-N-amyl nitrosamine-Induced Rat Oesophageal Tumourigenesis by Dietary Feeding of Diosmin and Hesperidine, Both Alone and in Combination.

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The modifying effects of diosmin and hesperidin during the initiation and postinitiation phases of oesophageal carcinogenesis initiated with N-methyl-N-amyl nitrosamine (MNAN) were investigated in male Wistar rats. Feeding of these compounds significantly decreased the expression of cell proliferation biomarkers (BrdU-labelling index, AgNORs and polyamine levels). A number of oesophageal neoplasms developed in rats treated with MNAN alone, and feeding of both compounds caused a significant reduction in the multiplicity of oesophageal carcinoma and papilloma. These findings suggest that diosmin and hesperidin supplementation is effective in inhibiting the development of oesophageal cancer induced by MNAN.