[*Spectrochim. Acta*, **55A**, 2877-2882 (1999)] [Lab. of Instrumental Center]

Polymorphism of Phenylpyruvic Acid Studied by IR, Raman and Solid State ^{13}C NMR Spectroscopy.

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Polymorphs I and II of phenylpyruvic acid are obtained as mixtures of both crystal forms or relatively pure crystals from different solvents. Polymorph I is more stable than polymorph II at room temperature. Spectral characteristics of these polymorphs are discussed on the basis of IR, Raman and solid state ^{13}C NMR spectra. Also, the assignment of the IR features observed in the 1600-1700 cm^{-1} region is reinvestigated by referring to the spectra of the heavy-atom substituted derivatives. It is suggested that the C=O stretching band is split by the crystal field for both polymorphs.

[*Mutat. Res.*, **428**, 165-176 (1999)] [Lab. of Radiochemistry]

Effect of Cigarette Smoke on the Mutagenic Activation of Environmental Carcinogens by Rodent Liver.

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To assess the effect of cigarette smoke (CS) on metabolic enzymes, male hamsters and rats were exposed for two weeks to CS. Mutagenic activities of seven heterocyclic amines (HCAs) in strain TA98 with rat or hamster liver S9 were elevated up to 3.7 times above controls, whereas no significant alteration of mutagenicity was observed with 2-aminofluorene, benzo[*a*]pyrene, and 3'-hydroxymethyl-*N*,*N*-dimethyl-4-aminoazobenzene in TA98 or with six *N*-nitrosodialkylamines in TA100. 7,8-Benzoflavone and/or furafylline considerably inhibited the mutagenic activation of IQ and Trp-P-1 with liver S9 from hamsters and rats. Immunoblot analyses of liver microsomes using anti-rat CYP antibodies revealed that CS exposure increased the levels of hamster cytochrome P450 (CYP) 1A2 (3.9-fold) and rat CYP1A2 (3.0-fold) and CYP1A1. The present findings indicate that cigarette smoking in combination with intake of heating protein-rich foods as a life style may markedly contribute to the human carcinogenesis by HCAs.

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Increase of Urinary Extracellular-Superoxide Dismutase Level Correlated with Cyclic Adenosine Monophosphate.

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The urinary extracellular superoxide dismutase (EC-SOD) level was significantly correlated with the urinary excretion of N-acetyl β-D-glucosaminidase (NAG), but not with serum EC-SOD. EC-SOD appears not to be leaked from the plasma by glomerular filtration, but rather to be secreted from the renal tubule or its surrounding tissues. The urinary EC-SOD level was also significantly correlated with the urinary cyclic adenosine monophosphate (cAMP) level. cAMP analogues and adenylate cyclase modulators significantly stimulated the expression of EC-SOD but not other SOD isozymes in cultured fibroblast cell lines. Moreover, injection of parathyroid hormone, in Ellsworth-Howard tests, increased urinary EC-SOD accompanied with the elevations of urinary cAMP. Together these observations suggest that factor(s) stimulate the adenylate cyclase-cAMP system regulate the urinary EC-SOD level.

[*Cancer Lett.*, **135**, 113-119 (1999)] [Lab. of Clinical Pharmaceutics]

Enhancement of Glucuronosyl Etoposide Transport by Glutathione in Multidrug Resistance-Associated Protein-Overexpressing Cells.

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We found that glutathione (GSH) affects the transport of glucuronosyl etoposide as a major metabolite of etoposide in multidrug resistance-associated protein (MRP)-overexpressing KB/VP-4 cells. The relative resistance level of KB/VP-4 cells to etoposide was 70-fold that of wild-type KB cells. Membrane vesicles prepared from KB/VP-4 cells exhibited markedly enhaced ATP-dependent transport of glucuronosyl etoposide as well as LTC_4. Transport of glucuronosyl etoposide was augmented in the presence of GSH. Treatment of KB/VP-4 cells with buthionine sulfoximine (BSO), an inhibitor of GSH synthesis, resulted in about 75% depletion of cellular GSH levels, a four-fold increase of the sensitivity to etoposide and depression of glucuronosyl etoposide efflux. These results suggest that GSH plays a role in the enhancement of MRP-mediated glucuronosyl etoposide transport.