

DOCTORAL DISSERTATION ABSTRACTS

EFFECT OF ROUTE OF INPUT ON THE HEPATIC DISPOSITION KINETICS OF COMPOUNDS

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Most studies involving the perfused liver have been concerned with single input via the portal vein (PV): yet physiologically the liver receives a dual supply, PV and the hepatic artery (HA). In the present study, various aspects of the hepatic disposition were studied as a function of route of input. A suitable experimental model was developed wherein the liver of a male rat was perfused simultaneously via the HA and PV. The perfusion experiments were conducted using Krebs-bicarbonate based perfusion medium (37°C) delivered in a single-pass mode at a total flow rate of 15 ml min⁻¹ (HA: 3 ml min⁻¹ and PV: 12 ml min⁻¹). The specific water space associated with the HA was estimated using three different methods - desiccation, linear regression and transit time, whereas its flow was evaluated using the transit time method. The physiological aqueous spaces of the liver (intravascular IV, interstitial IS, and intracellular IC) were determined as a function of route of administration using non-labelled and radio-labelled markers, after bolus administration. Permeability characteristics of the liver were investigated in terms of red blood cell (RBC) and hepatocyte permeability. The effect of RBCs on the hepatic distribution was studied using labelled urea and thiourea in the single PV perfused liver preparation. The effect of hepatocyte permeability on the hepatic distribution kinetics of salicylic acid was explored in the dual perfused liver preparation. The differences in availability as a function of route of input was examined using diclofenac and diazepam at different albumin concentrations (0.25-1%). A model based on dispersion principles was developed to describe the temporal outflow profiles of reference markers and drugs. The model consisted of two-components (the common and specific arterial spaces) in parallel: outflow profiles following bolus administration into the PV was described by the single component model and assumed to represent the common space, whereas the two-parallel component model was applied to the arterial input data.

THE BIOMONITORING OF POLYCYCLIC AROMATIC HYDROCARBONS (PAH) EXPOSURE IN THE CHILD LABORERS

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Polycyclic Aromatic Hydrocarbons (PAH) are abundant in environment. Therefore PAH exposure is occurred in both environmental and occupational. Main PAH sources are diesel and oil engine exhaust which produce with petroleum combustion, tobacco smoke, reaction products occurred during electrode and graphite production, smoke caused by during cooking, coal tar occurred pyrolysis of coal. 61 diesel exposed workers were compared 30 unexposed controls with respect to some genotoxicity parameters. The mean value (\pm SE) of urinary 1-OH pyrene excretions of workers was 4.71 (\pm 0.53) μ mol/mol creatinine and also mean urinary 1-OH pyrene for controls was found to be as 1.55 \pm 0.28 μ mol/mol creatinine. The mean values (SE \pm) of Sister Chromatid Exchange (SCE) frequency in peripheral lymphocytes from the workers and controls were 4.47 (\pm 0.09) and 4.06 (\pm 0.16) respectively. The mean (Micronucleus; MN/cell) frequencies of MN in the exposed and control groups were found as 1.87 (\pm 0.04) and 1.56 (\pm 0.06) respectively. Significant effects of work related exposure were detected in the urinary 1-OH pyrene excretion SCEs and micronuclei analysed in peripheral blood lymphocytes ($p < 0.0001$; $p < 0.05$; $p < 0.0001$ respectively). The effect of smoking were also evaluated by the applied genotoxicity tests. In conclusion, our data suggested that PAH exposure was evident and this PAH exposure contributed to the observed genotoxic damage in workers.

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OXIDATIVE STRESS AND LIPID PEROXIDATION IN PATIENTS WITH DILATED CARDIOMYOPATHY

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Indicators of oxidative stress and lipid peroxidation in patients with dilated cardiomyopathy (7 women, 16 men) and 21 healthy normal control (9 women, 12 men) were studied in this investigation. Eleven patients (3 women, 8 men; aged 37-75 years) had dilated cardiomyopathy with coronary artery disease (CAD), remaining 12 patients (4 women, 8 men; aged 31-66) had nonischemic dilated cardiomyopathy. Serum/plasma, erythrocyte membranes, and packed erythrocytes were separated from the blood samples obtained from the patients before IV dobutamine administration. Albumin, bilirubin, uric acid, malondialdehyde (MDA) or thiobarbituric acid reactive substances (TBARS), fluorescent products of lipid peroxidation (FPL), total thiol (TSH), protein thiols (PSH) and glutathione (GSH) levels were analyzed in sera/plasma samples. In erythrocyte membranes TSH and FPL contents, and susceptibility to peroxidation of membranes were studied. Superoxide dismutase and GSH contents of packed erythrocytes and susceptibility of erythrocytes to peroxidation were measured. All the measurements were carried out in patient group after 48 hours-dobutamine administration and in control group. There was no statistically significant difference for these parameters between ischemic and nonischemic patients groups, and between the values obtained before and after dobutamine administration ($P>0.05$). Albumin, TSH, PSH and GSH levels of patient group were lower than control group, but TBARS, uric acid and FPL levels were higher, significantly ($P<0.05$). TSH levels were lower but FPL and susceptibility to peroxidation values were higher in erythrocyte membranes of patient group ($P<0.05$). SOD and GSH content of erythrocytes from patients was lower than controls, but susceptibility to peroxidation was higher ($P<0.05$). In conclusion, patients with dilated cardiomyopathy, whether ischemic or nonischemic, are suffered from increased oxidative stress and lipid peroxidation. This may explain increased fatal arrhythmias and sudden death incidence in patients with dilated cardiomyopathy.

PHARMACEUTICAL BOTANICAL STUDIES ON ASPARAGUS SPECIES (LILIACEAE) GROWING IN TURKEY

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In this study, morphological, anatomical, chemical and microbiological features of each *Asparagus* species indigenous to Turkey were investigated.

In morphological studies; a new identification key was prepared to distinguish the species from each other, each species was described and the taxonomic characters of the species were explained by the original photographs and drawings. In addition; the maps showing the distribution of each species in Turkey were prepared by using the records in the herbarium and the localities stated in Flora of Turkey.

During this work, a species and a subspecies were newly defined for flora of Turkey and for the World of Science. Transverse sections of the cladodes, stems and roots of each species were drawn and were photographed. The anatomical features of these organs were determined by the help of these drawings and photographs.

The chemical works were realised under the two main titles; saponins and fixed oils. The saponin aglycone of the aerial parts and rhizomes were identified by TLC (Thin Layer Chromatography). It was determined that the rhizomes of *A. acutifolius*, *A. aphyllus* subsp. *orientalis*, *A. officinalis* and the cultivated plant contain diosgenin as a sapogenol. Among sterols, β -sitosterol and stigmasterol were also identified in aerial parts and rhizomes of all species.

After preparing the methyl esters of the fatty acids of the fixed oils included in the seeds, the fatty acid composition were determined by GLC-MS.

It was observed that the fixed oil which was extracted from the seed of the examined species of *Asparagus* was rich in oleic and linoleic acid content.

The antifungal and antibacterial effects of alcoholic and chloroform extracts of the aerial parts and rhizomes which were prepared separately were also studied.

It was observed that some species are effective on Gr (+) bacteria. It was also determined that the examined species are ineffective on Gr (-) bacteria and *Candida albicans*.