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Transferrin-conjugated cationic liposome (Tf-liposome) was developed as a targeted gene delivery system by using heterobifunctional cross-linking agent, SPDP, and gradient metrizamide ultracentrifugation method. Physico-chemical properties of Tf-liposome were determined by scanning/transmission electron microscopy (SEM/TEM) and dynamic laser-light scattering method (DLS) with the mean diameter being 584±15nm. Gel retardation assay was performed using various DDAB:DNA ratios and proved the 6:1 weight ratio formulation being the most compact with a slight positive zeta-potential. In vitro transfection was done in human cervical cancer cell line, HeLa, and the transfection efficiency of Tf-liposome was found to be 5-fold higher than that of un-conjugated (plain) DDAB liposome and 2-fold higher than that of Lipofectin™. Biocompatibility of Tf-liposome was also tested using human red blood cells (RBC) and their morphology remained unaffected after incubation with Tf-liposome at 10μg/ml concentration. In conclusion, a target-oriented gene delivery system of transferrin-conjugated cationic liposome (Tf-liposome) was made successfully and proved to be very efficient in DNA delivery into the cells in culture. Furthermore, its possible use as an in vivo gene delivery system is highly expected as suggested by its biocompatibility test using human RBC.

[PE1-12] [ 04/19/2001 (Thr) 15:30 - 16:30 / Hall 4 ]

## The studies of interaction between methamphetamine and melanin pigment in hair

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There were many studies that suggested the amount and type of melanin present were major factors in determining how much drugs deposited in hair after exposure but the mechanism of drug entrapment in hair had been unknown. In vitro methamphetamine (MA)-melanin interaction was firstly studied using ultrafilteration membrane systems to interpret the deposition mechanism of methamhetamine in hair. The solutions of MA-melanin in amber vials were shaken by Recipro shaker and equilibrated at ambient temperature (20±0.5℃) for 24 hours. The concentrations of free drug were determined with HPLC systems. The binding parameters, association constant (K) and the number (n) of binding site per weight (mg) of melanin, were obtained from the Scatchard equation. The binding or association constant (K) and the number (n) of binding site of methamphetmaine to melanin polymer were 604 L/mole and 3.46 X $10^{-5}$ M $mg^{-1}$, respectively. This binding constant indicated that the interaction of methamphetamine to melanin was somewhat stronger than the published binding constants of some small molecules (p-toluene sulfonic acid (1), etc) to polymers(serum albumin, polyvinylpyrrolidone, etc). The Scatchard plot showed curvature at high concentrations of methamphetamine. This curvature usually indicated the existence of more than one type of binding site. The IR spectrum methamphetamine-melanin mixture showed band shift from 3420 $cm^{-1}$ to 3376 $cm^{-1}$ at N-H stretching region of methamphetamine. This shifting of the N-H stretching band of methamphetamine to lower frequency would be from hydrogen bonding with some groups (would be carboxyl or hydroxyl groups) of melanin. This MA-melanin interaction suggested that melanin as one component of hair was contributing to methamphetamine deposition in hair.

[PE1-13] [ 04/19/2001 (Thr) 15:30 - 16:30 / Hall 4 ]

## Application of Vitamin E TPGS forming the solid dispersion with furosemide

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The techniques that can potentially enhance the dissolution rate and extent of absorption of poorly soluble drugs is the formation of solid dispersion with polymeric materials. To increase the dissolution rate of furosemide, vitamin E TPGS (d-alpha tocopheryl polyethylene glycol 1000 succinate) was used as a drug carrier. The 1:2(w/w) solid dispersion was prepared by solvent method. The dissolution test, X-ray diffraction, Infrared spectra, thermal analysis of furosemide test systems were carried out. The dissolution rate of furosemide-vitamin E TPGS solid dispersion was enhaced markedly than that from the physical mixture or intact furosemide. The X-ray diffraction, IR, DTA, and TGA studies showed the physiochemical modification of the furosemide from the solid dispersion. The crystalline peaks of furosemide alone or furosemide contained within a physical mixture were disappeared in the solid dispersion indicating the amorphous form. An interaction, in the solid dispersion such as an association between the functional groups of furosemide and vitamin E TPGS might have occurred at the molecular level, changing the physicochemical property and increased the dissolution of furosemide. The results showed that the extent of dissolution was significantly enhanced, following formation of the solid dispersion, and the solid dispersion techniques with vitamin E TPGS provide a promising way to increase the dissolution rate of poorly soluble drug.

[PE1-14] [ 04/19/2001 (Thr) 15:30 - 16:30 / Hall 4 ]

## Circadian Changes in Pharmacokinetics of Acebutolol Orally Administered to Rabbits

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Effect of circadian rhythm on the pharmacokinetics of acebutolol and its metabolite, deacetylacebutolol was studied in rabbits after a single oral administration of acebutolol, 20mg/kg, in the morning (09:00 A.M.) and in the evening (21:00 P.M.). The plasma data were subjected to simultaneous computer nonlinear least squares regression analysis using a two-compartment pharmacokinetic model.

The elimination rate constant(β) of acebutolol were 0.072 ±0.016 $hr^{-1}$ in the morning and 0.066 ± 0.013 $hr^{-1}$ in the evening. The total body clearance(CLt) and area under the plasma concentration-time curve(AUC) of acebutolol were 3.02 ±0.52 L/hr/kg and 6.79 ±1.21 μg/ml·hr in the morning and 2.41 ±0.43 L/hr/kg and 9.16 ±1.69 μg/ml·hr in the evening. The plasma concentrations of acebutolol in the evening were increased during 4-12hr compared to those of acebutolol in the morning. The CLt of acebutolol in the evening were decreased significantly ($p < 0.05$) compared to that of acebutolol in the morning and the AUC of acebutolol in the evening were increased significantly ($p < 0.05$) compared to that of acebutolol in the morning.

However, the pharmacokinetic parameters of its metabolite were not significantly different between in the morning and in the evening.

[PE1-15] [ 04/19/2001 (Thr) 15:30 - 16:30 / Hall 4 ]

## Pharmacokinetic Changes of Intravenous Diltiazem in Alloxan-Induced Diabetes Mellitus Rabbits

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Because physiological changes occurring in diabetes mellitus patients could alter the pharmacokinetics of the drugs used to treat hypertention resulting from diabetic complications,the pharmacokinetics of diltiazem were investigated after intrvenous administration of the drug (4 mg/kg) to control rabbits and rabbits with acute and chronic diabetes induced by alloxan. Impaired kidney and