Mechanistic studies on peptide conjugate formation from GHRP-6 and PLGA polymer

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We previously reported that peptide conjugates were formed during in vitro release test of growth hormone releasing peptide-6 (GHRP-6, His-DTrp-Ala-Trp-DPhe-Lys-NH2) containing PLGA microspheres. LC/MS/MS analysis had confirmed that glycolic and lactic acids originated from PLGA polymer were conjugated to the free amino group of N-terminal His and epsilon amino group of Lys5 of GHPR-6. In this presentation, we studied the reaction mechanism of the conjugation formation more systemically by incubating GHRP-6 and a hydrophilic 50:50 PLGA polymer (RG502H, Boehringer Ingelheim) in various conditions. Two critical physico-chemical phenomena between GHRP-6 and PLGA polymer were determined as peptide binding to the polymer and glycolic/lactic acids conjugation to the peptide. From various experimental evidences including higher conjugate formation at alkaline pH, aminolysis of PLGA catalyzed by amino group of GHRP-6 is suggested as a plausible reaction mechanism.

[PE1-2] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Prediction method on the effect of transdermal enhancer II: Modeling by Artificial Neural Network-Partial Least Squares Regression

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The final goal of this work is to develope a proper regression model for the prediction of the effect of various enhancers on the transdermal flux. In order to carry out this task, flux data were obtained under homogeneous experimental condition. The effect of enhancers (2 hydrophobic and 2 hydrophilic) on the flux of model compounds (antipyrene, atropine, benzoic acid, chloraminophenamide, nicotinic acid) were studied.
Molecular descriptors of enhancers and model compounds were related with flux data of enhancer-drug combinations. Flux data were preprocessed in several different ways prior to regression analysis. Several regression models such as multiple linear regression(MLR), principal component regression (PCR), partial least squres regression(PLSR), continuum regression(CR), artificial neural network with non-linear transfer functions, and ANN-PLSR were tested and compared. The best prediction so far was obtained with ANN-PLSR(Artificial Neural Network-Partial Least Squares Regression).

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[PE1-3] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Solubilization of an anesthetic drug in nonionic surfactant systems

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Propofol is an effective anesthetic drug having some desirable properties such as rapid onset and recovery, even after a prolonged infusion, and the absence of emetic sequalae.
In this study, solubilization of propofol by means of nonionic surfactant systems has been investigated. Pseudo-ternary phase diagrams have been constructed for systems comprising of propofol-water-nonionic surfactant-cosurfactant.
Monophasic, isotropic areas were seen to occur along the water-surfactant axis in most systems studied, and propofol-water-PEG 660 12-hydroxystearate-ethylalcohol system showed larger region than any other compositions. Optimum rateo of surfactant/cosurfactant was 5/1.
The droplet sizes in all prepared system, determined by light scattering techniques, were below than 150nm. No significant difference in droplet size and concentration was observed for 8 weeks at 40℃, when 1%(w/w) of drug was solubilized with 8%(w/w) of surfactant/cosurfactant. The results obtained show that it is possible to solubilize suitable amount of propofol with nonionic surfactant systems.

[PE1-4] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Characterization of hydrophobized pullulan with various hydrophobicity

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Pullulan is a bacterial polysaccharide consisting essentially of α-1,6 linked D-glucopyranose residues with a few percent of α-1,2,α-1,3, or α
-1,4-linked side chains. Pullulan is widely under investigation as a polymeric carrierin drug delivery systems. Because of its good biocompatibility, pullulan is also a suitable polymer to be used for the preparation of hydrogels, which are becoming increasingly important in the biomedical, pharmaceutical, and biotechnological fields. Pullulan acetate was synthesized by pullulan suspended in formamide and dissolved by vigorous stirred. Then, pyridine and acetic anhydride were added, and the mixture was stirred and precipitant was obtained and then purified by reprecipitation with distilled water and methanol. The resultant precipitant was vacuum-dried and characterized by FT-IR, XRD and DSC measurement. Core-shell type nanoparticles of hydrophobized pullulan could be self-assembled in water as nanospherical aggregates, and their phyco-chemical properties were significantly differenced against various hydrophobicity. In this study, we synthesized pullulan acetate with various hydrophobicity, and evulation of self-assembling pullulan nanospheres against various hydrophobicity.

[PE1-5] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Pluronic grafted poly-(L)-lysine as a new sythetic gene transfer

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Genes are attractive candidates as therapeutic agents, and the development of gene carriers is essentia for human gene therapy. In order to investigate the delivery of DNA into cells, poly-L-lysine-g-pluronic copolymer was synthesized by conjugating free amino group of poly-L-lysine and pluronic which was partially functionalized with 4-nitrophenyl carbonate groups. Physiochemical properties the new graft copolymers were characterized by 1H-NMR, gel retardation assay, z potential, and size measurement. 1H-NMR spectrum of copolymer shows peaks at ?1.13ppm, 1.37~1.6ppm, 3.0ppm, 3.5ppm, 3.66ppm which can be assigned to the reaction between poly-L-lysine and pluronic. Gel retardation assay, z potential and size measurement confirmed that the new gene carriers make a compact complex with plasmid DNA. DNA size was decreased from 900nm to 290nm and z potential was increased from ?0mV to +40mV by adding poly-L-lysine-g-pluronic. pCMV-?gal was used as a repoter gene, and in vitro gene trnasfection efficiency was measured in HeLa cells by using ONPG assay. The highest transfection efficiency was achieved at a 1:1 weight ratio of polymer:DNA and 3-fold increase in transfection