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

efficiency was achieved by treatment of a lysosomotropic agent, chloroquine. Compared with unmodified PLL, PLL-g-pluronic showed about 2-fold increase in transfection efficiency and lower cytotoxicity specifically at a 1:1 weigh ratio of polymer:DNA. In vivo gene expression experiment using this new polymer is under going.

[PE1-6] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Preparation and evaluation of polymeric nanoparticles composed of poly(L-Latic acid) and dextran

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In this study, we synthesized a new amphiphilic polymers composed of poly(L-Latic acid) (PLA) and dextran. PLA is one of the poly(a-hydroxy esters) with bioerodible characteristics, and it degrades into naturally occurring substances. We expected PLA to have more hydrophobic properties than polysaccharide dextran. Dextrans are colloidal, hydrophilic and water-soluble substances, inert in biological systems and do not affect cell viability. Dextrans can be degraded by the dextranase which was found to be present in the colon. Biodegradable core-shell structure nanoparticles were prepared from PLA and dextran by activation with carbonyldiimidazole. The physicochemical characteristics were evaluated by fluorescence spectroscopy, transmissiton electron microscope, x-ray diffractometry, and photon correlation spectroscopy. Indomethacin (IN) was loaded as a model drug, and IN release behaviors were observed in vitro.

[PE1-7] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Transferrin-Conjugated Cationic Liposome for In Vitro and In Vivo Gene Transfer

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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™.
Interleukin 12 (IL-12) has a pivotal role in controlling cell-mediated immunity through a number of important biological activities, such as secretion of interferon-γ(INF-γ), and systemic administration of IL-12 can inhibit the growth of both established s.c. tumors and experimental metastasis. We inoculated C-26, murine colon carcinoma cells into Balb/c mice subcutaneously. When tumor volumn reached 100mm3 (~ 4 days after tumor inoculation), mice were injected intravenously with IL-12 plasmid/Tf-liposome complexes twice a week for 3 weeks. As a result, significant suppression of tumor growth was achieved by the Tf-liposome/DNA treatment. IL-12 plasmid 10μg/Tf-liposome complex had superior suppression effect among tested and this effect was similar to the same amount of Lipofectin™/DNA complex. Results from different therapy regimen will also be presented.
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 both in vitro and in vivo.