of itraconazole-loaded microspheres were 16.18~25.74㎛. In morphology studies, bupivacaine-loaded microspheres showed an irregular shape and had a rough surface.

[PE1-18] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

In Vitro Evaluation of Three Positional Isomers of mono-PEGylated Salmon Calcitonin

Jung JY°, Youn YS, Oh SH, Hong ST, Lee JE, Lee SD, Lee KC

Drug Targeting Laboratory, SungKyunKwan University

Salmon calcitonin (sCT) is a therapeutic polypeptide hormone consisting of 32 amino acids (3432 Da). As with other bioactive peptide therapeutics, however, therapeutic use of sCT has been limited due to the problems of short circulating half-life and rapid proteolytic degradation. To get over this problem, the three positional isomers of mono-PEGylated sCT were prepared and among these, the best drug candiate for nasal application was chosen. sCT was conjugated with monomethoxy polyethylene glycol succinimidyl propionate (mPEG-SPA) 2K via covalent linkage. Three positional isomers of mono-PEGylated sCT were directly separated by reversed-phase column and the PEGylation sites of each isomer were identified by endoprteinase Lys-C digestion followed by MALDI-TOF mass spectrometry. To select the best candidtate, the In vitro biological activity in T47D human breast cancer cell line, the stability against various nasal enzymes and nasal membrane permeability in RPMI 2650 human nasal epithelial cell monolayer of three positional isomer were investigated. The findings of this study indicate that Lys18-residue modified mono-PEGylated sCT which has increased stability, preserved bioactivity, and enhanced membrane permeability would be the best drug candidate for therpeutic application via nasal route.

[PE1-19] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Encapsulation of Plasmid DNA in Liposomes: Preparation and Characterization

Park HyoMin°, Lee HwaJeong

College of Pharmacy, Ewha Womans University 11-1 Daehyun-dong, Seodaemun-gu, Seoul 120-750, Korea

Unlike cationic liposome/DNA complexes, neutral liposomes containing plasmid DNA are stable in blood and does not selectively entrapped in the lung. The objective of this study was to construct neutral liposomes containing plasmid DNA with optimal encapsulation efficiency. Plasmid DNA (pGL2 clone 753, ~ 6 kb) was encapsulated by the freeze/thawing method into liposomes composed of 1-palmitoyl-2-oleyl-sn-glycerol-3-phosphocholine (POPC), didodecyldimethylammonium bromide (DDAB), distearoylphosphatidyl-ethanolamine polyethylene glycol 2000 (DSPE-PEG 2000) and DSPE-PEG 2000-maleimide. The liposomes containing plasmid DNA were then extruded through two stacked polycarbonate filters with series of different pore sizes to obtain a narrow size distribution of the particles. The plasmid DNA entrapped in the liposomes was separated from free plasmid DNA by Sephadex CL-4B column chromatography. The encapsulation efficiency was markedly affected by the cationic lipid (DDAB) concentration, but to a low degree by the size of liposomes and by the amount of plasmid DNA.

[PE1-20] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Expression of *O*-acetyl disialoganglioside synthase in experimental rat and human liver fibrosis

Lee sung Hee°, Choi Jeong-Yong, Park Eun-Jeon, ZhaoYu-Zhe, Park Young Nyun, Chae Keon-Sang, Sohn Dong Hwan

College of Pharmacy, Wonkwang University, Iksan, Jeonbuk 570-749;Division of Biological Sciences, Chonbuk National University, Chonju, Jeonbuk 561-756;Yonsei University College of Medicine, Seoul 120-749, South Korea

The activation of the hepatic stellate cell (HSC) is a key step in liver fibrogenesis. Utilizing large scale sequencing of a 3'-directed cDNA library, we investigated expression profiles of quiescent and activated rat HSCs. During the activation process, *O*-acetyl disialoganglioside synthase (OAcGD3S) was identified as one of the significant upregulated factors. Upregulation of OAcGD3S in cultured HSCs was confirmed by both northern and western blot analyses. OAcGD3S expression in models of experimental liver fibrosis was investigated at the mRNA level using RT-PCR. The expression of OAcGD3S protein in activated rat HSCs and in experimental fibrotic livers was demonstrated by immunohistochemistry. In situ hybridization revealed OAcGD3S mRNA expression in areas of ductular proliferation. Furthermore, O-acetyl GD3 protein was detected in activated rat HSCs and human cirrhosis livers. This study shows that OAcGD3S is strongly expressed during liver fibrogenesis, and HSCs seem to be the major cellular sources of OAcGD3S in the liver.

[PE1-21] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Surface modulation of long term drug releasing microparticulates for optimization of release kinetics

Hwang Jeonghyo°, Song HyeWon, Lee SeungJin

Department of Pharmacy, College of Pharmacy, Ewha Womans University, Seoul, 120-750, Korea

With the aim of obtaining the early bone regeneration efficacy, poly (L-lactide) particulates were developed as a long-term drug carrier system.Biodegradable microparticulates have been used extensively as drug delivery devices.However, problems like poor encapsulation efficiencies of the drugs and complicated fabrication process are still remained to be solved.To overcome these problems, poly (L-lactide) microparticulates were prepared by using newly developed method which includes rapid freezing of drug dispersed polymeric solution and micronizing the freeze-dried polymeric matrices.To evaluate the delivery system, particulates were implanted in 8-mm (critical size) rat calvarial defects and examined 4 weeks after implantation.
PLLA polymer-drug solution was emulsified with pH 7.4 phosphate buffer and freeze dried. The resulting matrix was micronized by using micromill.The morphology of the microparticulates was examined by
SEM.In vitro release tests were performed for 35days. In vitro cytotoxicity of PLLA particulates was examined using the MTT assay with MG 63 cells. Bone regenerative effect of tetracycline was measured in rat calvarial critical-size defects.The defect was filled with particulates and rats were sacrifized 4 weeks after implantation. PLLA barrier membrane prevents outer soft tissue immigration into the bone defect. Microscopical examination of the retrieved specimens was undertaken using Olympus BH-2 light microscope.
The particulates showed porous structure. The pore size was 250-350㎛ in diameter. Since PLLA is usually impermeable to tetracycline, these particulates are porous to allow tetracycline release.

After initial burst release of tetracycline, the release rate was leveled-off. Therapeutic concentration range (10㎍/㎖) of tetracycline was continuously released from the PLLA