

Objectives: Galatosylated PEI was synthesized and characterized for gene delivery to hepatocytes. It was modified by conjugating with hydrophilic PEG to improve in vivo circulation. And we studied the possibility as an imaging modality for monitoring of gene delivery using gal-PEI derivatives. Methods: The substitution values of galactose in PEI were calculated by resorcinol/sulfuric acid method and quantity of PEG was calculated by comparing NMR peak. Cytotoxicity was determined by MTT. Galatosylated PEI-PEG derivatives were labeled with  $^{99m}\text{Tc}$  using stannous chloride and then determined their labeling efficiencies using ITLC. After injection via vein with  $^{99m}\text{Tc}$  Gal-PEI derivatives, images were acquired with a gamma camera. Size and zeta potential of DNA complex was measured and transfection experiments were performed on HepG2 and Hela cells. Results: The substitution value of LA was estimated by 1.2 mol%. The compositions of PEGs in Gal-PEI were confirmed to be 4.1 and 7.6 mol% (10%, 50%). The MTT assay showed that cytotoxicity of Gal-PEI was decreased with increasing the degree of PEG substitution. The labeling efficiencies were shown all above >90% until 1 h. The rabbit images showed that with increasing degree of PEG grafting, non-specific interactions with plasma components and lung endothelium were reduced. Size of complex was found to increase with increasing PEGylation (65.05 nm for 0%, 194 nm for 4.1%, and 296.75 nm for 7.6%). Zeta potential decreased in inverse proportion to degree of PEG substitution (19.81, 15.27, and 5.75 mV). As transfection with  $^{99m}\text{Tc}$  Gal-PEI-PEG 50%/DNA complexes (N/P=3.0), green fluorescent proteins were expressed just in galactose receptor positive-cell (HepG2). Conclusion:  $^{99m}\text{Tc}$  labeled DNA complexes were efficiently entered into the cells through endocytosis in vitro and GFP gene was expressed regardless of  $^{99m}\text{Tc}$ . These results suggest that Galatosylated PEI-PEG derivatives can be used hepatocyte targeting agent and imaging modality.

[PE3-6] [ 2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function ]

### **Chitosan-Iron casein succinylate nanoparticles as oral delivery systems : increasing the stability and enhancing the absorption of iron nanoparticles.**

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The objective of the study was to develop an oral delivery system to increase the stability and efficacy of iron casein succinylate. Aqueous nanoparticles were prepared using complex coacervation of the oppositely charged chitosan and iron casein succinylate with polyethyleneglycol (PEG). The physicochemical properties of nanoparticles were investigated using dynamic light scattering, zeta potential and scanning electron microscopy. Chitosan-iron casein succinylate interactions were investigated in solid state by differential scanning calorimetry (DSC) and FT-IR spectrometry. The mucoadhesive properties of nanoparticles were evaluated by studying the interaction between mucin and nanoparticles in aqueous solution. Iron release kinetics were investigated in vitro in the simulated gastric fluid (pH 1.2, 2 hr) and intestinal fluid (pH 6.8, 4 hr). An in vitro digestion/Caco-2 cell culture model was used to compare iron transport from ferrous gluconate, two kinds of organic iron (sodium ferric gluconate complex, iron-hydroxide polymaltose complex), iron casein succinylate and chitosan-iron casein succinylate nanoparticles. The nanoparticles of chitosan and iron casein succinylate mixed in a weight rate of 3:2, 1:1, 2:1 and 4:3 were stable for 5 weeks. The nanoparticles carried a positive charge from 48 to 61 mV and showed the size in the range from 600 to 850 nm. DSC and FT-IR showed that the covalent bond of chitosan and iron casein succinylate did not change. A strong interaction between nanoparticles and mucin was detected from mucoadhesive study. The amount of iron released at 6 hr was more than 60%. The nanoparticles were stable physically and chemically at 4°C for 5 weeks without preservatives. The permeability of iron was increased 25~50-fold (chitosan:iron casein succinylate=3:2, 1:1, 2:1 and 4:3) compared with iron casein succinylate solution. The chitosan-iron casein succinylate nanoparticles could increase the stability and enhance the absorption of iron.

[PF1-1] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]

### **Analysis of $\beta$ -blockers Use in Chronic Heart Failure**

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