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. Galactosylated PEI-PEG derivatives were labeled with ^{99m}Tc using stannous chloride and then determined there labeling efficiencies using ITLC. After injection via vein with ^{99m}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}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}Tc labeled DNA complexes were efficiently entered into the cells through endocytosis in vitro and GFP gene was expressed regardless of ^{99m}Tc. These results suggest that Galactosylated 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℃ 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 β-blockers Use in Chronic Heart Failure

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β-blockers are considered as standard therapy for patients with stable chronic heart failure (CHF) and to prolong survival and reduce hospitalizations. We examined the effects of the β-blocker on mortality, hospitalization and symptoms in patients with CHF and the related factors to the use of β-blockers. Patients in New York Heart Association class Ⅱ-Ⅳ were included if they were treated for heart failure from January 2002 to June 2002. At baseline, 6 months, and 12 months, they were assessed for the change of NYHA class and all deaths and hospital admissions. Demographic and clinical characteristics of the groups were compared to explore the related factors to the use of β-blockers. As results, 123 of 235 patients received β-blockers. Women were 62(50.4%), NYHA class Ⅱ was 80(65%) and the nonischemic cause of CHF were 74(60.2%) in β-blocker group. LVEF and the use of ACEI/ARB were the related factors to the use of β-blocker. Carvedilol was the most common β-blocker used and followed by atenolol and metoprolol. The average dosages were titrated to lower dosage than the recommended target doses. NYHA class was improved in the β-blocker group compared with the non β-blocker group at 6 months and 12 months(p=0.016, p=0.017, respectively). There was no significant difference in reasons for hospitalizations(p=1.000). Number of hospital admissions was lower in the β-blocker group(p=0.033). Treatment effects were independent of age, cause of heart failure, NYHA class, the use of diuretics, the use of ACEI/ARB or the concomitant use of ACEI/ARB and diuretics. In conclusions, β-blockers improved mortality, reduced the need for hospitalizations and improved NYHA class. Factors affecting use of β-blockers were LVEF and the use of ACEI/ARB.

[PF1-2] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Analysis of Spironolactone Use in Chronic Heart Failure

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Background Aldosterone has an important role in the pathophysiology of heart failure. Aldosterone promotes the retention of sodium, the loss of magnesium and potassium, sympathetic activation, parasympathetic inhibition, myocardial and vascular fibrosis, baroreceptor dysfunction, and vascular damage and impairs arterial compliance.Objectives We investigated the effects of additional spironolactone to angiotensin-converting enzyme inhibitor (ACEI) / angiotensin-II receptor blocker (ARB) in patients with heart failure.Methods In a retrospective study, we evaluated 290 patients who had heart failure, left ventricular systolic dysfunction and NYHA class of more than II. A total of 99 patients were received spironolactone, and 159 not received. We analyzed spironolactone dose, relationship on hospitalization and death, factors affecting of spironolactone use, and relative risks of hospitalization and death from all causes.Results Mean dose of spironolactone was 28.1±12.7mg and there were more patients with cardiac caused hospitalization in spironolactone group than non-spironolactone group(p=0.013). Factors affecting spironolactone use were LVEF≤35%, NYHA class III-IV, Age≤65yr, digitalis use. Spironolactone had better effect on death and hospitalization in cases of ischemic cause, NYHA class III, ACEI/ARB+loop diuretic+β-blocker use. Conclusion Spironolactone, aldosterone-receptor blocker, in addition to standard therapy, can reduce the risk of morbidity and death among patients with chronic heart failure.

[PF1-3] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Retrospective Evaluation of Heptaplatin Nephrotoxicity in Patients with Advanced Gastric Cancer

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There are contradicting reports on the nephrotoxicity of heptaplatin, a new platinum derivative. A retrospective study was performed to compare the toxicities of heptaplatin-containing regimens with the ones not. Seventy-seven patients with advanced gastric cancer who did not receive any chemotherapy within the last 3 months before the treatment were evaluated. Among them 38 patients received heptaplatin-containing regimens (heptaplatin/epirubicin/5-FU: 26, heptaplatin/5-FU: 12) and 39 patients received other regimens (cisplatin/epirubicin/5-FU:11, epirubicin/leucovorin/5-FU: 28). Serum creatinine (Scr) before and after the