Complexes

Chae Min Jung°, Chung Hesson, Kwon Ick Chan, Chung Jin Wook, Park Jae Hyung, Sohn Young Taek, Jeong Seo Young
Biomedical Research Center, Korea Institute of Science and Technology, Seoul, Korea Dept. of Pharmacy, Duksung Women's University, Seoul, Korea, Biomedical Research Center, Korea Institute of Science and Technology, Seoul, Korea, Dept. of Radiology, College of Medicine, Seoul National University, Seoul, Korea, Dept. of Pharmacy, Duksung Women's University, Seoul, Korea

A cationic lipid emulsion (o/w) containing lipiodol and 1, 2-dioleoyl-sn-glycero-3-trimethylammonium-propane (DOTAP) has been prepared as a gene delivery system. In order to increase the transfection efficiency of the lipiodol emulsion, 1, 2-dioleoyl-sn-glycero-3-phospho -ethanolamine (DOPE) and polyoxyethylene sorbitan monooleate (Tween 80) were incorporated as additional lipids. By including DOPE and Tween 80, the cationic emulsion became a more potent gene carrier under in vitro condition in the presence of serum, and under in vivo condition. The role of protamine sulfate on cationic lipid emulsion-mediated gene transfer was also tested. The particle size and the zeta potential of the lipiodol emulsion as well as the DNA/Carrier complexes were examined in order to evaluate the physical stability. The particle size of the DOTAP/DOPE/Tween 80 emulsion was 71 nm, and this particle was more stable than those in the DOTAP emulsion in PBS with or without serum. When the DOTAP/DOPE/Tween 80 emulsion was combined with DNA, the size and the zeta potential of the complex were 220~300 nm and +30mV, respectively. The DNA /Emulsion/Protamine sulfate complex delivered DNA effectively to spleen through a single intravenous injection in mice. The feasibility study of DNA/Carrier complexes as a local injection carrier was performed by injecting the complex via hepatic artery of rabbit VX2 tumor model. When the DNA/Emulsion (DOTAP/DOPE/Tween 80) complex was administrated to hepatic artery, DNA was localized at the tumor site more specifically when compared with the DNA/Emulsion (DOTAP) complex.

[PE1-7] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Enhanced Stability of Acetyl-L-Carnitine Tablet under Accelerated Storage Condition

Kwon Min Chang°, Wang Hun Sik, Shim Ji Yeon, Park Jun Sang
GL PharmTech Corp.

Acetyl-L-carnitine (ALC), an endogenous component of L-Carnitine, is the acetyl ester of carnitine that has been reported to be beneficial in depressive disorders and Alzheimer's disease.ALC is so hygroscopic that deliquescence took place when it absorbed moisture by 15%(w/w) in a week and then reached steady-state at 45%(w/w) in 40℃, 75% RH storage condition. Therefore it is necessary to prevent ALC from absorbing atmospheric moisture.For this purpose, we chose hydroxypropylmethylcellulose phthalate (HPMCP), an enteric polymer, as a film former. After two weeks' storage under 40℃, 75% RH without a package, HPMCP-coated ALC tablet absorbed moisture only below 20%(w/w), while control product, Nicetyl? tablet coated with cellulose acetate phthalate (CAP) represented moisture absorption up to 32%(w/w).This result demonstrated that HPMCP could be much more effective to protect the ALC tablets against moisture under severely humid circumstances as well as to reduce the cost for tight moisture-proof package.

[PE1-8] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Electrospun poly (lactic-co-glycolic acid)(PLGA) nanoparticles for controlled drug delivery system

Lee Jue-Yeon°, Lee Meong Hee, Park Won-Ho, Min Beong-Moo, Lee Seung-Jin
College of Pharmacy, Ewha Womans University, College of Pharmacy,Ewha Womans University, College of Engineering, Chungnam National University, College of Dentistry, DRI, Seoul National University

In many biodegradable polymers recently investigated, poly(lactic acid)(PLA) or poly(lactic-co-glycolic acid)(PLGA) have extensively been utilized as drug delivery systems for sustained release drug delivery. Recently, there has been increased interest in electrospinning, which can produce fibers that are sub-micron in diameter. This technique has been applied to various micro/nano fabrication areas using numerous polymers but

very few uses in the pharmaceutical area have been reported. The electrospinning technology is well suited to process natural biomaterials and synthetic biocompatible or bioabsorbable polymers for biomedical applications because it is rapid, efficient, and heat free process. The potential applications of microparticles produced by electrospinning include local drug delivery device and surface coating agent. In the present study, we investigated the effects of varying the processing parameters in electrospinning on the PLGA nanoparticles for drug delivery system. We have also demonstrated that the electrospinning could control the initial burst release of tetracycline from PLLA particulates. Tetracycline loaded PLLA particulates with 350-500㎛ diameter for long term drug delivery system were developed in our laboratory. These particulates release tetracycline in therapeutic concentration for 28 days with the initial burst. The initial burst was caused by drug exposed at the surface of particles. To reduce initial burst, we designed surface coating of PLLA particles with PLGA nanoparticles produced by electrospinning method. Scanning electron microscopy (SEM), release test, differential scanning calorimetry (DSC) were used to investigate the structure and morphology of the electrospun PLGA nanoparticles.

[PE1-9] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

In vitro and in vivo evaluation of erdosteine capsule

Shon HeeKyoung°, Park YoungJoon, Choi YongGak, Kang Heuill
Yuhan Research Institute, 27-3 Dangjeong-dong, Gunpo-si, Gyeonggi-do, # 435-715, Korea

Purpose. The purpose of this study is to compare in vitro dissolution characteristics and bioavailability in beagle dog of a hard gelatine capsule containing erdosteine (Yuhan Erdosteine capsule™) with those of commercial product (Erdos capsule™). Methods. Yuhan Erdosteine capsule™ was prepared using erdosteine 300 mg, lactose, magnesium stearate, and others by powder filling method. The dissolution characteristics of Yuhan Erdosteine capsule™ and Erdos capsule™ were determined by USP dissolution apparatus 2. The studies were conducted in 900ml of dissolution mediums (pH 1.2, 4.0, 6.8 and water) maintained at 37 ℃. Gentle agitation was provided by rotationg the dissolution paddle at 50 rpm. A randomized, two way crossover bioavailability study in healthy male beagle dogs was conducted after oral administration of Yuhan Erdosteine capsule™. Blood samples were collected at scheduled intervals and the plasma concentrations of erdosteine were analyzed by HPLC method. Results & Conclusion. The dissolution profiles of Erdosteine capsule™ were very similar to those of Erdos capsule™. AUC_{0-7} and Cmax of Yuhan Erdosteine capsule™ hr/ml and 11.14 ± 3.16 ug/ml, respectively. The relative□were 25.56 ± 6.01 ug bioavailability of Yuhan Erdosteine capsule™ to Erdos capsule™ was 105.5 %, 104.2 %, based on AUC0-7 and Cmax , respectively. These results met the bioequivalence criteria of the KFDA guideline. Therefore Yuhan Erdosteine capsule™ was revealed to be bioequivalent with Erdos capsule ™.

[PE1-10] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Study on Polymorphism of Cefotaxime Sodium, Cephradine, and Ceftriaxone Sodium

Sun Hee Park°, Young Taek Sohn
College of Pharmacy, Dongduk Women's University

Investigation of polymorphism has become a requirement in the pharmaceutical industry because the physical properties and bioavailabilities of crystalline drugs depend on their polymorphic form. Two polymorphic modifications and one pseudopolymorphic modification of cefotaxime sodium were prepared by recrystallization in organic solvents under variable conditions. Four polymorphic modifications of cephradine were prepared by recrystallization. Three polymorphic modifications and one pseudopolymorphic modification of ceftriaxone sodium were prepared by recrystallization. They were characterized by UV spectrophotometer, DSC, TGA and X-ray crystallography. The solubilities of all modifications were checked through the dissolution test. Comparing each solubility of cefotaxime sodium polymorphic forms (by 120 minutes), Form 1 is 99.30%, Form 2 is 85.09% and Form 3 is 45.91%. : Form 1 > Form 2 > Form 3. Comparing each solubility of cephradine polymorphic modifications (by 120 minutes), Form 1 is 100%, Form 2 is 75.55%, Form 3 is 98.90% and Form 4 is 77.83%. : Form 1 > Form 3 > Form 4 > Form 2. Comparing each solubility of ceftriaxone sodium polymorphic forms (by