

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 $\mu$ m 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**<sup>o</sup>, Park YoungJoon, Choi YongGak, Kang Heuill

*Yuhan Research Institute, 27-3 Dangejeong-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<sup>TM</sup>) with those of commercial product (Erdos capsule<sup>TM</sup>). **Methods.** Yuhan Erdosteine capsule<sup>TM</sup> was prepared using erdosteine 300 mg, lactose, magnesium stearate, and others by powder filling method. The dissolution characteristics of Yuhan Erdosteine capsule<sup>TM</sup> and Erdos capsule<sup>TM</sup> 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 °C. Gentle agitation was provided by rotating 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<sup>TM</sup>. 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<sup>TM</sup> were very similar to those of Erdos capsule<sup>TM</sup>. AUC<sub>0-7</sub> and C<sub>max</sub> of Yuhan Erdosteine capsule<sup>TM</sup> hr/ml and 11.14 ± 3.16 ug/ml, respectively. The relative  $\square$  were 25.56 ± 6.01 ug bioavailability of Yuhan Erdosteine capsule<sup>TM</sup> to Erdos capsule<sup>TM</sup> was 105.5 %, 104.2 %, based on AUC<sub>0-7</sub> and C<sub>max</sub>, respectively. These results met the bioequivalence criteria of the KFDA guideline. Therefore Yuhan Erdosteine capsule<sup>TM</sup> was revealed to be bioequivalent with Erdos capsule<sup>TM</sup>.

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

### **Study on Polymorphism of Cefotaxime Sodium, Cephadrine, and Ceftriaxone Sodium**

**Sun Hee Park**<sup>o</sup>, 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

120 minutes), Form 1 is 95.22%, Form 2 is 67.80%, Form 3 is 64.00% and Form 4 is 99.90%. : Form 4 > Form 1 > Form 2 > Form 3. The solubility of Form 1 placed on sale was lower than that of Form 4. Therefore, Form 4 of ceftriaxone sodium would be applied to enhance bioavailability. Each modification is also investigated after storage of 2 months at 52% and 0% humidity. All polymorphs except Form 2 of ceftriaxone sodium were not converted to another form at 52% and 0% humidity. However, Form 2 of ceftriaxone sodium was transformed to monohydrated form (Form 3 of ceftriaxone sodium) at 52% humidity. Form 2 of ceftriaxone sodium is regarded as a metastable form.

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

### **Collagen electrospun chitosan-PLLA membrane for guided bone regeneration**

Hyonjin Baek, Kyunghwa Kim, Jieun Jung, Juyeon Lee, young Ku, Chongpyung Chung, Seungjin Lee  
*Ewha Womans University, Seoul National University*

Recently, the barrier membranes have been applied for regenerating bone surrounding peri-implant defects in guided bone regeneration(GBR). GBR membrane should provide mechanical support sufficient to withstand in vivo forces and maintain wound space for bone regeneration. The ability to exclude unwanted tissues or cells(connective tissue and epithelium) is needed. In addition large surface area is conducive to tissue ingrowth. The search for ideal materials that biocompatible, bioresorbable and can support the growth and phenotypic expression of osteoblasts is a major challenge in the biomedical application for the repair of bone defects. In our study, collagen electrospun chitosan-PLLA membranes for GBR were fabricated by electrostatic fiber spinning. Fibrous meshes of collagen electrospun chitosan-PLLA membranes were composed of collagen nano-fibers(50-800nm) and chitosan micro-fibers(30-50 $\mu$ m). Chitosan fibers support sufficient mechanical strength and collagen fibers provide large surface area. We assumed that nano/micro-fiber composites have advantages of both nano-fibrous membrane and micro-fibrous membrane. PLLA membranes between the two nano/micro-fiber composite meshes have 2-10 $\mu$ m pore size pores were generated by an in-air drying phase inversion technique. collagen electrospun chitosan-PLLA membranes showed similar tensile modulus with Chitosan-PLLA membrane. After 1 days osteoblast incubation, cells were spindle-shaped and had several cytoplasmic extension or lamellopodia development. After 1 week of culture, membrane surface is partially covered with multi-layers of cells. Therefore, it is demonstrated that collagen electrospun chitosan-PLLA membranes has good cellular compatibility. Also, it might be beneficial to achieve significant bone augmentation as GBR.

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

### **Micro-and nanofibrous scaffold for enhanced cartilage regeneration**

Lee Myung Hee<sup>o</sup>, Shim In Kyong, Hwang Jung Hyo, Ahn Hyun Jung, Lee Sang Hoon, Lee Myung Chul, Lee Seung Jin

*Department of Pharmacy, Ewha Womans University, Department of orthopedic surgery, Seoul National University*

Extracellular matrix(ECM) is composed of the ground materials(proteoglycan) and nano size diameter fibrous proteins(ex. collagens) that together form a composite-like structure. In this study, fibrous scaffold with biomimetic architecture based on collagen nanofibers interpenetrated in PLGA/chitosan microfibrinous matrix. Chitosan was selected for its structure similarity to glycosaminoglycan and neutralizing capacity for PLGA acidic metabolite. Collagen nanofiber were prepared by electrospinning. Electrospinning fabricate ultra fibers ranging from 500-300 nm in a diameter, features a morphologic similarity to the ECM of natural tissue, which is characterized by a wide range of pore diameter distribution, high porosity, and effective mechanical properties. The strategy of this scaffold design includes; I) improvement of tissue compatibility of PLGA maintaining its mechanical strength and biodegradability, ii) enhancement of cell-matrix interaction provided by collagen nanofibers, iii) achievement of ideal biomimetic 3-D environment for chondrocyte culture and cartilage regeneration. Collagen nanofibers well incorporated into PLGA/chitosan microfibrinous network. In micro-and