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

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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

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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

particulates which was effective for obtaining optimal GBR efficacy.
The cellular growth and survival with PLLA particulates against osteoblasts showed 80-110% cellular activity indicating that the particulate system has no significant toxic effect.
Microscopic examination of samples developed with Masson - trichome stain revealed histology patterns for the particulates treated groups. No adverse cellular reac tion including macrophages or multinucleated giant cells was observed.The newly formed bone was observed at the margin of the defect and along the side of dura mater. long-term release of tetracycline from the PLLA particulates enhanced new bone
formation.
Tetracycline released from PLLA particulates enhanced the early bone healing and regeneration.
Tetracycline loaded biodegradable PLLA particulates functioned as a proper long term drug delivery device for guided bone regeneration.

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Evaluation on the stability of Vitamin preparations- Vitamin A

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Accelerated stability testing was performed on the different 7 dosage forms in order to evaluate the influences of the existence of other vitamins, minerals, excipients on the chemical stability of vitamin A in complicated vitamin drug products. The stability results suggested that increasing of storage time and temperature has resulted in increasing the rate of vitamin A decomposition and the shelf lives(t_{90}) under the test decreased as the storage temperature increased. Vitamin A content was analyzed by HPLC and method validated. All the data were treated as first order kinetics and determined their shelf lives(t_{90}) using Arrhenius plots. The results from Arrhenius plotting were 15.6, 31.0, 17.3 and 43.1, 26.2, 43.0, 21.8, 11.5 months for injection, hard capsule, chewable tablets, ointment, film coated tablet, powder, soft capsule of vitamin A at 25℃, respectively. Injection and ointment of vitamin A were very stable under thermal cycling test. The photostability of vitamin A preparations performed by ICH guidelines was showed vitamin A on the hard capsule, soft capsule and film coated tablet were stable. Though vitamin A on the injection, chewable tablets, ointment and powder were unstable in open containers, they were very stable in final packaging material for marketing. Our results would be helpful to evaluate the stability of multivitamin drug products and be applicable to quality control for vitamin preparations in pharmaceuticals.

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Nonwoven chitosan fibrous matrix with bioactive agents modified surface and drug release function as tissue engineering scaffold

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For polymeric material for tissue engineering, chitosan was selected with benefit of high tissue compatibility attributed and wound healing through its activation of growth factors. And nonwoven chitosan fibrous matrix has well interconnected porosity. But chitosan itself has some of limitations in inducing rapid bone regeneration at initial states incorpor-ated of bioactive materials such as growth factors and ECM molecules.
Chitosan fibers were prepared by extruding 4% chitosan solution 4% acetic acid into basic