The purpose of incorporating peptide drugs into a polymer matrix is to improve the therapeutic efficacy, suitable for parenteral administration to maintain the pharmacological activity for a prolonged period. Many studies have also been attempted to evaluate the polymer matrices. In this study, PLGA microspheres containing salmon calcitonin (sCT) using hydrophilic polymer (RG503H) was much faster compared to hydrophobic polymer (RG503) were prepared by a solvent extraction/evaporation method. Using capillary electrophoresis (CE) and matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS), the in vitro release rates of sCT from two different microspheres were determined, and demonstrated that the polymer properties affected the sCT release pattern from biodegradable PLGA microspheres. Degradation of microsphere and drug release occurred much faster in RG503H polymer than in RG503 polymer. Also, the complex peak between sCT and polymer fragments was detected and increased with the time during the release test. The sCT in RG503 polymer also demonstrated stronger interaction between sCT and polymer units than in RG503H indicating that the hydrophobicity of polymers might be the important factor for the interaction with peptides.

[PE1-24] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

In Vitro Stability of Peptides in Poly(Lactic-co-Glycolic Acid) Microspheres

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One of the critical aspects in the development of peptide/protein-loaded microspheres is the investigation of release characteristics of peptide/protein from microsphere matrix. The stability and chemical changes of peptides in microspheres during in vitro release test were investigated by using capillary electrophoresis (CE) and matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS). Leuprolide and human parathyroid hormone (1-34) (hPTH1-34) were employed as model systems. In the CE electropherogram of two peptides extracted from microspheres after incubation for 3 days at 37oC, the leuprolide microsphere showed no degradation product, while hPTH1-34 microspheres showed the extra peak in addition to the intact peptide. MALDI-TOF mass spectrum of hPTH1-34 extracted from microsphere showed three peaks, including hPTH1-34 (4114.91 m/z) and two peaks (4172.96 and 4228.84 m/z), whereas the leuprolide showed only the mass corresponding to the intact peptide (1208.95 m/z), showing the different stabilities within the microspheres. The two peaks from hPTH1-34 microsphere are corresponded to the association product of hPTH1-34 and polymer fragments. The in vitro release profiles of leuprolide and hPTH1-34 microspheres also showed different patterns. These results indicate that the interaction of peptide to polymer affects the release profiles from the microsphere.

[PE1-25] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Non-invasive method to encapsulate basic proteins into porous poly(DL-lactide-co-glycolide) microspheres

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Non-invasive method to encapsulate protein into PLGA microspheres has been tried by soaking blank porous PLGA microspheres into protein solution. The incorporation mechanism was systematically studied by varying incorporation parameters such as pH, salt and temperature using five model proteins with different physical properties such as molecular weight and pI. With including NaCl as a porosigen in the primary water phase, porous PLGA microspheres were prepared by W/O/W double emulsion solvent evaporation method using hydrophilic 50:50 PLGA polymer (RG502H, Boehringer Ingelheim) which contains free carboxyl end group. At neutral pH, 37°C, for 24hr, basic proteins, such as lysozyme and ribonulease A were incorporated more than 10% (weight