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Covalent attachment of polyethylene glycol (PEG) to proteins (PEGylation) is a procedure of growing interest for enhancing the therapeutic potential of protein pharmaceuticals. The PEGylation of recombinant human epidermal growth factor (rhEGF) as method to increase the stability was examined. The PEGylated rhEGF was prepared with succinimidyl propionate(SPA)-monomethoxy-PEG (SPA-mPEG, M.W. 20kD). The mono-PEGylated rhEGF was purified by size-exclusion chromatography and characterized by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). Thermal stability test was performed in PBS (10 mM, pH 7.4) at 70oC. Radioiodination of native rhEGF and mono-PEGylated rhEGF was performed with IODO-GEN method. The 125I-rhEGF and 125I-mono-PEGylated rhEGF were mixed with wound homogenate of rat skin and incubated at 36.5℃. Column-switching HPLC method using flow-through radioisotope detector (FTRD) was used for direct analysis of homogenate samples. In thermal stability test, native rhEGF remained 19% after incubation of 39 hours and was not detected after 64 hours, while mono-PEGylated rhEGF still remained 62% after incubation of 64 hours. After incubation in wound homogenate of rat skin for 7 hours, the remained amount of rhEGF and mono-PEGylated rhEGF were measured 37% and 80%, respectively. The degradation peak of rhEGF was detected in FTRD-HPLC chromatogram and the peak was increased with incubation time. Mono-PEGylated rhEGF did not show the degradation peak. In conclusion, this study indicates that PEGylation of rhEGF can improve its stability.

[PE1-21] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Preparation and in vitro release of LHRH agonist containing poly(d, l-lactide-co-glycolide) microspheres

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Triptorelin, goserelin, and leuprolide are luteinizing hormone-releasing hormone (LHRH) agonists widely used for the treatment of prostate cancer and endometriosis. A mixed oil in water solvent extraction/evaporation method with exactly same manufacturing parameters was employed to fabricate LHRH-agonists containing microspheres using 50:50 poly(d,l-lactide-co-glycolide) (PLGA). Encapsulation efficiency, yield, and size distribution were similar. SEM observation also showed similar internal and external morphologies. However, in vitro release test (33 mM phosphate buffer, pH 7.0 at 37°C), showed quite different profiles. Release rate of leuprolide was fastest and that of triptorelin was slowest. Further extensive studies including in vitro release tests in various different conditions and in vivo release efficacy should be followed to correlate well the in vitro-in vivo release profiles.

[PE1-22] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Direct Determination of the Actual Drug Content Incorporated into PLGA Microspheres by MALDI-TOF Mass Spectrometry

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Matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS) has been evaluated for direct determination of drug content incorporated into poly(D,L-lactic-co-glycolic acid) (PLGA) microspheres. Biodegradable PLGA (50/50) microsphere containing leuprolide acetate as