varied between 0.2 and 2㎛ by means of adjusting the system pressure and/or temperature. The proposed method is attractive as the basis of a new process for the preparation of drug delivery system.

[PE1-18] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Formulation of microemulsion-based hydrogel containing prostaglandin E1 ethyl ester

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Prostaglandin E1 analogues, especially prostaglandin E1 ethyl ester(PGE1-EE), have been focused as a therapeutic agent for erectile dysfunction due to its higher skin penetration property than that of PGE1. A microemulsion-based hydrogel(MHG) containing PGE1-EE was formulated through phase diagram with polyoxyl castor oils, EtOH and medium chain triglycerides(MCTs). In vitro drug penetration characteristics of MHG was investigated using Franz diffusion cell and receptor solution (pH 7.4 PBS : EtOH = 90 : 10) containing PGE1 was assayed by validated HPLC method. PGE1-EE was stable in receptor solution for 6hrs but PGE1-EE was cleaved to PGE1 by skin esterase during penetration. Microemulsion promoted penetration of PGE1-EE, showing the result of 2~3 times higher penetration than that of control hydrogels, e.g. sodium alginate gel. Finally, in vivo pharmacodynamic effects of MHG, such as ICP(Intra Cavernosal Pressure), duration of erection, increment of penile length were investigated with wild male cats.

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

Formation of peptide adduct during in vitro release of GHRP-6 containing poly(dl-lactide-co-glycolide) microspheres

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GHRP-6 is a synthetic growth hormone-releasing hexapeptide (His-DTrp-Ala-Trp-DPhe-Lys-NH2) which elicits a dosage-related release of growth hormone in vitro and in vivo. GHRP-6 was encapsulated into 50:50 poly(d,l-lactide-co-glycolide) (PLGA) microspheres using oil in water solvent extraction/evaporation method. Spherical microspheres with smooth surface structures were obtained with high encapsulation efficiency. In vitro release test was carried out in 33 mM phosphate buffer, pH 7.0 at 37°C. During in vitro release test, several degradation and/or adduct peaks were detected and some of them were identified by LC/MS/MS. Glycolic acid and lactic acid attributed to the erosion of PLGA during the incubation seemed to be conjugated to the free amino group of N-terminal His and epsilon amino group of Lys5 of GHPR-6. These results indicate that peptide adduct formation should be considered when planning to develop a sustained release peptide formulation using PLGA polymers.

[PE1-20] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Increased Stability of Recombinant Human Epidermal Growth Factor by Poly(Ethylene Glycol) Conjugation

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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