a model system was prepared by a solvent extraction/evaporation method. The leuprolide-loaded PLGA microsphere was dissolved by acetonitrile containing 0.1% TFA, and then content of leuprolide in the microsphere was directly determined by MALDI-TOF MS using alpha-cyano-4-hydroxy cinnamic acid as a matrix. Triptorelin was used as an internal standard. The relative peak height of leuprolide was calculated and plotted versus its contents. This plot showed linearity between 5 and 500 ug/mL of leuprolide and the precision was found to be in the range of 0.3 to 2.3% relative standard deviation. The results were compared to the data determined by capillary electrophoresis and HPLC. This new approach was found to be sensitive, convenient, and reliable. It is expected to be applied to various related studies including stability, peptide/protein-polymer interaction, and in vitro release study. It also provides the merits of speed, high resolution, small sample requirements, ease of determination, and simple data manipulations over other analytical tools.

[PE1-23] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Stability study of PEGylated Salmon Calcitonin

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PEGylation of salmon calcitonin (sCT) has been studied to improve the bioavailability by increasing the stability of sCT. PEGylated sCT was obtained by conjugation with succinimidyl carbonate-polyethylene glycol (sc-mPEG, m.w. 5,000). Mono- and di-PEGylated sCTs were separated by GFC and showed molecular ion peaks at m/z 8339 and m/z 13274 by MALDI-TOF/MS. Mono-PEGylated sCTs were further separated into three positional isomers (M1-M3) by RP-HPLC. By LC-MS/MS analysis of tryptic digests, PEGylated sites of three isomers were identified. That is, the position of PEGylation in M1, M2 and M3 was Cys1, Lys18 and Lys11 of sCT, respectively. HPLC-UV analysis of the degradation of mono-PEGylated sCTs and sCT showed that mono-PEGylated sCTs were chemically more stable than sCT and M1 was the most stable among three mono-PEGylated sCTs. The metabolic stability study of sCT and N-terminus modified mono-PEGylated sCT using purified lysosomal enzymes, cathepsin B1 and D indicated that mono-PEGylated sCT, M1 was more stable than sCT against purified lysosomal enzymes.

[PE1-24] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Preparation and Evaluation of Prostaglandin E1 (PGE1) Intraurethral Solutions for Erectile Dysfunction

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Preparation and Evaluation of Prostaglandin E1 (PGE1) Intraurethral Solutions for Erectile Dysfunction. Byoung-Ju Park*, Seung-Ho Lee, Qi-Zhe Quan, Han-Gon Choi, Jong Dal Rhee and Chul Soon Yong.

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Purpose. To prepare and evaluate PGE1 intraurethral solutions. Methods. PGE1 intraurethral solutions were prepared with polyethyleneglycol 400, propylene glycol monolaurate, and benzyl alcohol. The stability of PGE1 in intraurethral solution was investigated using a validated HPLC technique. In pentobarbital anesthetized wild cats, increases in intracavernous pressure(ICP), penile length and duration of erectile response were determined after application of PGE1 intraurethral solution. For the possible urethral mucous irritation, histological examinations were also performed. Results. It was found that PGE1 intraurethral solution was stable over 1 yr at 4℃. ICP of intraurethral solution(83.7± 15.2mmHg) was less than that of intracavernosal injection 1g of PGE1(102.5±17.7mmHg) as control.

The normal penile length(18±5mm) was increased to 39±8mm after application of intraurethral solution, which was similar to that after intracavernosal injection 1g of PGE1(38±6mm). Duration of erectile response of intraurethral solution(287±34min), however, was much longer than that of control (32±8min). Histological examination revealed no or very little irritancy. Conclusions. PGE1 intraurethral solution for erectile dysfunction could be developed employing feline erection model.

[PE1-25] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

The investigation on adhesive properties of an anti-immflammatory plaster containing ketoprofen

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This study was conducted to get the available information that could be applied into development of a drug-in-adhesive (DIA) type plaster containing ketoprofen (KP). When an anti-immflammatory DIA type plaster is developed, we should consider several properties such as drug absorption, drug stability, skin irritation, appearance, and adhesion on skin. Because plasters are applied on skin for long time (above 12 h), adhesive property is very important factor in DIA-plaster formulation. Actually, main patient's discontent on commercial products is that plasters do not show acceptable adhesive property as good as a patient is satisfied. Therefore, it is required to develop a plaster with reasonable skin adhesion. DIA-type plaster has an adhesive-layer consisted of adhesive and additives such as drug and enhancers, etc. These additives usually convert original PSA property to unwanted direction. Thus, it is difficult to control the adhesive property of an adhesive-layer. Additionally, even if same adhesive-layer formulation is applied to various backings, one final plaster adhesive property is different with one another. In this study, adhesive properties of each DIA formulation containing KP were observed according to the combination of an acrylic adhesive, KP, penetration enhancers, and backings. The adhesive property of a formulation was evaluated by in-vitro test such as 180o peel adhesion, ball tack, and shear test.

[PE1-26] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Evaluation of Disintergration Test of Soft Capsules

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The crosslinking process in gelatin causes formation of a swollen, rubbery, water insoluble gelatin resulting in increasing disintegration time. The effect of crosslinking and disintegration medium on dissolution time and the effect of disintegration apparatus on disintegration of soft capsules exceeding 20.0 mm in diameter were studied.
Soft capsules were filled with three solutions of aqueous formaldehyde in PEG(0.05, 0.3, 0.5 %), stored at ambient conditions for 96 hr, emptied, disintegration tested scanned in NIR spectrophotometer. The more increased concentration of formaldehyde, the more increased disintegration time in water, KP disintegration medium I and USP simulated gastric fluid. But in USP simulated gastric fluid, the differences of disintegration time among crosslinking amounts were less than in water.
In the case of marketed samples, the differences of disintegration time among test mediums were not different and accepted by KP disintegration test criteria.
We conducted disintegration test with KP apparatus and USP apparatus B in the soft capsules of which diameter was over 20.0 mm. The disintegration time between KP apparatus and USP apparatus