[PE1-31] [10/19/2001 (Fri) 09:00 ~ 12:00 / Hall D]

Direct Determination of Salmon Calcitonin Incorporated into PLGA Microsphere 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 as a reliable and efficient method for the determination of salmon calcitonin (sCT) incorporated into microspheres. Biodegradable poly(lactic-co-glycolic acid) (PLGA, 50/50) microsphere containing sCT was prepared by a solvent extraction/evaporation method. The PLGA microsphere containing sCT was dissolved by acetonitrile containing 0.1% TFA, and then content of sCT in the microsphere was directly determined by MALDI-TOF MS with the precision in the range of 2.3 to 5.4% relative standard deviation. Human parathyroid hormone (1-34) was used as an internal standard. The in vitro release profile of sCT by MALDI-TOF MS corresponded well to the data determined by capillary electrophoresis and HPLC with sample extracted using organic solvent. This new approach was found to be convenient and reliable. It is expected to be applied to quantitate other peptides or proteins from microsphere. It provides the merits of speed, high resolution, small sample requirements, ease of determination, and simple data manipulations over other analytical tools.

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Application of PEG-coated liposomes for oral delivery of peptide: Effect of liposome composition on the gastrointestinal absorption of rhEGF

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The purpose of the present study was investigated possibility of oral delivery of a peptide drug, recombinant human epidermal growth factor (rhEGF) as a model drug. PEG-coated liposome with rhEGF was prepared and evaluated for improving gastrointestinal stability and absorption. Encapsulation of rhEGF into liposomes suppressed the degradation of rhEGF in the Caco-2 cell homogenats compared with rhEGF solution. The flux of DPPC liposome across Caco-2 cell monolayer from the apical to basolateral side was 3 times greater than that PC liposome and solution, whereas the flux of PC liposome and soution were without significant differences. After oral administration liposomes and rhEGF solution in rats, the AUC, C_{max} and T_{max} of DPPC and PC liposome were increased compared with rhEGF solution. These results indicated that PEG-coated liposomes could be developed as a oral delivery system for rhEGF with improved encapsulation efficiency. Moreover, it is suggested that the DPPC liposome coated with PEG might have a potential as oral delivery systems for other protein and peptide drugs.

[PE1-33] [10/19/2001 (Fri) 09:00 ~ 12:00 / Hall D]

The effect of NPE, hormone distrupter, on the barrier function of epithelial membranes

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Nonylphenol ethoxylate(NPE) is a widely used surfactant and known hormone disrupter. In previous study, NPE is readily absorbed and rapidly removed from the body by gastrointestinal and renal excretion routes. P-glycoprotein(P-gp) that confers cellular multidrug resistance to many cytotoxic compounds may be an ideal candidate for this excretory role and can transport nonionic detergents like NPE. NPE similar to Tergitol NP-9 is identified in human urine. It was reported that high concentration of NPE might enhance the membrane transport due to cell membrane damage.However the effect of NPE on epithelial membranes is not yet studied in lower concentrations may be similar to the physiological level. In this study, the effect is examined using the Caco-2 and LLC-PK1 cell lines. TEER was also measured to know the effect of NPE on the tight-junction with EVOM.Caco-2 and LLC-PK1 cells were grown to confluency on a polycarbonate membrane inserts to permit loading of paracellular markers(mannitol and inulin), a transcellular transport drug(Ketoprofen), and P-gp substrates(Rhodamine 123 and Daunomycin) in the presence of NP-9 and other NPE. When NPE was put either in the apical or basal side, TEER was significantly decreased and the transport of mannitol, a paracellular marker, was increased and these changes were reversible in 2hrs. There was no significant change in the transport of Ketoprofen. P-gp induction by NPE pretreatment didn't affect the transport of P-gp substrates. In conclusion, the effect of NPE on the barrier function of epithelial membranes is not by P-gp induction but by tight junction opening.

[PE1-34] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Agitation condition does not affect the correlation between in vitro permeability and in vivo bioavailability of drugs.

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It has been well-known that a strong correlation is observed between in vitro permeability and in vivo bioavailability. But its curve was different in each labs. The permeability of drugs across Caco-2 cell monolayers have been measured and varied under each different agitation condition. Also there is a report that the permeability of some hydrophobic drugs were increased by the increasing rate of agitation. So we studied the effect of the agitation on the permeability of each drug and the relationship between the difference of Papp by the agitation(△Papp) and the hydrophobicity of drugs. Also we investigated the effect of △Papp on the correlation curve between in vitro permeability and in vivo bioavailability. The transport of drugs were examined under two different agitation condition(60 rpm, 0rpm, respectively) using Caco-2 cell monolayers.
As a result, permeability(Papp) of propranolol, phenylpropanolamine and YH-439 was slightly increased by the agitation. But, Papp of mannitol, cimetidine, ranitidine, hydrocortisone, loxoprofen, theophylline, tacrine and benzylpenicillin was not affected by the agitation. Also △Papp was not related with hydrophobicity of drug and the agitation didn't change the curve indicating the relationship between the permeability and the bioavailability.
In conclusion, it may not be necessary to consider the effect of agitation when we intend to predict in vivo bioavailabililty from the permeability of drugs across Caco-2 cell monolayer.

Poster Presentations - Field E2. Pharmacokinetics

[PE2-1] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Population pharmacokinetics of aceclofenac in Korean healthy subjects using NONMEM