directions(the apical-to-basolateral (A-to-B), basolateral-to-apical(B-to-A)),suggestive of a passive diffusional process. However, the transport mechanism of berberine is not yet studied using in vitro cell line . Also in another previous study, berberine modulates expression of P-glycoprotein. This result implies that berberine may be transported in carrier-mediated system. Therefore we elucidated the transport mechanism of berberine using in vitro absorption model, Caco-2 cell monolayers.
Caco-2 cells were grown to confluency on a polycarbonate membrane inserts to permit loading of berberine on either the apical or basolateral side of the cell monolayer. we performed concentration and temparature dependency and inhibition studies.
Polarized transport of berberine was observed with B-to-A permeability being 20-fold greater than A-to-B permeability. B-to-A transport of berberine was concentration and temperature dependent, and was reduced by P-glycoprotein inhibitor such as verapamil.
In summary this study demonstrated that berberine is secreted across the Caco-2 cell monolayers via P-glycoprotein-mediated efflux. Thus this study provide that berberine can be substrates of P-glycoprotein.

[PE1-27] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Preparation and properties of mono-PEG modified interferon-a having different molecular weight of the PEG portion

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Pegylation, conjugation process with poly(ethylene glycol) (PEG), may be an effective method for delivering therapeutic proteins and modifying their pharmacokinetic properties. PEG-protein conjugates exhibit: (1) enhanced solubility (2) decreased antigenicity (3) decreased proteolysis and (4) reduced rate on kidney clearance. These effects are mostly dependent on the molecular weight of the attached PEG. The attachment of PEG to the proteins might result in decreasing the biological activity by masking the active site of protein.
The present studies investigated the effects of PEG molecular weight size on the properties of PEG modified interferon-a (IFN-a). Mono-PEGylated IFN-as were prepared by conjugation with various PEGs of different size and purified. Their physico-chemical properties, biological activities and the pharmacokinetics were examined.
The results showed that the covalent attachment of PEG into IFN-a did not change the protein conformation, and endowed with increased stability against temperature and enzyme digestion. Depending on the increase in PEG size, their biological activity decreased due to the stearic hindrance, whereas phamacokinetic parameters such as circulating half-life increased. And it is expected that these circulating half-life extension would give rise to increase in overall in vivo biological activity of PEGylated-IFN-a even though its bioactivity itself decreases.

[PE1-28] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Sustained Release of Recombinant Human Growth Hormone From Biodegradable Polymer Matrices

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Sustained-acting formulations for recombinant human growth hormone (rhGH) were prepared by a phase separation (dispersion/solvent evaporation-extraction) method from hydrophilic 50:50 poly(D,L-lactide-co-glycolide) (PLGA) polymers, MW 5 000 and MW 10 000.
The rhGH-loaded PLGA 5K (Formulation I) and 10K (Formulation II) microspheres showed similar particle