protein/weight microspheres), whereas acidic proteins such as ovalbumin, bovine serum albumin and human growth hormone were incorporated less than 1%. As the pH of the incorporation medium decreases, incorporation capacity was also decreased. Ionic strength and temperature of the incorporation media were also determined as critical factors of the incorporation capacity. These results suggest that the incorporation is mainly caused by ionic interaction between free carboxyl group of the polymer and positive charges of the basic proteins. Conclusively, this non-invasive method of encapsulation of protein into biodegradable PLGA polymeric matrix can be successfully applied to basic proteins with high drug loading.

[PE1-26] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

THE INTESTINAL ABSORPTION OF HEPARIN DISACCHARIDE USING SEVERAL ABSORPTION ENHANCERS IN CACO-2 MONOLAYERS

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The effect of several absorption enhancers was studied using the Caco-2 cell monolayers on the intestinal absorption of heparin disaccharide, a repeating unit of heparin of which the structure is highly charged and heterogeneous. The absorption enhancing activity of a series of compounds was determined by the changes in transepithelial resistance(TEER) and the transport amount of heparin disaccharide across the Caco-2 cell monolayer by HPLC using SAX column. Among the absorption enhancers, dipotassium glycyrrhizinate, 18β- glycyrrhetinic acid, caprate and taurine decreased TEER and increased the permeability of heparin disaccharide in a dose- and time-dependent manner without severe cytotoxicity. Dibutyryl adenosine 3',5'-cyclic monophosphate, which is an endogeneous cAMP analogue, decreased TEER and increased the transport of heparin disaccharide by almost 10% for control without any toxicity. The combination of sodium deoxycholate and dipotassium glycyrrhizinate or 18β- glycyrrhetinic acid or taurine made the absorption more effective than they were used alone. Our results indicate that these absorption enhancers can widen the tight junction, which is a paracellular absorption route of the hydrophilic compounds, such as heparin, chondroitin sulfate and protein drugs. The oral administration of heparin as well as heparin oligosaccharides may be possible using the selective enhancers together.

[PE1-27] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Preparation and evaluation of microspheres containing GFP for oral vaccine delivery system

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In order to design the oral vaccine delivery system, we prepared the alginate microspheres containing GFP (Green Fluorescent Protein) as a model drug by spraying method.
To optimize the preperation conditions of microspheres, we investigated the effects of various parameters including nozzle pressure, nozzle pening angle, and concentrations of sodium alginate and calcium chloride . The prepared microspheres were evaluated by measuring their size and loading efficiency, and morphology.
The particle size of microspheres was affected by the concentration of sodium alginate and calcium chloride, and nozzle opening angle, and nozzle diameter. As the concentration of sodium alginate increased, GFP loading efficiency and particles size of microsphere also increased. But more than 1.5%(w/v) sodium alginate solution too viscous, So it was difficult to spary the solution, and particles shape was not spherical.The pressure over 2kgf/cm2 didn't affect the size of particles.
As a result,the spraying method enabled us to prepare microspheres for oral vaccine delivery

system. In this study, the better loading efficiency and more spherical particles were shown when using concentration of sodium alginate 1%(w/v).

[PE1-28] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Formulation of PLGA microspheres containing ovalbumin and their immunogenicity in BALB/c mice

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A model protein, ovalbumin(OVA), was entrapped in poly(lactide-co-glycolide) polymers to demonstrate the effect of formulation conditions and the microparticles were administered subcutaneously to female BALB/c mice as a single dose. Microspheres were prepared by a W/O/W multiple emulsion solvent evaporation method and their in vitro characterization was performed. The same microspheres were used in a series of in vivo studies to evaluate the immune response after single subcutaneous injection. Microspheres were characterized for particle size, encapsulation efficiency, morphology, gel permeation chromatography and in vitro drug release in a PBS solution (pH 7.4, 37 ℃). Protein denaturation was evaluated by size exclusion chromatography, SDS-PAGE and isoelectric focusing and circular dichroism. The primary IgG antibody responses obtained with OVA microparticles were compared to those obtained with OVA solution and OVA absorbed to alum. Low loading efficiencies of less than 20% were observed and in vitro release of OVA showed the burst effect in all batches of different microspheres, followed by gradual release over the next 6 weeks. The structural integrity of OVA was unaffected by the formulation process by this method and enzyme-linked immunosorbent assays demonstrated that the single subcutaneous administrations of ovalbunim-loaded PLGA microspheres induced good antibody responses. These microcapsules providing the controlled release of antigens may be valuable in advanced vaccine formulations for the parenteral protein drug delivery.

[PE1-29] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Effect of temperature and oleic acid on the electrical properties of skin

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Electrically, skin is usually represented as a parallel combination of capacitance and resistance. From the stripping experiments, it has been shown that the stratum corneum is mainly responsible for the electrical properties of the skin. The capacitance is believed to originate from the lipid matrix-keratin cell complex of the stratum corneum; the resistance appears to be primarily associated with the ion conducting pores in the skin. These pores are mainly locating at appendages on skin, such as hair follicles and sweat glands, though there are some unidentified pathways whose contribution to the flow of current is dependent on the magnitude of current. Impedance measurements have shown that resistance and/or capacitance may be affected by various factors such as ionic strength of the skin-bathing medium, pH and chemical treatment. The effect of iontophoresis on resistance and capacitance has also been studied.

In order to optimize or maximize the benefits from iontophoresis, it is very important to understand the electrical properties of the skin. In this work, we have measured the electrical impedance of skin as a function of frequency and the Nyquist plot was carried out. Resistance (R) of skin was determined from this plot by multiplying the real part value at frequency (f_c) giving the highest imaginary part value by two. The capacitance (C) was calculated from the equation $C=\tan\Theta/(2\pi f_c R)$, where Θ is shift in phase of the sinusoidal current. Using hairless mouse skin, the effect of temperature (between 5 and 30 ℃) and oleic acid treatment on these properties were evaluated.