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[Lab. of Pharm. Engineering]

**Pulmonary Delivery of Insulin with Nebulized DL-Lactide/Glycolide Copolymer (PLGA) Nanospheres to Prolong Hypoglycemic Effect.**

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Insulin loaded PLGA nanospheres having weight mean diameters of 400 nm were prepared by the modified emulsion solvent diffusion method in water. Eighty five percent of the drug was released from the nanospheres at the initial burst, followed by prolonged releasing of the remaining drug for a few hours in saline at 37 °C. The aqueous dispersions of PLGA nanospheres were nebulized by a sieve type ultrasonic nebulizer to discrete droplets of 5-7 μm in mean diameters, 75% of which were successfully delivered into the alveolar fraction in a cascade impactor inhaled at 28.3 L/min. The nebulized PLGA nanospheres were administered via a spacer by using a constant volume respirator into the trachea of the fasted guinea pig for 20 min. After the administration of 3.9 I.U./kg insulin with the PLGA nanospheres, the blood glucose level was reduced significantly and the hypoglycemia was prolonged over 48 h, compared to the nebulized aqueous solution of insulin as a reference (6 h).

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[Lab. of Pharm. Engineering]

**Comparison of Lipiodol Water-in-Oil-in-Water Emulsion and Oil-in-Water Emulsion: Acute Toxicity and Deposition in Liver after Hepatic Arterial Administration in Rats.**

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Lipiodol is an oily contrast medium widely used as an embolizing material for transcatheter arterial embolization (TAE) therapy, an effective method for treating unresectable hepatocellular carcinoma. We investigated the acute toxicity and deposition in the liver of lipiodol water-in-oil-in-water (w/o/w) emulsion encapsulating epirubicin hydrochloride after hepatic arterial administration to rats, and compared results with those of the oil-in-water (o/w) emulsion conventionally used for TAE therapy. The concentration of epirubicin hydrochloride in the liver was increased and its residence was prolonged by encapsulating it in the w/o/w emulsion membranes. The toxic effects of epirubicin hydrochloride and lipiodol on the normal hepatic cells were reduced, resulting in a decrease in both glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) activity.

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[Lab. of Pharm. Engineering]

**Mixed Base of Hydrophilic Ointment and Purified Lanolin to Improve the Drug Release Rate and Absorption of Water of Minocycline Hydrochloride Ointment for Treatment of Bedsores.**

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A desired ointment bases for better treatment of bedsores was developed to improve the release rate of minocycline hydrochloride (MH) and the water absorption capacity using various types of hydrophobic to hydrophilic ointment base. The influence of purified lanolin (PL) on the release behavior of MH from hydrophilic ointment (HO) base was primarily focused on. It was found that the release rate of drug increased with increase in the hydrophilicity of the base. A linear correlation between the apparent release rate-constant of drug from the HO and PL mixed ointment base at various combination ratios and the elution of ointment base was noted. The HO ointment base containing 30% PL had the highest apparent release rate constant of MH. The mixed ointment base with the lowest viscosity showed the highest absorption of water and elution of ointment base.

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[Lab. of Pharm. Engineering]

**Prolonged Circulation Time of Doxorubicin-loaded Liposomes Coated with a Modified Polyvinyl Alcohol after Intravenous Injection in Rats.**

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The purpose of this study was to evaluate the functions of a modified polyvinyl alcohol (PVA-R), which has a hydrophobic moiety, as a coating material for liposomes to be loaded with the anticancer drug, doxorubicin. The size-controlled liposomes were prepared by the hydration method followed by extrusion. Drug encapsulation and surface modification with polymers (PVA and PVA-R) were carried out simultaneously using a modified pH gradient method. The effects of polymer coating on the behavior of the liposomes in vivo were evaluated by measuring the circulation time and biodistribution of the drug after i.v. administration of the liposomal drug in rats. The PVA-R-coated liposomes showed a more prolonged circulating time for the drug with less uptake by the reticuloendothelial system after i.v. administration in rats, compared with non-coated liposomes.