

[*Drug Delivery System*, **14**, 387-394 (1999)]

[Lab. of Pharm. Engineering]

Formulation and in vivo evaluation of w/o/w emulsion encapsulating Epirubicin hydrochloride for the transcatheter arterial embolization therapy for hepatocellular carcinoma.

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We developed a novel w/o/w emulsion formulation containing medium-chain triglyceride(MCT) as an oily phase and Imeron 300 as an aqueous phase with functions of embolizing and sustaining drug-release in trans-catheter arterial embolization(TAE) therapy for hepatocellular carcinoma. When normal rats were treated with the hepatic arterial injection of the MCT w/o/w emulsion encapsulating EPI, there was non dysfunction trans aminase of GOT and GPT in normal liver. The increased drug retention in liver after the arterial administration of EPI in a w/o/w emulsion form in rats bearing a hepatic tumor revealed the usefulness of this device for the drug targeting to the hepatic tumor.

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[Lab. of Pharm. Engineering]

Validation of a Microwave Sterilizer for Injection Ampules.

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A program for validating the microwave sterilizer, which is a new type of sterilizer, was established and implemented. This program includes the following tests specific to microwave sterilizers: the internal pressure strength of ampules, the acceptable range of sterilizing temperature, performance and calibration of the infrared thermometer and the plane blackbody, maintaining of sterilizing temperature, the processing speed (sterilizing time), the unacceptable ampules selection mechanism, microwave leaks, and a microbiological challenge test of the ampule head space using a biological indicator. Injectable preparations of mecobalamin and diprophylline were used as models for validation of the microwave sterilizer. The bioburden approach was used for injectable mecobalamin preparation, and the over-kill approach was used for injectable diprophylline preparation. The basis for practical use of this microwave sterilizer has been confirmed by the establishment and implementation of this validation program.

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[Lab. of Pharm. Engineering]

Compaction Properties of Composite Particles Consisting of Lactose with Sodium Alginate Prepared by Spray-Drying.

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Composite particles of lactose with a small amount of sodium alginate were prepared by spray-drying (SD) in an effort to improve the compactibility of the polymer for direct compression. The tensile strength of compacts formed from the SD composite particles containing sodium alginate ($\leq 10\text{wt}\%$) was as high as that of spray-dried amorphous lactose. The improved compaction was attributed to the higher relaxation pressure and lower elastic recovery of the composite particles compared with α -lactose monohydrate. However, increasing the sodium alginate content of the SD composite particles above 10wt% led to a marked reduction in the tensile strength of the resultant tablets. Scanning electron micrographs revealed that composite particles with a good compactibility fused totally in the tablets while composite particles containing 15% or more sodium alginate retained their shape, even after compression.

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[Lab. of Pharmaceutics]

The Cleavage Site Specificity of Human Prostate Specific Antigen for Insulin-like Growth Factor Binding Protein-3.

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The cleavage site of human insulin-like growth factor binding protein-3 (hIGFBP3) by urinary prostate specific antigen was examined. hIGFBP3 was incubated with urinary prostate specific antigen (PSA) and its proteolyzed fragments were separated by a reversed phase HPLC followed by N-terminal amino acid sequence analysis, demonstrating that the cleavage mainly occurred at Tyr-159. The syntetic peptide including Tyr-159 was also cleaved at the same site, although its reaction rate was relatively low. These results indicate that hIGFBP3 is specifically cleaved at Tyr-159 by PSA. hIGFBP3 was previously reported to be cleaved at five sites including Arg-97, Arg-132, Tyr-159, Phe-173 and Arg-179 by another group, however, PSA preparation is possibly contaminated by trypsin-like protease. In contrast, our purified urinary PSA had only a chymotrypsin-like activity, demonstrating that PSA has the high substrate specificity for hIGFBP3.