[*J. Org. Chem*, **63**, 9794-9800 (1998)] [Lab. of Pharm. Anal. Chem.]

Importance of Substituent Intramolecular Charge-transfer Effect on the Molecular Conformation of Diphenyl Ethers.

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The conformational control of diphenyl ethers by the electronic effect of substituents has been demonstrated by spectral measurements and their analyses based on CNDO/S-CI calculations, and by minimum-energy optimization using the method of ab initio MO calculations with 6-31G(d) basis sets. Introduction of an electron-accepting substituent at the para-position of either of diphenyl ether fixes the oxygen-bridged phenyl rings in the stable skew form though unsubstituted diphenyl ether adopts the non-rigid form. The strong electron-donating substituent attached at the para-position allows the diaryl ether moiety to be rigid in the preferable skew or twist conformation. The intramolecular charge-transfer interaction caused by strongly interacting substituents is important to govern the conformation of diphenyl ethers, and the substituent attached at para-position of either of diphenyl ether can control the conformation of whole molecule, depending on the electron donating/accepting character of the substituent.

[*Europ. J. Pharm. Biopharm.*, **45**, 41-48 (1998)] [Lab. of Pharm. Engineering]

Properties of a Peptide Containing DL-Lactide/glycolide Copolymer Nanospheres Prepared by Novel Emulsion Solvent Diffusion Methods.

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Novel emulsion solvent diffusion (ESD) methods in water or oil were developed to prepare the peptide (TRH and elcatonin)-loaded PLGA nanospheres, via the coprecipitation of drug and polymer in the emulsion droplets induced by the diffusion of solvent. The content and recovery of the peptide and nanospheres prepared by the ESD method in oil were superior to those of nanospheres prepared using other methods. The drug release properties from nanospheres depended on their preparation processes. The rate of the nanospheres prepared by the ESD method was determined by the diffusion of drug in the rigid matrix structure. The drug release behavior of nanospheres prepared by the phase separation method exhibited a triphasic release pattern.

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Physical Stability of Size Controlled Small Unilamellar Liposomes Coated with a Modified Polyvinyl Alcohol.

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The purpose of this work is to evaluate the improvement in physical stability of polymer coated liposomes. Small unilamellar liposomes (DMPC: DCP: Chol. = 7:3:1) 100nm in diameter were coated with polyvinyl alcohol (PVA) and a modified PVA, which bears a alkyl chain at the end of molecule (PVA-R). The amount of PVA-R coating increased with increasing polymer concentration. PVA-R coated liposomes showed almost complete retention of particle size and a larger entrapped content during freeze-drying and rehydration, while a dramatic increase in particle size and a reduction in the percentage entrapped, were observed for non-coated and PVA-coated liposomes. Aggregation of liposomes in calf serum was effectively prevented by coating liposomes with PVA-R.

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Particle Design of Wogon Extract Dry Powder for Inhalation Aerosols with Granulation Method.

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Aerosolization of Wogon extract powder (WEP) is difficult due to its strong adhesiveness to the inhalation device (Spinhaler) on emitting. To improve inhalation property, WEP was granulated by slugging, tumbling and agitation methods. The inhalation properties were measured in vitro with a cascade impactor and a twin impinger. The inhalation behaviors of granules were determined by granulation method employed and inhalation conditions such as inhaled air flow rate. It was found that a key factor determining the inhalation property was the mechanical strength and the particle size of the granules. A proportional correlation between the residual fraction in the inhalation device and the respirable fraction (RF) of the cascade impactor or the twin impinger was observed. Tumbling granulation method provided the largest EI, and improved the inhalation property of original WEP.