〔Chem. Pharm. Bull., **40**, 196-201 (1992)〕 [Lab. of Pharm. Engineering]

Contorol of Prolonged Drug Release and Compression Properties of Ibuprofen Microsponges with Acrylic Polymer, Eudragit RS, by Changing Their Intraparticle Porosity.

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Prolonged-release spherical micro-matrices of ibuprofen with Eudragit RS were prepared using a novel emulsion-solvent diffusion method. Those particles were termed "microsponges" due to their characteristic sponge-like texture and unique dissolution and compression properties, unlike conventional microcapsules or microspheres. The internal porosity of microsponges could be easily controlled by changing the concentration of the drug and the polymer in the emulsion droplet (ethanol). With lower concentration of ibuprofen in the ethanol, the resultant microsponges had a higher prosity, about 50 %. The drug release rate from the microsponges was interpreted by the Higuchi model of spherical matrices, which depended only on their internal porosity of the microsponges when size distribution and drug content were the same. The tortuosities in the microsponges were found to be almost constant (3-4) irrespective of porosity, suggesting the same internal texture. Microsponge compressibility was much improved over the physical mixture of the drug and polymer owing to the plastic deformation of their sponge-like structure.

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Preparation of Powdered Phospholipid Nanospheres by Fluidized-Bed Granulating in an Aqueous System with Sugars.

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Phospholipid nanosphere dispersions incorporating a lipophilic drug were prepared by the heating method. Prepared dispersions were powdered by depositing them on sugar nuclei in a fluidized-bed granulator in an aqueous system. Resultant free-flowing powders, which were agglomerates of sugar with phospholipid, reproduced phospholipid nanosphere dispersions when rehydrated with water. Incorporation of a lipophilic drug, *e.g.*, tocopherol, into the nanospheres or increasing of phospholipid concentration in the formulation increased the sizes of rehydrated nanospheres compared to the orignal dispersion before powdering due to the fusion or aggregation of the nanospheres. Proper selection of sugar nuclei, decreasing the sizes of original phospholipid nanospheres for powdering and addition of polyhydric or sugar alcohols into the sprayed dispersion, however, significantly reduced the aggregation of rehydrated nanosphere. All procedures from the preparation of the original nanosphere dispersion to its powdering were performed in an aqueous system without use of any organic solvent.

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Hollow Microspheres for Use as a Floating Controlled Drug Delivery System in the Stomach.

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Hollow microspheres (microballoons), loaded with drug in their outer polymer shells, were prepared by a novel emulsion-solvent diffusion method. The ethanol : dichloromethane solution of drug (tranilast or ibuprofen) and an enteric acrylic polymer were poured into an agitated aqueous solution of polyvinyl alcohol that was thermally controlled at 40 ℃. The gas phase generated in the dispersed polymer droplet by the evaporation of dichloromethane formed an internal cavity in the microsphere of the polymer with the drug. The drugs incorporated in the solidified shell of the polymer were found to be partially or completely amorphous. The flowability and packability of the resultant microballoons were much improved compared with the raw crystals of drug. The microballoons floated continuously over the surface of acidic dissolution media containing surfactant for>12 h *in vitro*. The drug release behavior of the microballoons was characterized as an enteric property, and drug release rates were drastically reduced depending on the polymer concentration at pH 6.8.