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[Lab. of Pharm. Engineering]

### **A Study of Microwave Sterilizer for Injection Ampules (No. 5): Evaluation of Sterilization Effect on the Head Space of Ampules.**

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The heating characteristics, heating parameters, and sterilizing effect of a new type of sterilizer (microwave sterilizer) for the head space of ampules were investigated. A thermographic analysis of the temperature of the head space of the ampules revealed that this system can heat both the solution and the head space to the same level of accuracy, and that the neck of the ampules is a cold spot when they are heated with this device. The two hot-air heaters were used for heating the head space of the ampules, and the microwave output was used for heating the solution within them. Multiple regression analysis was conducted to examine the relationship between the temperature of the cold spot of the head space and these three parameters. This analysis yielded the liner relationship ( $R = 0.998$ ). The following biological indicators were put into the cold spot of the ampule head to evaluate the sterilizing effectiveness of this device: spores of *Aspergillus niger*, *Bacillus subtilis* and spores of *Bacillus steamthermophilus*.

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[Lab. of Pharm. Engineering]

### **The Development of an Aqueous Polymeric Enteric Coating System with Hydroxypropylmethylcellulose Phthalate Nanoparticles.**

Hiromitsu YAMAMOTO, Ikumasa OHNO, Hirofumi TAKEUCHI and Yoshiaki KAWASHIMA\*

A new aqueous polymeric enteric coating system was developed with the aqueous dispersions of hydroxypropylmethylcellulose phthalate (HPMCP) nanoparticles prepared by the emulsion solvent diffusion method. The average diameter of HPMCP nanoparticles was 120nm. The enteric coating of riboflavin granules with the present system was successfully conducted using a fluidized bed coating. To obtain satisfactory acid resistance of the coated granules with HPMCP nanoparticles, the coating film thickness needed to be 10  $\mu\text{m}$  or more. The coating amount required to obtain satisfactory acid resistance of the coated granules with HPMCP nanoparticles was found to be much smaller than with the pulverized HPMCP available on the market. This is because the coating film with HPMCP nanoparticles was closer and more uniform than that with pulverized HPMCP particles. The equation to predict the amount of polymer required for satisfactory enteric coating was proposed in the present study.

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[Lab. of Pharm. Engineering]

### **Preparation of Spherically Granulated Crystals of Waxy Drug (Tocopherol Nicotinate) for Direct Tableting by Spherical Crystallization Technique.**

Hiromitsu YAMAMOTO, Yasuyo SAKAI, Tomoaki HINO, Hirofumi TAKEUCHI and Yoshiaki KAWASHIMA\*

Spherically microagglomerated crystals of waxy drug (tocopherol nicotinate) for direct tableting were successfully prepared by a spherical crystallization technique. The micromeritic properties of the original tocopherol nicotinate crystals, such as flowability, packability, and mixing characteristics with excipients were drastically improved for tableting. The surface-modified agglomerated crystals with deposition of colloidal silica reduced sticking (caking) properties under loading and exudation of drug from agglomerated crystals under compression. The agglomerated crystals provided acceptable tablets with easily disintegrating and releasing functions by compressing with suitable additives.

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[Lab. of Pharm. Engineering]

### **A New Powder Design Method to Improve Inhalation Efficiency of Pranlukast Hydrate Dry Powder Aerosols by Surface Modification with Hydroxypropylmethylcellulose Phthalate Nanospheres.**

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A new particle design method to improve the aerosolization properties of a dry powder inhalation system was developed using surface modification of hydrophobic drug powders (pranlukast hydrate) with ultrafine hydrophilic particles, hydroxypropylmethylcellulose phthalate (HPMCP) nanospheres. The mechanism of the improved inhalation properties of the surface-modified particles and their deposits on carrier particles (lactose) was clarified *in vitro*. Surface modification of hydrophobic drug particles with HPMCP nanospheres to improve hydrophilicity was extremely useful in increasing the inhalation efficiency of the drug itself and the drug deposited on carrier; this was attributed to increased dispersibility in air and emission from the device, for spray- and freeze-dried particles, respectively.