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Effect of dissolution rate and/or solubility of nano-formulation on oral absorption of poorly water soluble drug

Nano-pulverization by wet beads milling is one of the methods to make nanocrystal powder to improve the dissolution rate of the poorly water-soluble drugs. We have been studied the nano-pulverization of poorly water-soluble drugs to improve their bioavailability by the rotation/revolution pulverizer 1-4). NP-100 (Thinky Co., USA) could pulverize a small number of drugs (100 mg ~ 10 g) to nanoparticles in a few minutes useful at the discovery research and NP-500TWIN for a medium amount of drugs (5 g ~ 200 g) useful at the safety studies. It was reported that the solubility of compound dramatically increased with the particles smaller than 200 nm according to the Ostwald-Freundlich equation. However, it is difficult to measure the concentration of the compound dissolved in the nanoparticle suspension. In this study, the solubility of the nano-pulverized drug (GF; Griseofulvin) was estimated by measuring the permeation rate of GF through the semi-permeable membrane and the effect of the solubility on the oral absorption of GF was also estimated. Original GF (D50 = 8.60±0.24 μm) was pulverized to nano-sized particles (D50 = 0.116±0.006 μm) and micro-sized particles (D50 = 2.51±0.10 μm). The three kinds of powders were all crystalline. The powder (10 mg) was added in the donor chamber and the concentration of GF in the receiver chamber through the semi-permeable membrane was measured. The permeation rate of nano-sized particles was 1.5-folds higher than that of micro-sized particles. These results showed that the concentration of GF with nano-sized particles in the donor chamber was higher than that with micro-sized particles. The oral absorption of GF with the three kinds of powders was studied at the dose of 20 mg/kg in rats. The AUC0-8 (μg.h/mL) with nano-sized particles was 1.6-folds larger than that with micro-sized particles. The oral absorption of GF was thought to be improved by the increase of solubility. The nano-formulation influences the oral absorption of the poorly water-soluble drugs on the dissolution rate and the solubility.

Biography

Naofumi Hashimoto received his Bachelor of Science degree (1975) and his PhD in Pharmaceutical Sciences (1989) from the Kanazawa University in Japan. He joined the Setsunan University in Japan, College of Pharmacy as Professor of Pharmaceutical Sciences in 2007 after 30 years in the pharmaceutical industries. Prior to joining the Setsunan University, his held research positions in Pharmaceutical R&D for Pfizer and Shionogi Pharmaceutical Company. He is recognized for his expertise in the physical-chemical and biopharmaceutical characterization of compounds at the discovery and pre-formulation stages. His current research interests include oral bio performance assessment by nano-pulverization of poorly water-soluble compounds. He is a councilor of APSTJ in Japan.

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