EVALUATION SYSTEM ON IN VIVO NASAL ABSORPTION OF DRUG FROM DRY POWDER FORMULATIONS
Ryosuke Tatsuta1, Daisuke Inoue1,2, Tomoyuki Furubayashi2, Yutaka Higashi2, Hidemasa Katsumi3, Toshiyasu Sakane3, Akira Yamamoto1, Ken-ichi Ogawara1, Toshikiro Kimura1 and Kazutaka Higaki1
1Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, 1-1-1 Tsushimanaka, Kita-ku, Okayama 700-8530, Japan, 2School of Pharmacy, Shujitsu University, 1-6-1 Nishigawara, Naka-ku, Okayama 703-8516, Japan and 3Kyoto Pharmaceutical University, 5 Nakauchi-cho, Misasagi, Yamashina-ku, Kyoto 607-8414, Japan.

[Purpose] Dry powder formulations with high adherence to nasal mucosa are expected to improve the nasal drug absorption by prolonging nasal formulation residence time (FRT). However, no systematic investigation has been performed on the nasal drug absorption from powder formulations. The purpose of this study is to establish the evaluation system and to investigate the nasal drug absorption from powder formulations in vivo. [Methods] Dry powder formulation and solution of acyclovir (ACV) were administered nasally to rats under the physiological condition, and the plasma concentration-time profiles of ACV were determined with LC/MS. The clearance of fluorescent microsphere (FMS) from the nasal cavity was evaluated to determine FRT. [Results and Discussion] Compared with the solution, the plasma concentration-time profile following nasal administration of powder ACV showed the slow initial increase, prolonged time to reach the maximum concentration (Tmax) and lower bioavailability. Nasal clearance of FMS was very rapid with initial half-life of 5 min. These findings suggest that the decrease in the rate and extent of ACV absorption would be due to the rapid clearance of the formulation itself and the slow rate of drug dissolution from the powder. [Conclusions] The nasal absorption of ACV from the powder decreased because of rapid nasal clearance and slow dissolution rate of ACV, which was found by our novel evaluation system.

DEVELOPMENT OF IN VITRO EVALUATION SYSTEMS ON NASAL MUCOCILIARY FUNCTION AND RELATIONSHIP BETWEEN MUCOCILIARY FUNCTION AND NASAL DRUG ABSORPTION
Daisuke Inoue1,2, Ryosuke Tatsuta2, Tomoyuki Furubayashi1, Hidemasa Katsumi3, Toshiyasu Sakane3, Akira Yamamoto1, Ken-ichi Ogawara1, Toshikiro Kimura2, Kazutaka Higaki2 and Yutaka Higashi1
1School of Pharmacy, Shujitsu University, 1-6-1 Nishigawara, Naka-ku, Okayama 703-8516, Japan, 2Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, 1-1-1 Tsushimanaka, Kita-ku, Okayama 700-8530, Japan and 3Kyoto Pharmaceutical University, 5 Nakauchi-cho, Misasagi, Yamashina-ku, Kyoto 607-8414, Japan

【Purpose】Purposes of this study are to develop an evaluation system on the ciliary beat frequency (CBF) in order to clarify the relationship between CBF and mucociliary clearance (MC), and to investigate the effect of MC change on nasal drug absorption. 【Methods】Drugs that are reported to change the ciliary function (benzalkonium, β-adrenergics, acetylcholine and anticholinergics) were used. In vitro MC measurement: Fluorescent microsphere (FMS), a marker of MC, was applied on the rat nasal septum and its movement was photographed. A distance of FMS moving per minute was used as an index of MC. In vitro CBF measurement: The sequence of images of the cilia were captured at the rate of 100 frames per second through a microscope equipped with a high speed digital imaging system. CBF was determined from the analysis of serial images. 【Results and Discussion】β-Agonists increased MC slightly and CBF significantly. Acetylcholine showed significant increases of MC and CBF. In contrast, β-antagonists, anticholinergics and benzalkonium significantly decreased both of them. The change in MC was well correlated with that in CBF, suggesting the validity and accuracy of these evaluation systems. We are now investigating the effect of MC/CBF on the nasal drug absorption. 【Conclusions】The evaluation systems newly developed in this study were useful tools for assessing the ciliary function.