Gender Differences in Pharmacokinetics and Tissue Distribution of Three Perfluorinated Compounds in Rats Based on the Simultaneous Determination Method Using UPLC-MS/MS

S-J. Kim¹, S-H. Heo¹, D-S. Lee¹, Y-B. Lee², H-Y. Cho¹
¹College of Pharmacy, CHA University, ²Chonnam National University

Purpose
The main purpose of this study was to investigate the gender differences in pharmacokinetic (PK) characteristics and tissue distribution of 3 perfluorinated compounds (PFCs) consisted of perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), and perfluorohexane sulfonic acid (PFHxS) in both male and female rats. Additionally, we aimed to develop and validate a simultaneous determination method for the quantitation of the 3 PFCs in rat plasma and tissues using UPLC-MS/MS.

Methods
For this study, a simultaneous determination method of the 3 PFCs in rat plasma and tissues was developed and validated using a UPLC-MS/MS system. The study was conducted based on in vivo study after a single oral and intravenous administration of 3 PFCs to rats. The biological samples consisted of plasma, 9 tissues (brain, heart, liver, lung, spleen, kidney, G.I. tract, adipose tissue, and muscle), urine, and feces. The PK parameters such as area under the concentration-time curve from time zero to infinity (AUC₀-∞), terminal elimination half-life (t₁/₂), volume of distribution (Vₐ), and apparent clearance (CL) were calculated by non-compartmental and compartmental analysis using WinNonlin™ software (Ver. 6.4, Pharsight®, a Certara™ Company).

Results
The mean t₁/₂ of the 3 PFCs in female and male rats was in the range of 0.15–0.19 and 1.6–1.8 days for PFOA, 23.5–24.8 and 26.4–28.7 days for PFOS, and 0.9–1.7 and 20.7–26.9 days for PFHxS, respectively. The CL of the 3 PFCs in female and male rats was 612.8–645.1 and 40.3-47.4 mL/day/kg for PFOA, 8.5-9.8 and 7.3-9.2 mL/day/kg for PFOS, and 124.8-227.9 and 7.2-9.0 mL/day/kg for PFHxS, respectively. The 3 PFCs were highly distributed in the liver and kidney followed by lung, heart, and spleen. PFOA and PFHxS showed significant gender different PKs in rats. The developed and validated simultaneous determination method of the 3 PFCs was also within the accepted criteria of the international guidance.

Conclusion
The simultaneous determination method of 3 PFCs in rat plasma and tissues was developed and validated successfully. The gender differences in PK characteristics and tissue distribution of the 3 PFCs were well estimated by in vivo study.