Physiologically Based Toxicokinetic Modeling of PFAS in Dairy Goats

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Abstract

Per- and polyfluoroalkyl acids (PFAAs) are persistent environmental contaminants of concern food safety. When PFAAs bioaccumulate in dairy livestock, contaminated milk becomes a relevant exposure pathway for humans. Quantitative toxicokinetic models are therefore needed to rapidly link feed contamination to internal dose and milk concentrations.

We integrated data from an in vivo feeding study into a physiologically based toxicokinetic (PBTK) model describing gastrointestinal uptake, systemic distribution, enterohepatic circulation, and elimination in dairy goats. The linear ODE system was solved analytically, enabling efficient parameter estimation via global optimization of a Tobit likelihood to account for measurements below quantification limits. Model performance was evaluated using predefined criteria ($R^2 > 0.7$, geometric mean fold error < 2, $|\text{bias}| < 0.2$); 16 of 30 PFAAs met these benchmarks.

Fisher information-based identifiability analysis showed that global elimination and enterohepatic circulation parameters were well constrained, whereas renal and fecal excretion rates were weakly informed and correlated with alternative clearance pathways. Coupling the PBTK model to a physiology submodel providing time-resolved dry matter intake, body weight, and milk yield for representative dairy goat breeds, we performed covariance-aware Monte Carlo simulations based on a leave-one-animal-out jackknife to derive maximum allowable feed concentrations ensuring that the 95 % upper confidence bound of milk levels remains below EU indicative limits. Estimated thresholds were $0.06\,\mu g\,kg^{-1}$ feed for PFOS and 1.4–$1.8\,\mu g\,kg^{-1}$ feed for PFHxS.

This work provides a PBTK model for predicting internal dose and milk transfer across a broad spectrum of PFAAs in dairy goats.