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Supplemental Material

Physiologically Based Pharmacokinetic (PBPK) Modeling of the Bisphenols BPA, BPS, BPF, and BPAF with New Experimental Metabolic Parameters: Comparing the Pharmacokinetic Behavior of BPA with Its Substitutes

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Figure S2. Eadie Hofstee plots of enzyme kinetics of BPS, BPF, and BPAF with human liver and intestinal microsomes. Shown are averages (black circles) and ranges from minimal to maximal reaction velocities (whiskers). Abbreviations: BPAF, bisphenol AF; BPF, bisphenol F; BPS, bisphenol S; $c_{substrate}$, substrate concentration; v, reaction velocity.

Figure S3. Measured and modeled serum concentration–time profiles of BPS and BPS-g after peroral dosing with 8.75 µg BPS/kg bw. Individual measurements (black circles) represent observed serum concentrations (average ± standard deviation) of 7 adults (Oh et al. 2018). Concentration profiles for the respective volunteers (grey solid lines) were modeled using (A) the adjusted PBPK model for BPA further adjusted with BPS-specific metabolism parameters (Table 7) and (B and C) the BPS-specific model calibrated to assume a higher peroral uptake and increased clearance rates of BPS and BPS-g assuming either (B) no EHR or (C) a BPS EHR rate of 67% (see Table 5 for uptake parameters). Abbreviations: BPA, bisphenol A; BPS, bisphenol S; bw, bodyweight; EHR, enterohepatic recirculation; g, glucuronide.

Figure S4. Modeled concentration profiles of unconjugated BPS obtained with the basic PBPK model in serum (A) and gonads (B) for infants (6 days-3 months), toddlers (1-3 years), children (3-10 years), adolescents (10-18 years), and adults (18-45 years) after 500 ng/kg bw single peroral and dermal exposures (t=0) respectively (rough average of peroral and dermal high BPA exposure estimates for adults by the EFSA CEF Panel (2015)), see Table 5 for uptake parameters. Females are represented by solid lines, males are represented by dotted lines. Abbreviations: BPS, bisphenol S; bw, bodyweight; c, concentration; PBPK, physiologically based pharmacokinetic.

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Figure S6. Modeled concentration profiles of unconjugated BPF obtained with the basic PBPK model in serum (A) and gonads (B) for infants (6 days-3 months), toddlers (1-3 years), children (3-10 years), adolescents (10-18 years), and adults (18-45 years) after 500 ng/kg bw single peroral and dermal exposures (t=0) respectively (rough average of peroral and dermal high BPA exposure estimates for adults by the EFSA CEF Panel (2015)), see Table 5 for uptake parameters. Females are represented by solid lines, males are represented by dotted lines. Abbreviations: BPF, bisphenol F; bw, bodyweight; c, concentration; PBPK, physiologically based pharmacokinetic.

Figure S7. Modeled concentration profiles of unconjugated BPAF obtained with the basic PBPK model in serum (A) and gonads (B) for infants (6 days-3 months), toddlers (1-3 years), children (3-10 years), adolescents (10-18 years), and adults (18-45 years) after 500 ng/kg bw single peroral and dermal exposures (t=0) respectively (rough average of peroral and dermal high BPA exposure estimates for adults by the EFSA CEF Panel (2015)), see Table 5 for uptake parameters. Females are represented by solid lines, males are represented by dotted lines. Abbreviations: BPAF, bisphenol AF; bw, bodyweight; c, concentration; PBPK, physiologically based pharmacokinetic.

Figure S8. Measurements of Hormann et al. (2014) (symbols) against modeled individual serum profiles (solid lines) of unconjugated BPA, BPA-g, and BPA-s in three volunteers. They handled receipt paper for 4 min with both hands which were wetted with skin sanitizer and ate 10 French fries with a contaminated hand afterwards during 4 min. One hand was then cleaned and the other hand stayed contaminated until the end of blood collection (90 min in total, see Table S9 for study-specific parameters). Abbreviations: BPA, bisphenol A; g, glucuronide; s, sulfate.

Input tables

Table C1. Input table “Probanden” used in the basic PBPK model code for BPA.

Table C2. Input table “physAge” used in the basic PBPK model code for BPA.

Table C3. Input table “VarInputFem” used in the PBPK model code for the 2D Monte Carlo Analysis of BPA in women (18-45 years).

Table C4. Input table “ChemData” used in the PBPK model code for the 2D Monte Carlo Analysis of BPA in women (18-45 years).

Model code

References