**Supplementary Table S2. Properties of the drugs and their metabolites used in the PBPK models.**

Molecular weight (MW), octanol/water partition coefficient (logP), fraction unbound (Fu), acid dissociation constant (pKa), water solubility, and intestinal permeability via the transcellular route. Molecular weights, logP, Fu, and pkA values, as well as water solubilities are taken from DrugBank[1], HMDB[2], or were predicted by use of the software ChemAxon[3] or ALOGPS[4]. In some cases, logP ($logP_{initial}$) and Fu values ($Fu_{initial}$) as well as initial intestinal permeabilities provided by the modeling software[5] (Intestinal $permeability_{calc}$) are slightly adjusted ($logP_{model}$, $Fu_{model}$, Intestinal $permeability_{model}$) to best describe the clinical PK data. Diclofenac, DFN; hydroxy, OH; acyl glucuronide, AGLU; celecoxib, CEL; carboxy, COOH; glucuronide, GLU; zileuton, ZLT; sulfoxide, SO; licofelone, LCF; rifampicin, RIF; desacetyl, DA.

| ID | Drug/Metabolite | MW [g/mol] | $logP_{initial}$ | $logP_{model}$ | $Fu_{initial}$ | $Fu_{model}$ | Compound type | pkA | Water Solubility [mg/l] | Intestinal $permeability_{calc}$ [dm/min] | Intestinal $permeability_{model}$ [dm/min] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | CEL | 381.37 | 3.90 | 3.70 | 0.03 | 0.017 | acid | 10.70 | 3.30 | 3.60E-05 | 9.00E-05 |
| 1 | OH-CEL | 397.37 | 3.10 | 3.30 | n/a | 0.043 | acid | 10.70 | 4.50 | 1.19E-05 | 1.19E-05 |
| 1 | COOH-CEL | 411.35 | 3.24 | 3.30 | n/a | 0.039 | acid | 3.98 | 3.20 | 9.95E-06 | 9.95E-06 |
| 2 | DFN | 296.15 | 4.51 | 3.54 | <0.003[§] | 0.0022 | acid | 4.15 | 2.37 | 8.58E-05 | 9.37E-06 |
| 2 | 3'-OH-DFN | 312.15 | 3.96 | 3.68 | n/a | 0.0018 | acid | 3.82 | 10.00 | 9.40E-05 | 9.40E-05 |
| 2 | 4'-OH-DFN | 312.15 | 3.96 | 3.82 | n/a | 0.0034 | acid | 3.76 | 9.60 | 1.27E-04 | 1.27E-04 |
| 2 | 5-OH-DFN | 312.15 | 3.96 | 2.98 | n/a | 0.0021 | acid | 3.81 | 11.00 | 1.83E-05 | 1.83E-05 |
| 2 | DFN-AGLU | 472.27 | 2.31 | 2.14 | n/a | 0.0041 | acid | 3.23 | 35.70 | 3.23E-07 | 3.23E-07 |
| 3 | LCF | 379.88 | 5.39 | 4.04 | n/a | 0.0068* | acid | 4.83 | 1.11 | 1.00E-03 | 8.50E-04 |
| 3 | LCF-AGLU | 511.00 | 4.37 | 4.37 | n/a | 0.0841** | [acid, base] | [3.8, 8.9] | 1.46 | 2.96E-05 | 2.96E-05 |
| 3 | OH-LCF | 395.88 | 5.42 | 5.42 | n/a | 0.0232** | acid | 4.64 | 1.58 | 1.00E-03 | 1.00E-03 |
| 4 | RIF | 822.94 | 2.70 | 2.92 | 0.2[$] | 0.15 | [acid, base] | [1.7, 7.9] | 1400 | 1.01E-07 | 1.00E-05 |
| 4 | DA-RIF | 780.90 | 2.57 | 2.10 | n/a | 0.05 | [acid, base] | [6.9, 7.9] | 48.00 | 1.90E-08 | 5.00E-05 |
| 5 | ZLT | 236.29 | 0.90 | 1.40 | 0.07 | 0.095 | acid | 8.84 | 500.00 | 8.46E-07 | 4.20E-05 |
| 5 | ZLT-SO | 252.29 | 0.40 | 0.40 | n/a | 0.069 | acid | 8.92 | 622.00 | 6.23E-08 | 6.23E-08 |
| 5 | OH-ZLT | 252.29 | 1.76 | 1.76 | n/a | 0.069 | acid | 8.73 | 84.00 | 1.43E-06 | 1.43E-06 |
| 5 | ZLT-GLU | 412.414 | 0.07 | -0.50 | n/a | 0.205 | [acid, base] | [4.05, 3.06] | 147.00 | 8.59E-10 | 8.59E-10 |

* fitted to experimental data

** predicted by Gertz et al.[6]

[§] Davies et al.[7]

[$] Acocella et al.[8]

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