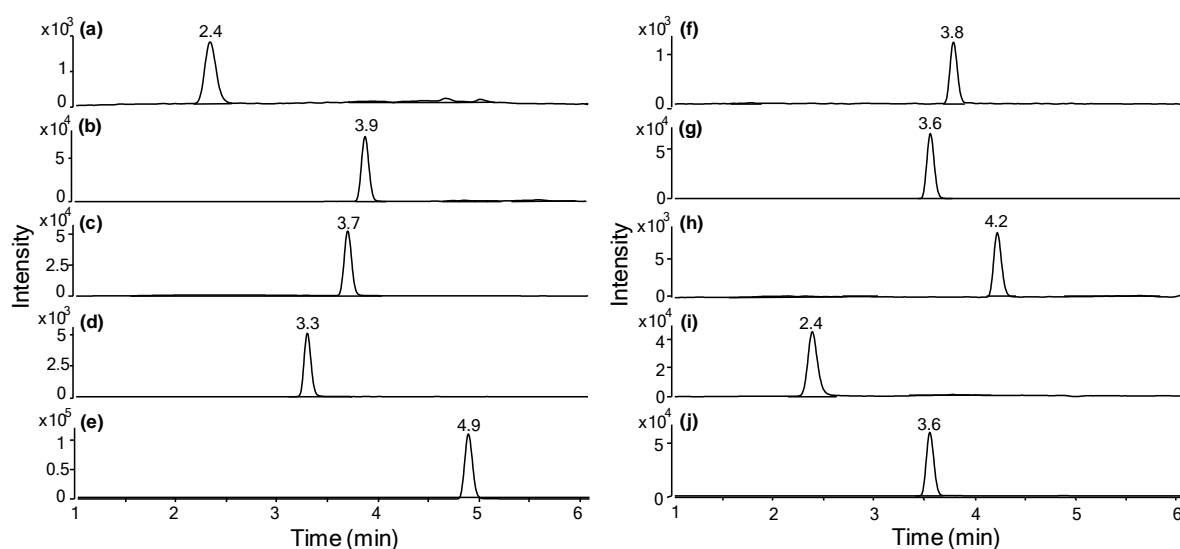


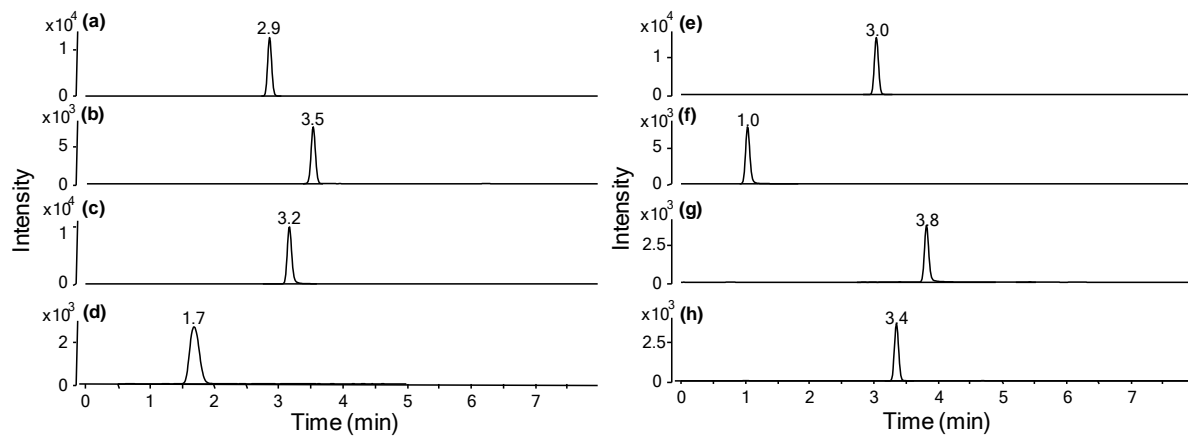
## Supplementary Materials

# In Vitro Interaction of AB-FUBINACA with Human Cytochrome P450, UDP-Glucuronosyltransferase Enzymes and Drug Transporters

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**Figure S1.** SRM chromatograms of CYP metabolites formed from human liver microsomal incubation of eight CYP cocktail substrates with NADPH and two IS. (a) acetaminophen, (b) 7-hydroxycoumarin, (c) hydroxybupropion, (d) *N*-desethylamodiaquine, (e) 4'-hydroxydiclofenac, (f) 4'-hydroxymephenytoin, (g) 1'-hydroxybufuralol, (h) 1'-hydroxymidazolam, (i) <sup>13</sup>C<sub>2</sub>,<sup>15</sup>N-acetaminophen, and (j) d<sub>9</sub>-1'-hydroxybufuralol (IS).



**Figure S2.** SRM chromatograms of UGT metabolites formed from human liver microsomal incubation of six UGT cocktail substrates with UDPGA and two IS. : (a) SN-38 glucuronide, (b) chenodeoxycholic acid 24-acyl- $\beta$ -glucuronide, (c) trifluoperazine *N*-glucuronide, (d) *N*-acetylserotonin glucuronide, (e) mycophenolic acid glucuronide, (f) naloxone 3- $\beta$ -D-glucuronide. (g) meloxicam (IS), and (h) propofol glucuronide (IS).

**Table S1.** Concentration ranges and correlation coefficients of the calibration curves and precision (coefficient of variation, CV) and accuracy values for CYP and UGT metabolites.

| analytes  | SRM transition ( <i>m/z</i> )<br>(collision energy, eV) | polarity         | Concentration range<br>(pmol) | Correlation<br>coefficient | QC<br>(pmol) | Intra-day ( <i>n</i> = 5) |        |
|---|---|------------------|-------------------------------|----------------------------|--------------|---------------------------|--------|
|   |   |                  |                               |                            |              | Accuracy (%)              | CV (%) |
| acetaminophen   | 152.1→110.1 (8)   | ESI <sup>+</sup> | 5-200                         | 0.9971                     | 15, 70, 140  | 96.8                      | 5.4    |
| 7-hydroxycoumarin                                       | 163.0→107.0 (12)  | ESI <sup>+</sup> | 15-600                        | 0.9963                     | 45, 120, 420 | 98.7                      | 6.9    |
| hydroxybupropion  | 256.1→238.0 (5)   | ESI <sup>+</sup> | 1-40                          | 0.9973                     | 3, 8, 28     | 99.7                      | 8.6    |
| <i>N</i> -desethylamodiaquine                           | 328.1→283.0 (55)  | ESI <sup>+</sup> | 15-600                        | 0.9970                     | 45, 210, 420 | 95.9                      | 8.4    |
| 4'-hydroxydiclofenac                                    | 312.0→231.0 (17)  | ESI <sup>+</sup> | 1-100                         | 0.9908                     | 3, 20, 70    | 97.3                      | 6.8    |
| 4'-hydroxymephenytoin                                   | 235.2→150.0 (8)   | ESI <sup>+</sup> | 0.5-20                        | 0.9946                     | 1.5, 7, 14   | 94.8                      | 8.2    |
| 1'-hydroxybufuralol                                     | 278.3→187.0 (8)   | ESI <sup>+</sup> | 0.5-20                        | 0.9993                     | 1.5, 7, 14   | 96.9                      | 6.3    |
| 1'-hydroxymidazolam                                     | 342.1→324.1 (8)   | ESI <sup>+</sup> | 5-200                         | 0.9981                     | 15, 70, 140  | 99.6                      | 9.0    |
| SN-38 glucuronide                                       | 568.9→392.9 (30)  | ESI <sup>+</sup> | 1-300                         | 0.9967                     | 3, 30, 210   | 105.5                     | 5.4    |
| chenodeoxycholic acid 24-acyl- $\beta$ -<br>glucuronide | 567.1→391.2 (34)  | ESI <sup>-</sup> | 1-300                         | 0.9980                     | 3, 30, 210   | 102.9                     | 10.1   |
| trifluoperazine <i>N</i> -glucuronide                   | 583.9→407.9 (26)  | ESI <sup>+</sup> | 4-1200                        | 0.9998                     | 12, 120, 840 | 98.8                      | 9.9    |
| <i>N</i> -acetylserotonin glucuronide                   | 394.9→219.0 (10)  | ESI <sup>+</sup> | 1-300                         | 0.9956                     | 3, 30, 210   | 97.9                      | 6.5    |
| mycophenolic acid glucuronide                           | 495.0 →319.0 (20)                                       | ESI <sup>-</sup> | 1-300                         | 0.9958                     | 3, 30, 210   | 98.1                      | 7.9    |
| naloxone 3- $\beta$ -D-glucuronide                      | 503.9→309.9 (32)  | ESI <sup>+</sup> | 1-300                         | 0.9971                     | 3, 30, 210   | 100.3                     | 8.4    |