**Table 2.** Summary of CYP450 and OAT3 inhibition parameters with rivaroxaban as probe substrate and ketoconazole, erlotinib or nilotinib as the putative inhibitors

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| *In Vitro* Inhibition parameters | | Ketoconazole | Erlotinib | Nilotinib |
| MBI of CYP3A4 | *KI* (µM) | - | 10.98 | 4.44 |
| *kinact* (h-1) | - | 2.28 | 2.00 |
| *kinact / KI*  (µM-1 h-1) | - | 0.21 | 0.45 |
| MBI of CYP2J2 | *KI* (µM) | - | 1.31 | -  -  - |
| *kinact* (h-1) | - | 1.06 |
| *kinact / KI*  (µM-1 h-1) | - | 0.81 |
| Reversible Inhibition of CYP3A4 | IC50 (µM)  R1a  Mode  *Ki* (µM)  α | -  -  Mixed  0.094b  3.28 | 20.24  1.014  -  -  - | 6.05  1.019  -  -  - |
| Reversible Inhibition of CYP2J2 | IC50 (µM)  Mode  *Ki* (µM) | -  Competitive  0.082b | 1.81  Competitive  0.76 | 0.30  Competitive  0.12 |
| Fraction Unbound in the *In Vitro* Incubation | fuinc | 1 | 0.92 | 0.43  Optimized to 1 |
| Inhibition of P-gp-Mediated Efflux of Rivaroxaban | IC50 (µM)  *Ki* (µM) | 0.34  0.17b |  |  |
| Inhibition of OAT3-Mediated Uptake of E3S | IC50 (µM) | 6.90 | - | 5.12 |
| Mode | Non-Competitive | - | Non-Competitive |
| *Ki* (µM) | 14.96 | - | 3.54 |
| Inhibition of OAT3-Mediated Uptake of Rivaroxaban  (Protein-Free Buffer) | IC50 (µM) | 0.58 | - | 0.062 |
| Mode | Non-Competitive | - | Competitive |
| *Ki* (µM) | 0.93 | - | 0.013 |
| Inhibition of OAT3-Mediated Uptake of Rivaroxaban  (5% w/v Human Serum Albumin) | IC50 (µM)  IC50,u (µM)  *Ki,u* (µM) | 1.29  0.037c  0.037e | -  -  - | 0.61  0.0098d  0.0098e |

aR1 is the predicted ratio of the victim drug’s area under the plasma concentration-time curve in the presence and absence of an inhibitor for basic models of reversible inhibition.

R1 = 1 + (Imax,u/*Ki*) whereImax,uis the maximal unbound plasma concentration of the interacting drug.

bValues reported were derived previously from Cheong *et al.* (2019).

cIC50,u = fup,ketoconazole (0.029) × IC50 (1.29 µM) = 0.037 µM

dIC50,u = fup,nilotinib (0.016) × IC50 (0.61 µM) = 0.0098 µM

eIC50,u corrected to *Ki,u* using the appropriate Cheng Prusoff equation based on the identified mode of inhibition. As described by Zhang *et al.* (2005), IC50,u = *Ki,u* for non-competitive inhibition and IC50,u = *Ki,u* × (1+S/Km) for competitive inhibition.