

Table S2 Final population pharmacodynamic parameters of the included studies

Study (year)	Analytical method	Formula	Fixed effect parameters		Between-subject variability	Residual unexplained variability
aPTT						
Mueck et al. (2007)[1]	kaolin-activated test	$\text{aPPT} = \text{aPTT}_0 \times (1 - \frac{\text{E}_{\max} \times C_p}{\text{EC}_{50} + C_p})$	aPPT ₀ E _{max} (s) EC ₅₀ (μg/L) slope (s/(μg/L))	31 42.6 497 0.0467	6.7% / 15.3% /	11.2 s
Tanigawa et al. (2013)[2]	kaolin-activated test	$\text{aPTT} = \text{aPTT}_0 + \text{slope} \times C_p^{1-\text{Hill}} \times C_p$	aPTT ₀ slope Hill	32.6 0.0658 0.000156	9.6% 31.8% /	9.1%
Zdovc et al. (2019)[3]	Pathromtin® SL	$\text{aPPT} = \text{aPPT}_0 + \text{slope} \times C_p$	aPTT ₀ (s) slope (s/(μg/L))	32.9 2.02	16.5% /	13.1%
Esmaeili et al. (2022)[4]	Fisherbrand™	$\text{aPPT} = \text{aPPT}_0 + \text{slope} \times C_p$	aPTT ₀ (s) slope (s/(μg/L))	35.0 0.033	15% 28%	13%
Heptest						
Mueck et al. (2007)[1]	Haemachem	$\text{Heptest} = \text{Heptest}_0 \times (1 - \frac{\text{E}_{\max} \times C_p}{\text{EC}_{50} + C_p})$	Heptest ₀ (s) E _{max} (s) EC ₅₀ (μg/L)	16.2 64 441	5.5% / 7.7%	2.3 s
Tanigawa et al. (2013)[2]	NA	$\text{Heptest} = \text{Heptest}_0 \times (1 - \frac{\text{E}_{\max} \times C_p^{\text{hill}}}{\text{EC}_{50} + C_p^{\text{hill}}})$	Heptest ₀ (s) E _{max} (s) EC ₅₀ (μg/L) Hill	17.9 43.2 240 × [1 + 0.147 × (ALB - 4.28)] 1.18	13.8% / 19.64% /	7.0%
Anti-Xa activity						
Zhao et al. (2022)[5]	Biophen DiXal	$\text{Anti-Xa} = \text{slope} \times C_p^{\text{Hill}}$	slope Hill	0.513 × 1.116 (if postprandial status) (fixed*) 1.10 (fixed*)	11.0% (fixed*) /	22.0% 12.0 μg/L
Esmaeili et al. (2022)[4]	STA®-Liquid Anti-Xa	$\text{Anti-Xa} = \frac{\text{E}_{\max} \times C_p^{\text{hill}}}{\text{EC}_{50}^{\text{hill}} + C_p^{\text{hill}}}$	E _{max} (IU/mL) EC ₅₀ (μg/L) Hill	4 180 1.44	/ 24% 108%	31%
PiCT						

Girgis et al. (2014)[6]	Pefakit® PiCT® kit	PiCT= PiCT ₀ +slope×C _p ^{1-Hill} ×C _p	PiCT ₀ (s) slope (s/(μg/L)) Hill	7.97×[1-0.0016×(CrCl-76)] 0.0954 0.000263×[1+0.00293×(CrCl-76)]	46.2% 5.56% /	22.1%
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Abbreviations: ALB: albumin; aPTT: activated partial thromboplastin time; aPTT₀: baseline of aPTT; C_p: rivaroxaban plasma concentration; CrCl: creatinine clearance; EC₅₀: concentration generating 50% of the maximum effect; E_{max}: the maximum effect; PiCT: prothrombinase-induced clotting time; PiCT₀: baseline of PiCT; TBIL: total bilirubin.

Fixed to estimates from model of healthy volunteers.

Reference:

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4. Esmaeili, T.; Rezaee, M.; Abdar Esfahani, M.; Davoudian, A.; Omidfar, D.; Rezaee, S. Rivaroxaban population pharmacokinetic and pharmacodynamic modeling in Iranian patients. *J. Clin. Pharm. Ther.* **2022**, *47*, 1284-1292.
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6. Girgis, I. G.; Patel, M. R.; Peters, G. R.; Moore, K. T.; Mahaffey, K. W.; Nessel, C. C.; Halperin, J. L.; Califf, R. M.; Fox, K. A.; Becker, R. C. Population pharmacokinetics and pharmacodynamics of rivaroxaban in patients with non-valvular atrial fibrillation: results from ROCKET AF. *J. Clin. Pharmacol.* **2014**, *54*, 917-27.