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Development and verification of a full physiologically-based pharmacokinetic model for sublingual buprenorphine in healthy adult volunteers that accounts for nonlinear bioavailability

Matthijs W. van Hoogdalem, Ryota Tanaka, Trevor N. Johnson, Alexander A. Vinks, Tomoyuki Mizuno

Division of Translational and Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA (M.W.v.H., R.T., A.A.V., T.M.); James L. Winkle College of Pharmacy, University of Cincinnati, Cincinnati, Ohio, USA (M.W.v.H.); Certara UK Limited, Sheffield, UK (T.N.J.); Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, Ohio, USA (A.A.V., T.M.); Center for Addiction Research, College of Medicine, University of Cincinnati, Cincinnati, Ohio, USA (A.A.V., T.M.)

Table S1. Exploration of optimal linear regression model between the area under the curve (AUC)- or peak concentration (C_{\max})-optimized ideal proportion and the sublingual tablet or solution dose in milligrams.

Formulation	Parameter	Equation	R^2
Solution	AUC	Proportion = $48.3 - 1.29 \times \text{Dose}$	0.709
		Proportion = $65.9 - 36.4 \times \log(\text{Dose})$	0.832
		$\log(\text{Proportion}) = 1.73 - 0.023 \times \text{Dose}$	0.907
		$\log(\text{Proportion}) = 1.98 - 0.573 \times \log(\text{Dose})$	0.815
	C_{\max}	Proportion = $33.5 - 0.529 \times \text{Dose}$	0.489
		Proportion = $40.7 - 14.8 \times \log(\text{Dose})$	0.572
		$\log(\text{Proportion}) = 3.51 - 0.020 \times \text{Dose}$	0.552
		$\log(\text{Proportion}) = 3.76 - 0.539 \times \log(\text{Dose})$	0.582
Tablet	AUC	Proportion = $32.9 - 0.99 \times \text{Dose}$	0.882
		Proportion = $44.6 - 24.7 \times \log(\text{Dose})$	0.838
		$\log(\text{Proportion}) = 1.85 - 0.057 \times \text{Dose}$	0.705
		$\log(\text{Proportion}) = 2.25 - 1.14 \times \log(\text{Dose})$	0.436
	C_{\max}	Proportion = $23.9 - 0.528 \times \text{Dose}$	0.659
		Proportion = $31.6 - 14.7 \times \log(\text{Dose})$	0.783
		$\log(\text{Proportion}) = 3.23 - 0.035 \times \text{Dose}$	0.730
		$\log(\text{Proportion}) = 3.65 - 0.882 \times \log(\text{Dose})$	0.700

For each formulation and each parameter, four varieties of the linear model, either untransformed or with Dose, Proportion_i, or both logarithmically transformed using a decimal logarithm of base 10, were explored. The coefficient of determination (R^2) was calculated with the DescTools package (v0.99.44, Signorell *et mult. al.*) for R. The mean R^2 of untransformed, or with Dose, Proportion_i, or both logarithmically transformed linear models were 0.685, 0.756, 0.724, or 0.633.