

A Comprehensive Physiologically Based Pharmacokinetic Model for Predicting Vildagliptin Pharmacokinetics: Insights into Dosing in Renal Impairment

Mahnoor Pasha ¹, Ammara Zamir ¹, Muhammad Fawad Rasool ^{1*}, Hamid Saeed ², Tanveer Ahmad ³, Nawaf Shalih Alqahtani ⁴, Lamya Saif Alqahtani ⁵ and Faleh Alqahtani ^{6*}

¹Department of Pharmacy Practice, Faculty of Pharmacy, Bahauddin Zakariya University, 60800, Multan, Pakistan; mahnoorpashaoc15@gmail.com (M.P); ammarazamir20@gmail.com (A.Z); fawadrasool@bzu.edu.pk (M.F.R)

² Section of Pharmaceutics, University College of Pharmacy, Allama Iqbal Campus, University of the Punjab, 54000, Lahore, Pakistan; hamid.pharmacy@pu.edu.pk (H.S)

³ Institute for Advanced Biosciences (IAB), CNRS UMR5309, INSERM U1209, Grenoble Alpes University, La Tronche, 38700, France; tanveer.ahmad@univ-grenoble-alpes.fr (T.A)

⁴King Abdulaziz Medical City- Riyadh Region Ministry of National Guard, Health Affairs; Alkahtanina3@mngha.med.sa (N.S.A)

⁵Department of Cardiology, Prince Sultan Cardiac Center, Riyadh, 11625, Saudi Arabia; lalqahtani@pscc.med.sa (L.S.A)

⁶Department of Pharmacology and Toxicology, College of Pharmacy, King Saud University, Riyadh, 11451, Saudi Arabia; afaleh@ksu.edu.sa. (F.A)

* Correspondence: fawadrasool@bzu.edu.pk (M.F.R), afaleh@ksu.edu.sa (F.A)

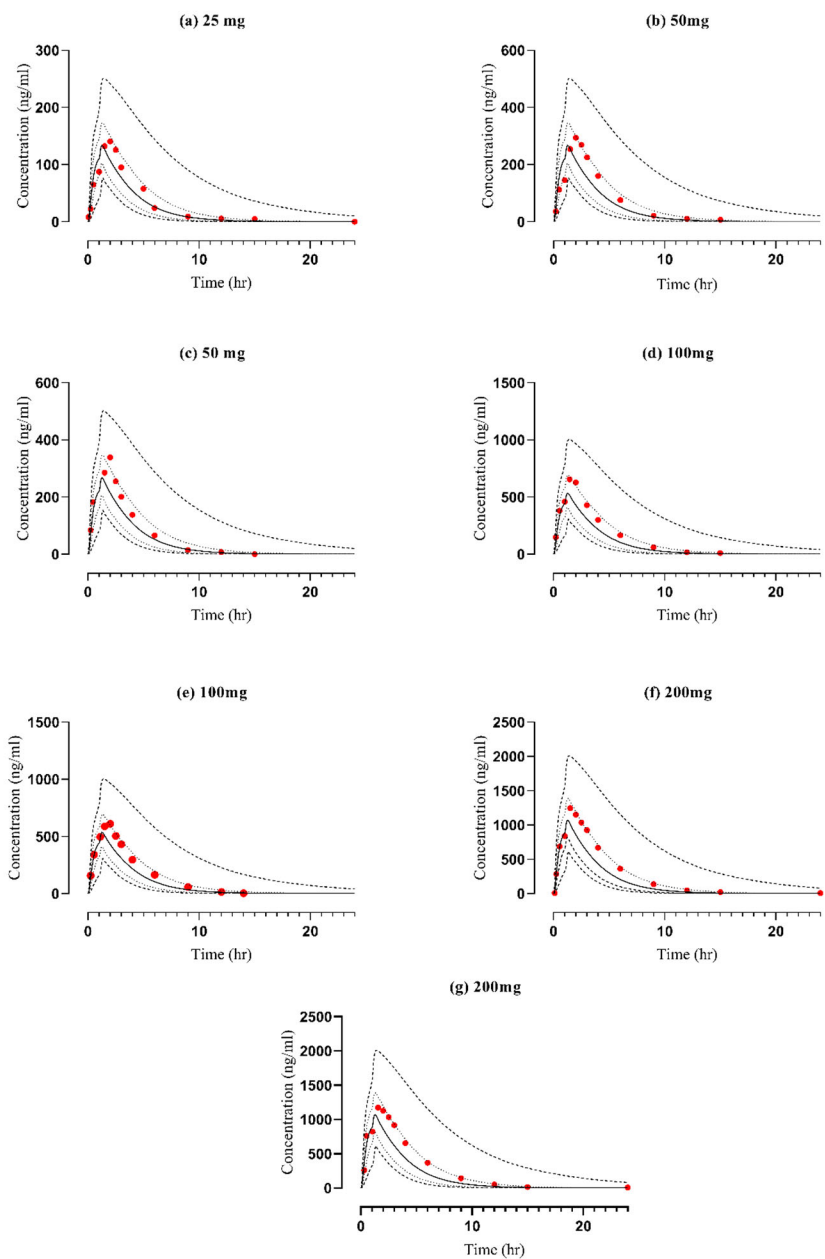


Figure S1: Comparison of observed and predicted plasma concentration vs time profiles of vildagliptin at different oral doses. (Dose in mg) (a) 25^[1], (b) 50^[1], (c) 50^[1], (d) 100^[1] and (e) 100^[1], (f) 200^[1], and (g) 200^[1] respectively. (· · ·): Values of reported data, (—): Values of simulated data, (- - -): highest and lowest values, (...) : 5th and 95th percentile.

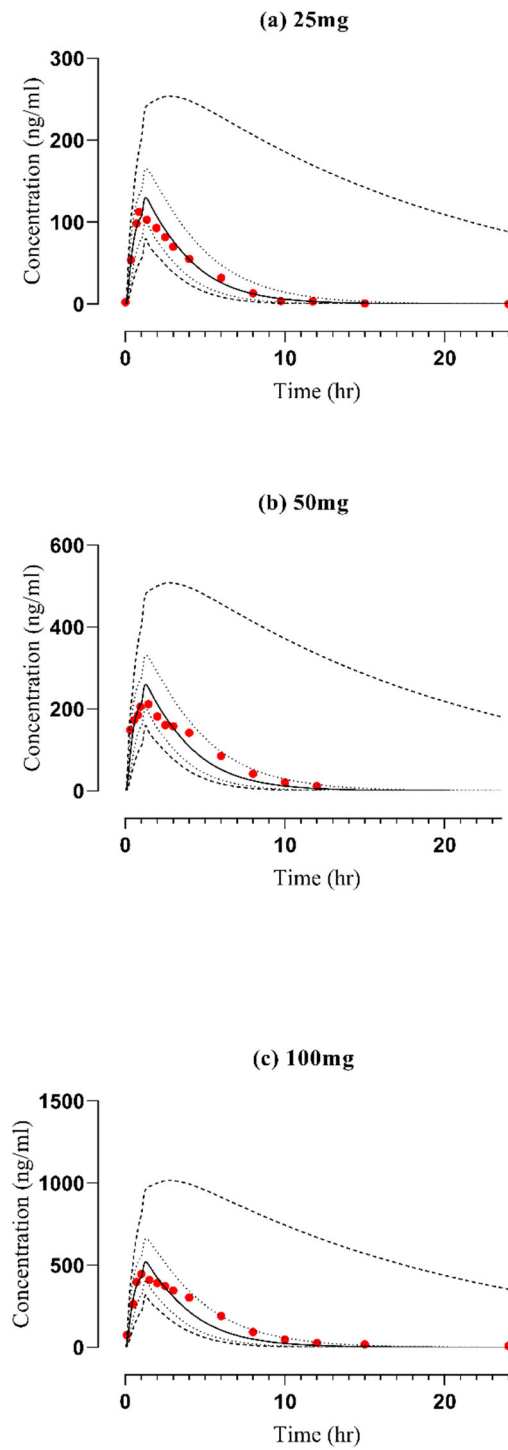


Figure S2: Comparison of observed and predicted plasma concentration vs time profiles of vildagliptin at different dosage levels. (Dose in mg) (a) 25^[2], (b) 50^[2], and (c) 100^[2] respectively. (...): Values of reported data, (—): Values of simulated data, (---): highest and lowest values, (---): 5th and 95th percentile

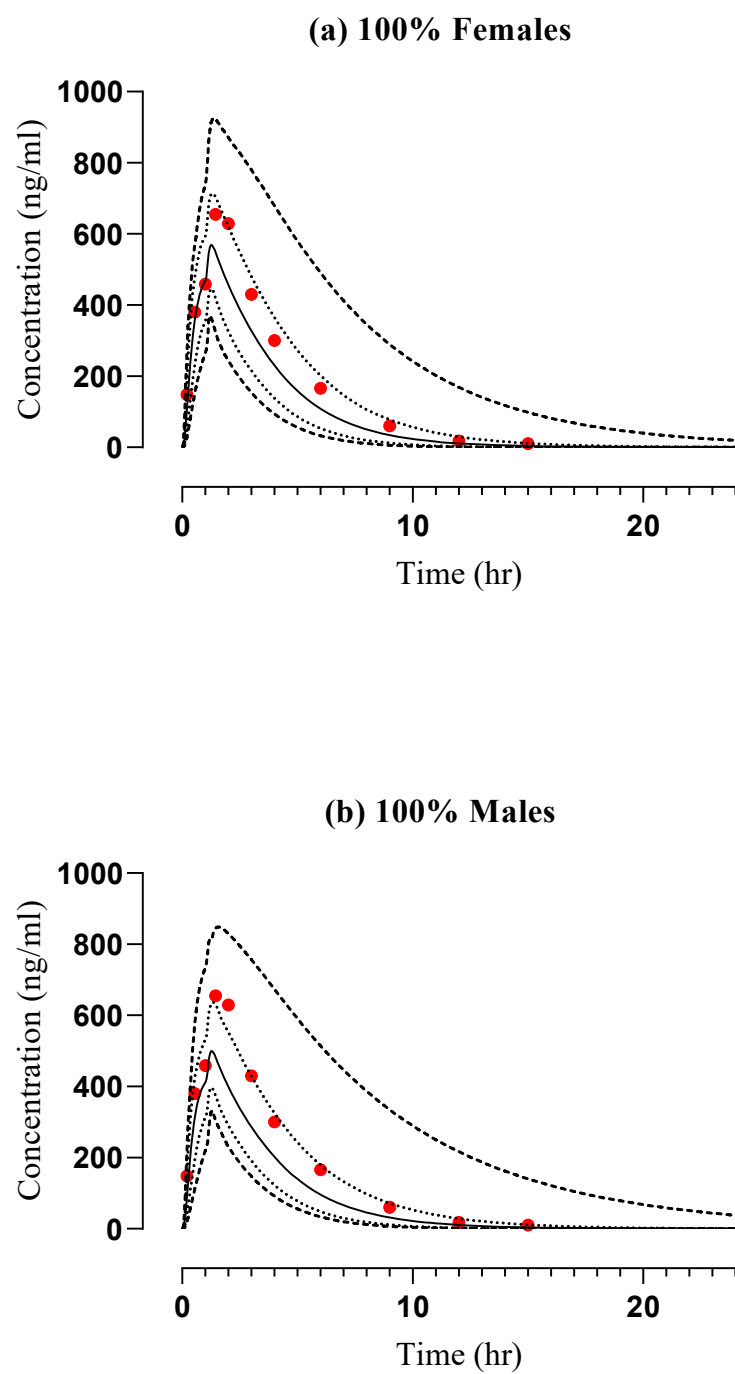


Figure S3: Comparison of observed and predicted plasma concentration vs time profiles of vildagliptin in males and females. Oral dose of 100 mg^[1] showing that gender imbalance has no effect on simulations. (· · ·): Values of reported data, (—): Values of simulated data, (---): highest and lowest values, (·····): 5th and 95th percentile

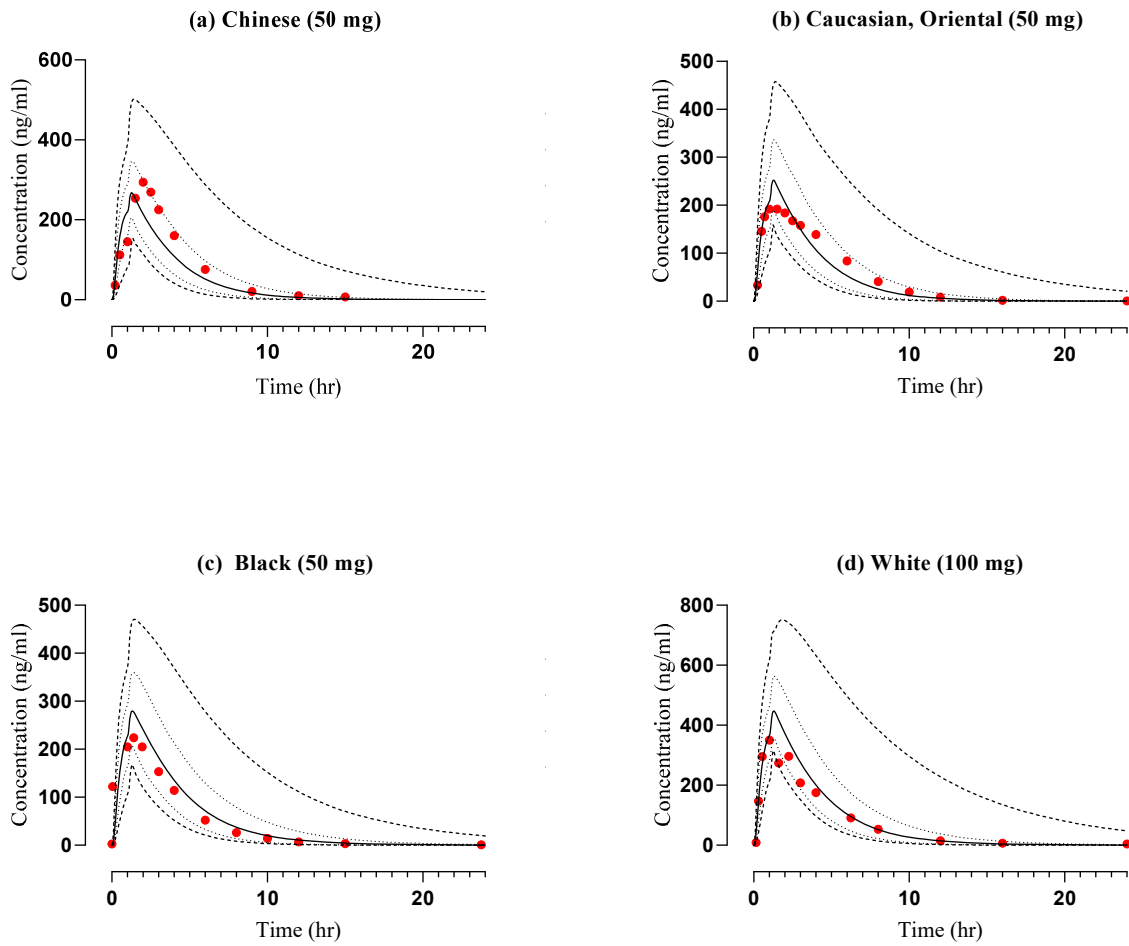


Figure S4: Comparison of observed and predicted plasma concentration vs time profiles of vildagliptin in different ethnic populations (...): Values of reported data, (—): Values of simulated data, (- - -): highest and lowest values, (...): 5th and 95th percentile

Table S1: Vildagliptin half-life ($t_{1/2}$) in healthy and diseased population

Dose (mg)	Half Life ($t_{1/2}$) from predicted data	Reference
Oral administration in Healthy individuals		
25 ^a	2.07	[1]
25 ^b	2.06	[1]
25	2.13	[2]
50 ^a	1.98	[1]
50 ^b	1.92	[1]
50	1.93	[2]
50	1.95	[3]
100 ^a	2.06	[1]
100 ^b	2.01	[1]
100	2.1	[2]
100	2.08	[4]
200 ^a	2.06	[1]
200 ^b	2.11	[1]
200	2.13	[2]
IV administration in Healthy individuals		
25	2.06	[3]
Oral administration in the CKD population		
50	1.99	[5]
50 (Mod)	3.30	[5]
50(severe)	4.88	[5]

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