

Table S1: Summary of Pharmacokinetic parameters (treatment-wise)

PK Parameters	Statistics	Cohort 1					Cohort 2		
		Treatment A	Treatment B	Treatment C	Treatment D	Total	Treatment E	Treatment F	Total
	N	24	24	24	24	96	24	23	47
AUC_{inf_obs} (h.ng/mL)	Mean(±SD)	16558(± 3026.8)	17447(± 4658.6)	17664(± 3447.7)	17205(± 3285.0)	17218(± 3624.4)	14589(± 2835.9)	15866(± 4353.0)	15214(± 3674.2)
	Median	16809	16028	17042	16777	16787	14704	16240	15070
	CV%	18.28%	26.70%	19.52%	19.09%	21.05%	19.44%	27.44%	24.15%
AUC_{last} (h.ng/mL)	Mean(±SD)	15965(± 3025.0)	16936(± 4534.3)	17099(± 3451.0)	16704(± 3299.6)	16676(± 3592.0)	14177(± 2780.1)	15498(± 4243.1)	14823(± 3594.5)
	Median	16401	15670	16570	16436	16261	14244	15883	14741
	CV%	18.95%	26.77%	20.18%	19.75%	21.54%	19.61%	27.38%	24.25%
C_{max} (ng/mL)	Mean(±SD)	2422.5(± 560.78)	2466.3(± 480.60)	2584.6(± 496.66)	2615.4(± 488.17)	2522.2(± 505.92)	2496.3(± 549.99)	2924.3(± 945.08)	2705.7(± 790.70)
	Median	2410.0	2370.0	2530.0	2555.0	2485.0	2480.0	2890.0	2730.0
	CV%	23.15%	19.49%	19.22%	18.67%	20.06%	22.03%	32.32%	29.22%
t_½ (h)	Mean(±SD)	5.39(± 1.66)	4.67(± 1.58)	5.10(± 1.89)	4.96(± 1.79)	5.03(± 1.73)	4.89(± 1.94)	4.48(± 1.16)	4.69(± 1.60)
	Median	4.90	4.21	4.69	4.34	4.69	4.03	4.06	4.06
	CV%	30.78%	33.80%	37.11%	36.10%	34.32%	39.66%	25.96%	34.19%
λ_z (1/h)	Mean(±SD)	0.14(± 0.04)	0.16(± 0.06)	0.15(± 0.05)	0.15(± 0.04)	0.16(± 0.05)	0.16(± 0.05)	0.16(± 0.04)	0.16(± 0.04)
	Median	0.14	0.16	0.15	0.16	0.15	0.17	0.17	0.17
	CV%	28.57%	33.54%	30.09%	29.21%	30.74%	30.79%	24.71%	27.63%

Treatment A – metformin (2 g) was administered with breakfast 20 min after one insulin tregopil (10 mg) tablet Treatment B – metformin (2 g) was administered with breakfast 20 min after 1 placebo tablet

Treatment C – metformin (2 g) was administered with breakfast 20 min after 3 placebo tablets

Treatment D – metformin (2 g) was administered with breakfast

Treatment E – metformin (2 g) was administered in fasting condition 20 min before breakfast

Treatment F – 3 placebo tablets and metformin (2 g) were administered in fasting condition 20 min before breakfast.