Electronic supplementary material

Clinical Pharmacokinetics

The Effect of Food Intake on the Pharmacokinetics of Oral Basal Insulin: A Randomised Crossover Trial in Healthy Male Subjects

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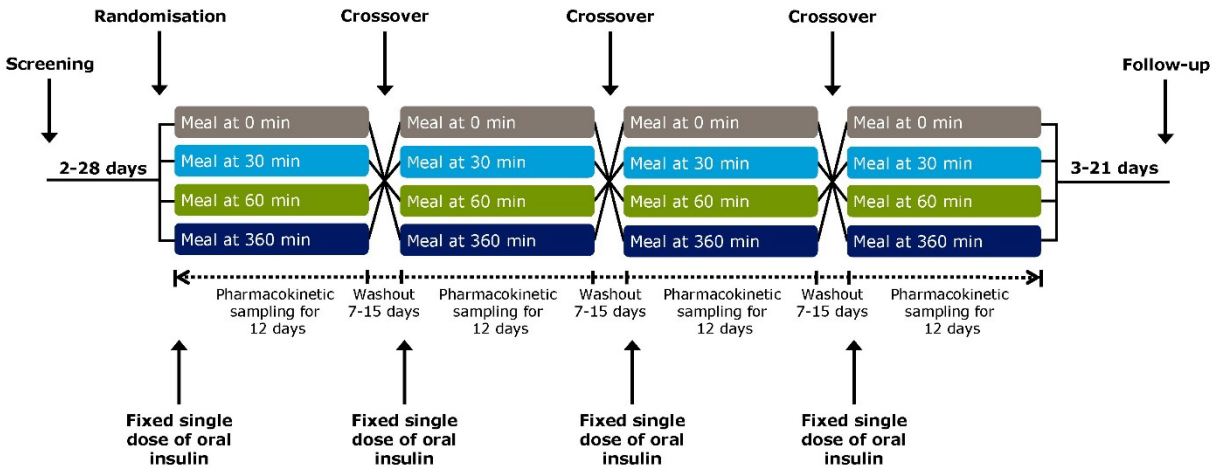

Fig. S1 Trial design.

Table S1 Pharmacokinetic blood sampling scheme

Nominal time (hh:mm)	Insulin 338	Capric acid
00:00[a]	X	X
00:05	X	X
00:10	X	X
00:15	X	X
00:20	X	X
00:25	X	X
00:30	X	X
00:40	X	X
00:50	X	X
01:00	X	X
01:15	X	X
01:30	X	X
01:45	X	X
02:00	X	X
02:15	X	X
02:30	X	X
02:45	X	X
03:00	X	X
03:30	X	X
04:00	X	X
05:00	X	
06:00	X	X
08:00	X	X
10:00	X	
12:00	X	X
14:00	X	
16:00	X	
18:00	X	
20:00	X	
22:00	X	
24:00	X	X
27:00	X	
30:00	X	
36:00	X	
48:00	X	
72:00	X	
96:00	X	
120:00	X	
168:00	X	
216:00	X	
288:00	X	

[a] Within 15 min pre-dose.

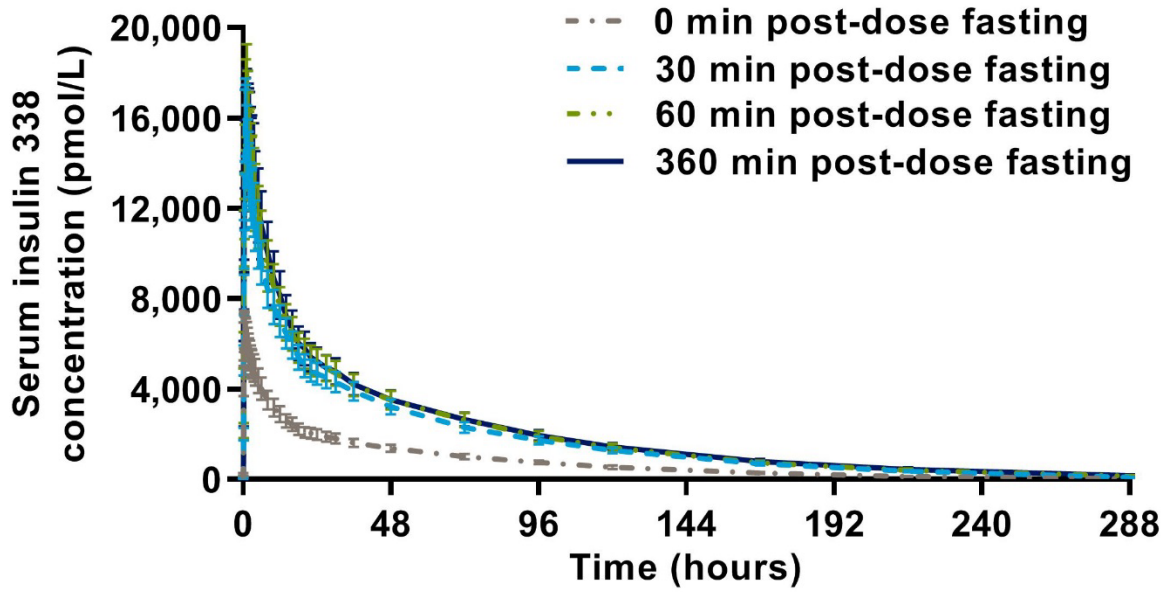

Fig. S2 Mean serum insulin 338 concentration-time profiles after oral administration and varying duration of post-dose fasting in healthy males. Error bars show standard error of the mean.

Table S2 Total variability in $AUC_{Ins338,0-\infty}$ and $C_{max,Ins338}$ after an oral single dose of insulin 338 and varying duration of post-dose fasting in healthy male subjects

	Post-dose fasting period				p value
	0 min	30 min	60 min	360 min	
$AUC_{Ins338,0-\infty}$					
Total variability (CV%)	106.1	131.5	91.4	82.4	0.11
$C_{max,Ins338}$					
Total variability (CV%)	122.2	163.2	90.0	84.5	<0.01

Total variability consists of both the within-subject day-to-day variability and the between-subject variability.
Data are estimated CV%. The p value is from a likelihood ratio test, investigating if the model with different variances for the 4 post-dose fasting periods could be reduced to a model with a common variance for all 4 post-dose fasting periods.
$AUC_{Ins338,0-\infty}$, area under the concentration-time curve for insulin 338 from time zero to infinity; $C_{max,I338}$, maximum concentration of insulin 338; CV%, percentage coefficient of variation.

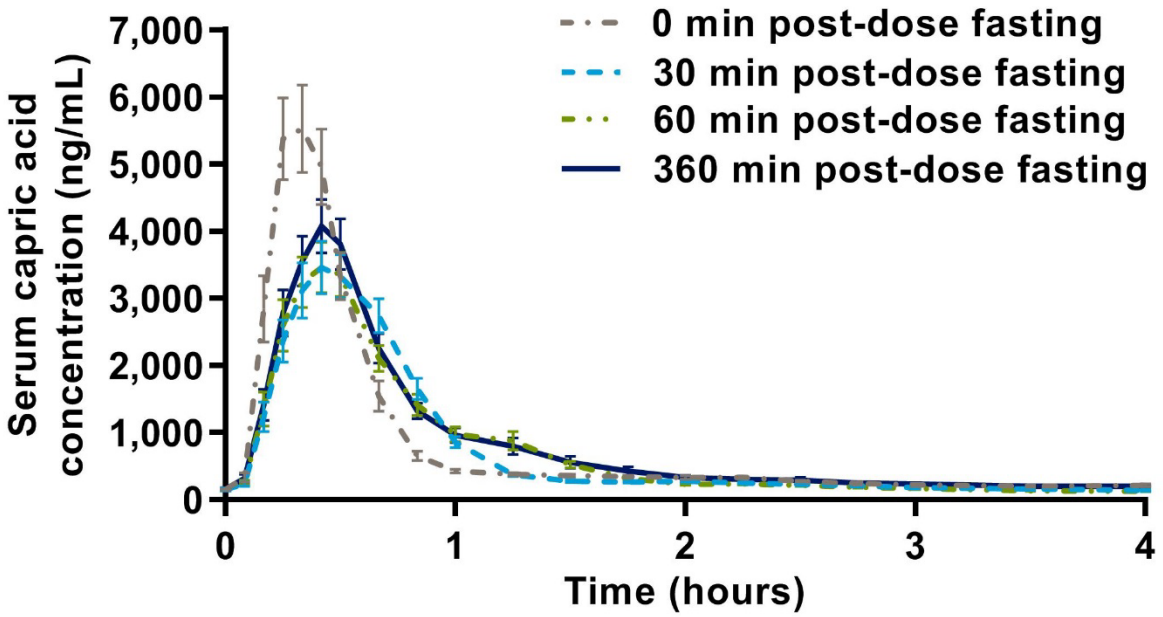

Fig. S3 Mean serum capric acid concentration-time profiles after oral administration of insulin 338 and varying duration of post-dose fasting in healthy males. Error bars show standard error of the mean.

Table S3 Summary of $AUC_{Capric\ acid,0\text{-}6h}$, $C_{max,Capric\ acid}$ and $t_{max,Capric\ acid}$ after an oral single dose of insulin 338 and varying duration of post-dose fasting in healthy male subjects

	Post-dose fasting period			
	0 min	30 min	60 min	360 min
$AUC_{Capric\ acid,0\text{-}360min}$ (ng·h/mL)				
Geometric mean	3,500	3,034	3,070	3,552
CV%	31.6	26.0	28.4	28.4
Median	3,442	2,979	3,061	3,563
Min-Max	1,579-6,803	1,494-5,281	1,594-5,265	1,933-6,074
$C_{max,Capric\ acid}$ (ng/mL)				
Geometric mean	5,079	4,304	4,094	4,730
CV%	64.2	46.9	49.7	43.1
Median	7050	4890	4630	5590
Min-Max	440-18,000	616-10,400	836-10,100	1,350-9,730
$t_{max,Capric\ acid}$ (min)				
Geometric mean	23.0	28.9	30.5	28.9
CV%	137.6	35.6	54.5	76.4
Median	20	30	30	25
Min-Max	10-240	10-50	10-75	10-135

$AUC_{Capric\ acid,0\text{-}360min}$, area under the concentration-time curve for capric acid from time zero to 360 min; $C_{max,Capric\ acid}$, maximum concentration of capric acid; CV%, percentage coefficient of variation; Max, maximum; Min, minimum; $t_{max,Capric\ acid}$, time to maximum concentration for capric acid.