

SUPPLEMENTARY DATA

Supplementary Table 1 Demographic and Clinical Characteristics of Study Population

Characteristic	Study Subjects
Number	10
Age (years)	42.9 (8.1)
Sex	
Male	7 [70%]
Female	3 [30%]
Race	
White	10 [100%]
Weight (kg)	83.7 (18.9)
BMI (kg/m ²)	26.2 (3.8)
Duration of disease (years)	22 (11)
HbA1c (%)	7.3 (0.7)
Fasting glucose (mg/dL)	137 (43)
Fasting insulin (pmol/L)	155 (80)
Fasting C-peptide (nmol/L)	<0.167
Daily Insulin dose (U/kg/day)	0.633 (0.150)

Data presented are mean (SD), with the exception of the sex and race, which are presented as n[%]. The lower limit of quantification for the C-peptide assay was 0.167 nmol/L

Supplementary Table 2 Summary of adverse events

Preferred Term	Placebo	Prandial Insulin	RE 50 mg	RE 150 mg	RE 500 mg
	N=10	N=10	N=10	N=10	N=10
Subjects with Any AE	3 (30%)	4 (40%)	5 (50%)	6 (60%)	4 (40%)
Headache	2 (20%)	2 (20%)	3 (30%)	2 (20%)	2 (20%)
Abdominal pain lower	0	0	0	0	1 (10%)
Dyspepsia	0	0	0	1 (10%)	0
Nausea	0	0	1 (10%)	0	0
Catheter site reaction	0	1 (10%)	0	0	0
Discomfort	0	0	0	1 (10%)	0
Bronchitis	0	0	0	1 (10%)	0
Muscle strain	1 (10%)	0	0	0	0
Thermal burn	0	0	0	1 (10%)	0
Insomnia	0	1 (10%)	0	1 (10%)	1 (10%)
Dry throat	0	0	1 (10%)	0	0
Events of Interest					
Hypoglycemia	5 (50%)	5 (50%)	3 (30%)	5 (50%)	6 (60%)
Related to drug	3 (30%)	5 (50%)	2 (20%)	3 (30%)	4 (40%)

Values are number of people reporting an event (%).

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Supplementary Table 3 Summary of derived glucose parameters

Parameter	Placebo	Prandial Insulin	RE 50 mg	RE 150 mg	RE 500 mg
	N=10	N=10	N=10	N=10	N=10
Weighted Mean Glucose (0-4h), mg/dL ¹	261 (42)	201 (70)	231 (48)	212 (42)	215 (40)
Adjusted Wt. Mean Glucose (0-4h), mg/dL ¹	157 (44)	81 (54)	119 (36)	109 (35)	110 (42)
Δ from placebo ²			-49	-42	-43
			(-76, -22)	(-67, -17)	(-70, -17)
Δ from prandial insulin ²			28	35	34
			(2, 54)	(8, 62)	(7, 61)
Weighted Mean Glucose (0-10h), mg/dL ¹	293 (58)	176 (56)	239 (66)	223 (62)	233 (60)
Adjusted Wt. Mean Glucose (0-10h), mg/dL ¹	190 (69)	56 (40)	128 (60)	120 (59)	127 (64)
Δ from placebo ²			-65	-69	-62
			(-93, -38)	(-96, -42)	(-80, -24)
Δ from prandial insulin ²			53	49	66
			(25, 81)	(20, 78)	(37, 94)

¹ Values are mean (SD)

² Values are difference in least square means by analysis of covariance (95% CI)

Supplementary Table 4 Urine pharmacodynamic parameters

	Placebo	Prandial Insulin	RE 50 mg	RE 150 mg	RE 500 mg
Total Urine Volume (ml), 0-24h					
n	10	10	10	10	9
Mean (SD)	4628 (747)	4623 (829)	5268 (1078)	4962 (886)	5274 (899)
Fluid Balance (ml)					
n	10	10	10	10	10
	-473 (1076)	-231 (985)	-1233 (841)	-840 (773)	-943 (513)
Glucose Excreted (g), 0-24h					
n	10	10	10	10	9
Mean (SD)	58.5 (45.5)	24.3 (34.5)	104.2 (41.0)	108.3 (37.2)	138.6 (44.1)
Creatinine Excreted (mg), 0-24h					
n	10	10	10	10	9
Mean (SD)	1462 (357)	1562 (395)	1587 (381)	1546 (480)	1635 (346)
Creatinine Clearance (ml/min), 0-24h					
n	10	10	10	10	10
Mean (SD)	113.6 (30.3)	124.0 (35.5)	120.9 (30.1)	121.3 (38.0)	128.2 (25.5)
Fractional Glucose Excretion in Urine, %					
n	10	10	10	10	9
0-24h	11.1 (5.76)	5.7 (5.13)	25.4 (4.74)	29.9 (6.00)	34.5 (10.00)

Fluid balance was determined as the sum of measured oral and intravenous fluid input minus total urine volume for 24 hours. Glucose and creatinine excretion were measured from a 24 hour urine collection. Fractional glucose excretion in urine was estimated as the % of filtered glucose in the kidney that was excreted as glucose.