

ELECTRONIC SUPPLEMENTARY MATERIAL

Fig. S1 Urinary volume (a) and water intake (b) during canagliflozin treatment. Data are mean \pm standard deviation.

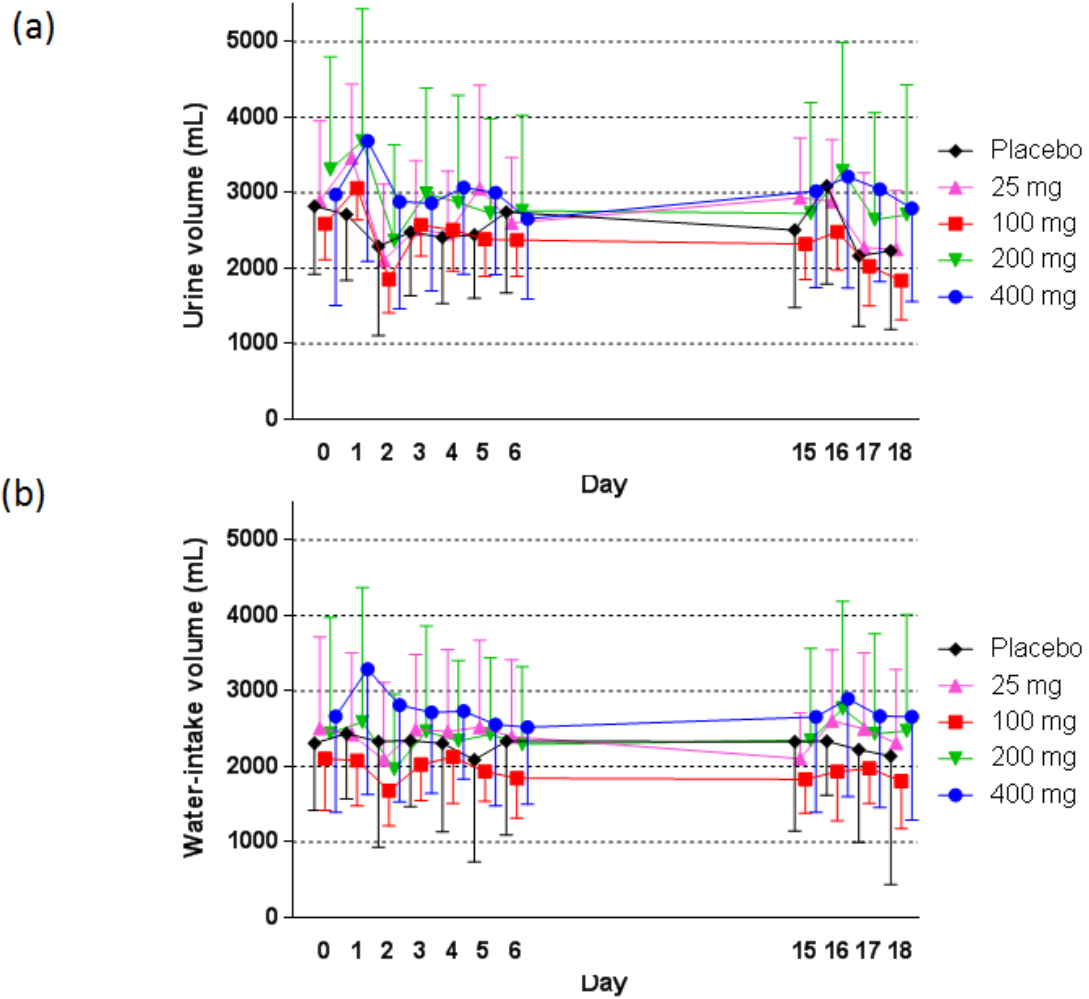


Fig. S2 Systolic (a) and diastolic (b) blood pressure–time profiles on Days 0, 1, and 16 after canagliflozin administration. Data are mean \pm standard deviation. *SBP* systolic blood pressure, *DBP* diastolic blood pressure

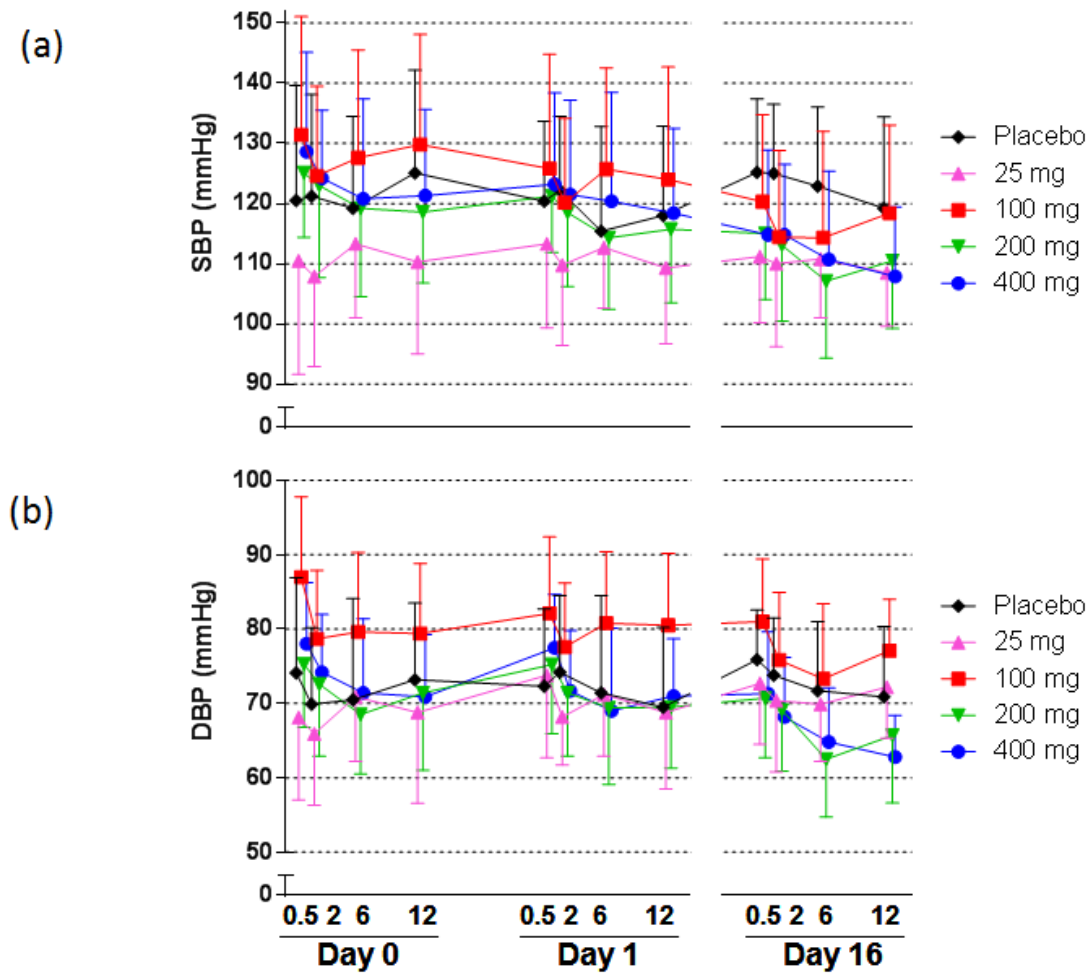


Table S1 Changes in fasting plasma glucose and serum insulin

Mean (SD)	Placebo		Canagliflozin							
			25 mg		100 mg		200 mg		400 mg	
FPG, mg/dL										
Day 1	183	(39)	165	(19)	156	(20)	163	(15)	168	(28)
ΔDay 2	-2	(7)	-8	(6)	-19	(12)	-32	(11)	-41	(17)
ΔDay 17	-6	(26)	-25	(16)	-29	(22)	-51	(16)	-60	(25)
24-h mean PG, mg/dL										
Day 0	233	(45)	213	(19)	200	(27)	209	(31)	217	(34)
ΔDay 1	-3	(16)	-25	(10)	-19	(17)	-30	(15)	-43	(15)
ΔDay 16	-11	(33)	-42	(16)	-29	(28)	-57	(24)	-75	(29)
SI, fasting, μU/mL										
Day 1	5.2	(2.6)	5.2	(2.1)	4.9	(2.3)	4.3	(2.0)	6.3	(3.9)
ΔDay 2	1.1	(1.4)	0.6	(1.2)	-1.0	(1.0)	-1.5	(1.4)	-2.2	(1.7)
ΔDay 17	0.7	(1.4)	0.8	(1.9)	-1.1	(1.3)	-0.9	(1.5)	-1.7	(1.6)
24-h mean SI, μU/mL										
Day 0	18.9	(10.6)	20.9	(16.9)	19.8	(9.6)	10.2	(3.5)	18.7	(12.9)
ΔDay 1	-0.3	(2.5)	-3.4	(6.9)	-2.2	(4.8)	-1.5	(1.8)	-4.1	(3.3)
ΔDay 16	-1.0	(2.0)	-4.0	(7.4)	-2.9	(3.1)	-0.7	(2.7)	-2.9	(4.4)

SD standard deviation, *FPG* fasting plasma glucose, *SI* serum insulin

FPG: 1 mg/dL = 0.0555 mmol/L; insulin: 1 μU/mL = 6.945 pmol/L

Table S2 Urinary electrolyte excretion in 24 hours

Mean (SD)	Day	Placebo	Canagliflozin				
			25 mg	100 mg	200 mg	400 mg	
Sodium	mEq	Baseline	191.57 (41.70)	225.61 (38.76)	216.47 (35.49)	130.79 (51.40)	140.81 (57.08)
	ΔmEq	1	-21.25 (36.64)	29.73 (43.45)	54.12 (41.80)	44.32 (49.89)	36.15 (33.35)
		2	-37.22 (28.59)	-40.70 (31.19)	-18.88 (56.44)	-14.44 (34.33)	-18.04 (33.56)
		3	-31.28 (28.34)	-4.79 (51.89)	29.54 (29.74)	15.58 (38.07)	16.22 (46.73)
		4	-8.11 (33.99)	14.28 (57.11)	61.76 (41.72)	-0.29 (25.68)	1.85 (28.50)
		5	5.68 (45.21)	21.56 (58.85)	30.62 (46.97)	-1.23 (30.57)	2.65 (32.77)
		6	-28.59 (49.12)	-25.58 (47.38)	-19.19 (28.08)	3.64 (28.48)	-12.68 (43.55)
		15	-13.72 (35.98)	51.81 (63.23)	7.47 (35.14)	9.71 (35.19)	22.63 (61.63)
		16	-5.12 (33.72)	5.19 (53.48)	-24.73 (40.99)	14.66 (49.27)	24.78 (49.95)
		17	-58.21 (30.24)	-57.64 (48.87)	-73.54 (38.15)	-14.63 (28.01)	3.68 (44.42)
18	-47.64 (27.41)	-41.54 (34.14)	-56.24 (49.50)	-17.34 (27.67)	-11.75 (38.40)		
Potassium	mEq	Baseline	45.166 (11.183)	44.269 (8.152)	43.858 (7.568)	39.114 (9.842)	46.358 (14.304)
	ΔmEq	1	0.184 (4.932)	4.280 (5.670)	8.803 (5.677)	7.024 (8.014)	3.252 (10.677)
		2	-6.299 (7.577)	-9.470 (6.345)	-8.501 (7.817)	-3.925 (6.688)	-4.742 (10.588)
		3	-4.876 (8.071)	-1.698 (7.775)	3.202 (6.415)	2.824 (9.988)	-3.382 (9.786)
		4	-4.996 (5.131)	-2.239 (7.367)	0.826 (8.908)	0.540 (9.967)	-4.088 (8.900)
		5	-5.164 (9.063)	-0.195 (9.379)	0.073 (8.879)	0.399 (11.223)	-2.984 (8.946)
		6	-10.268 (7.895)	-4.752 (6.813)	-3.349 (9.009)	1.974 (10.591)	-4.630 (11.245)
		15	-2.881 (5.140)	0.091 (8.423)	5.235 (9.534)	2.980 (5.726)	1.502 (16.191)
		16	-1.898 (6.009)	-3.442 (5.794)	0.447 (8.765)	2.956 (8.149)	-1.281 (11.671)
		17	0.089 (23.143)	-6.107 (6.597)	-3.235 (7.652)	-0.424 (8.886)	-0.044 (12.235)
18	-8.784 (6.121)	-4.960 (10.342)	-4.985 (9.474)	0.662 (11.152)	-3.035 (9.017)		

	mEq	Baseline	179.61 (41.83)	213.12 (33.46)	206.75 (35.74)	129.88 (53.64)	143.46 (62.59)
Chloride	ΔmEq	1	-21.73 (31.67)	23.73 (43.84)	48.72 (39.02)	37.99 (43.28)	27.09 (28.95)
		2	-34.96 (27.68)	-53.96 (26.65)	-34.61 (55.82)	-27.08 (31.22)	-37.01 (31.67)
		3	-33.72 (25.81)	-11.08 (51.78)	19.15 (33.18)	-0.67 (32.98)	-11.59 (40.37)
		4	-11.93 (29.53)	-3.31 (48.37)	40.02 (44.42)	-15.39 (23.52)	-21.75 (26.87)
		5	5.37 (45.65)	13.84 (51.93)	18.20 (48.06)	-14.81 (26.22)	-17.98 (30.29)
		6	-34.73 (42.91)	-37.11 (39.17)	-29.77 (30.96)	-4.50 (27.60)	-28.85 (39.58)
		15	-17.38 (33.86)	47.64 (58.99)	1.33 (41.74)	7.19 (31.91)	9.08 (56.96)
		16	-9.72 (33.26)	1.57 (48.90)	-26.33 (36.00)	8.81 (40.05)	7.08 (46.46)
		17	-50.32 (28.83)	-59.33 (46.62)	-70.22 (35.52)	-20.19 (24.59)	-8.95 (42.09)
		18	-47.94 (29.44)	-44.32 (28.75)	-52.69 (47.08)	-22.13 (26.83)	-23.54 (35.02)
	mg	Baseline	177.448 (59.840)	172.233 (62.022)	180.974 (66.494)	193.388 (81.102)	211.774 (84.723)
Calcium	Δmg	1	-27.568 (19.840)	-19.904 (30.800)	-23.228 (31.220)	-25.703 (21.318)	-37.937 (20.705)
		2	-25.138 (45.104)	1.314 (33.852)	18.852 (22.630)	-33.561 (52.259)	-34.330 (27.035)
		3	-31.154 (29.833)	-32.993 (36.905)	-20.230 (29.724)	-30.089 (32.091)	-19.099 (39.842)
		4	-8.555 (42.378)	-25.558 (25.406)	-4.119 (25.652)	-42.846 (42.591)	-23.190 (46.577)
		5	-10.606 (36.917)	-14.433 (32.250)	-17.856 (35.647)	-30.909 (40.119)	-27.516 (45.014)
		6	-38.308 (36.881)	-38.393 (45.227)	-31.101 (42.559)	-39.952 (33.565)	-41.196 (55.194)
		15	-26.609 (33.421)	7.650 (38.051)	-0.456 (30.301)	-30.780 (44.531)	-23.455 (61.516)
		16	-9.507 (33.654)	20.658 (37.618)	3.545 (33.798)	-23.658 (58.913)	-19.859 (61.746)
		17	-19.456 (51.302)	-7.710 (38.305)	-12.658 (26.920)	-29.660 (51.224)	2.854 (58.871)
		18	-27.027 (41.766)	6.297 (34.398)	4.339 (29.907)	-28.527 (45.683)	-11.148 (61.059)

	mg	Baseline	84.356 (27.730)	81.991 (19.341)	77.048 (11.855)	91.272 (27.163)	98.086 (30.709)
Magnesium	Δmg	1	-2.158 (18.353)	-9.784 (10.310)	-18.296 (10.623)	-30.156 (14.467)	-37.695 (14.381)
		2	-2.391 (18.674)	9.743 (12.615)	19.913 (12.675)	-10.733 (19.418)	-13.078 (14.49)
		3	-4.322 (15.727)	-11.896 (9.636)	-0.671 (8.288)	-13.665 (17.396)	-10.454 (15.265)
		4	1.713 (20.302)	-6.528 (9.803)	13.23 (13.520)	-11.811 (16.562)	-3.360 (20.758)
		5	0.192 (23.288)	8.502 (25.203)	14.506 (13.088)	-6.768 (12.305)	-6.594 (14.842)
		6	-9.264 (21.995)	-5.669 (13.310)	10.701 (9.982)	-7.106 (11.519)	-9.936 (18.606)
		15	-3.030 (19.106)	9.288 (19.043)	8.819 (17.892)	5.281 (18.571)	11.073 (25.534)
		16	7.681 (15.558)	16.155 (14.294)	16.451 (11.703)	6.774 (22.162)	8.121 (26.287)
		17	8.723 (15.556)	19.404 (16.575)	26.605 (13.310)	4.573 (23.484)	25.705 (27.212)
		18	-3.396 (18.594)	28.343 (18.442)	33.876 (14.254)	2.183 (16.959)	10.906 (16.874)
	mg	Baseline	667.442 (146.987)	762.557 (127.104)	825.593 (127.634)	654.491 (119.384)	677.438 (123.725)
Inorganic phosphorus	Δmg	1	9.435 (122.097)	-228.096 (113.863)	-240.501 (96.574)	-101.994 (126.41)	-154.463 (95.128)
		2	-38.305 (89.406)	48.013 (91.207)	50.997 (91.301)	108.788 (94.566)	161.924 (120.722)
		3	-16.189 (161.166)	-140.364 (125.632)	-122.946 (120.974)	102.604 (140.808)	201.906 (145.555)
		4	63.842 (158.104)	1.254 (92.293)	76.452 (108.489)	55.614 (95.226)	170.215 (113.188)
		5	11.965 (151.733)	-36.354 (111.248)	-8.516 (91.331)	74.690 (145.196)	166.743 (123.038)
		6	-40.174 (123.480)	13.853 (143.580)	18.594 (94.351)	58.687 (77.332)	139.720 (140.589)
		15	-48.286 (110.391)	0.128 (116.229)	30.316 (102.054)	18.084 (89.494)	47.340 (157.115)
		16	10.541 (138.422)	-53.40 (91.442)	-58.157 (122.926)	38.156 (148.240)	36.073 (200.775)
		17	-3.728 (111.781)	52.488 (104.319)	5.795 (79.034)	49.905 (127.263)	92.078 (113.624)
		18	-87.282 (128.705)	-90.183 (96.711)	-42.588 (88.040)	57.935 (129.751)	116.452 (157.906)

SD standard deviation