

Supplementary Data

Simultaneous Quantitation of Ramipril and Ramiprilat in drug formulations: A Clinical LC-MS/MS Study

S1. Table of Demographic Data of each subject.

Subject No	Subject Initial	Screening Date	Date of Birth (DD/MM/YYYY)	Sex	Age	Height (Meter)	Weight (Kg)	BMI	Smoker*/ Non-Smoker
01	AAMA001	17/07/21	10/12/1998	Male	23	1.71	81	27.7	No
02	KIHG014	17/07/21	05/05/2000	Male	21	1.79	79	24.7	No
03	MSSA044	22/07/21	05/05/2001	Male	20	1.73	63	21.0	Yes
04	ARAA038	17/07/21	11/01/2001	Male	21	1.74	76	25.1	Yes
05	AAKE030	17/07/21	31/03/1992	Male	29	1.80	96	29.6	Yes
06	MAKE029	17/07/21	30/01/2003	Male	18	1.73	70	23.4	No
07	YNDA041	17/07/21	30/04/1996	Male	25	1.74	71	23.5	No
08	MSMA015	17/07/21	04/11/1998	Male	23	1.64	65	24.2	Yes
09	MAHA037	17/07/21	04/02/1974	Male	47	1.73	88	29.4	No
10	ANAN033	17/07/21	27/12/2002	Male	19	1.80	85	26.2	No
11	AAAA026	17/07/21	17/08/1981	Male	40	1.69	80	28.0	No
12	MRAA036	17/07/21	01/03/2003	Male	18	1.81	98	29.9	Yes
13	BJFA034	17/07/21	21/11/2002	Male	19	1.80	65	20.1	No
14	ZHAA035	17/07/21	29/05/2002	Male	19	1.81	69	21.1	No
15	ANMI016	17/07/21	08/09/1999	Male	22	1.74	80	26.4	Yes
16	ASTA031	17/07/21	01/01/1994	Male	28	1.75	65	21.2	Yes
17	KHMO011	17/07/21	27/10/1999	Male	22	1.71	71	24.3	Yes
18	AHMO010	17/07/21	14/08/1997	Male	24	1.65	65	23.9	Yes
19	AWMO008	17/07/21	20/10/1996	Male	25	1.73	82	27.4	Yes
20	MHMO007	17/07/21	06/10/1998	Male	23	1.83	90	26.9	Yes
21	BWMU004	17/07/21	10/09/1992	Male	29	1.80	95	29.3	Yes
22	DKDA019	17/07/21	12/07/1993	Male	28	1.73	60	20.0	Yes
23	AMAY013	17/07/21	06/07/1998	Male	23	1.73	87	29.1	No

24	YADB012	17/07/21	15/04/2003	Male	18	1.70	69	23.9	No
25	MIAS017	17/07/21	15/01/1991	Male	31	1.75	70	22.9	No
26	MAIA023	17/07/21	19/05/1993	Male	28	1.79	74	23.1	Yes
27	AAIT025	17/07/21	09/11/1993	Male	28	1.78	75	23.7	Yes
28	AMSA024	17/07/21	14/01/1974	Male	48	1.73	73	24.4	Yes
29	ZMSA028	17/07/21	09/04/2002	Male	19	1.81	61	18.6	Yes
30	MJIZ027	17/07/21	22/12/2000	Male	21	1.79	60	18.7	Yes
31	SHIO022	17/07/21	21/11/1986	Male	35	1.82	62	18.7	Yes
32	AKAA005	17/07/21	21/01/1991	Male	31	1.60	75	29.3	Yes
33	ASMS003	17/07/21	06/03/1973	Male	48	1.63	78	29.4	No
34	MOMS002	17/07/21	05/10/1980	Male	41	1.73	86	28.7	Yes
35	MSAA020	17/07/21	31/08/1993	Male	28	1.75	90	29.4	Yes
36	IRIA042	17/07/21	21/05/1995	Male	26	1.68	61	21.6	No

Arithmetic Mean	27	1.74	75	24.9	Yes= 22/ No = 14
SD	8.5	0.06	11.0	3.6	
CV %	32	3.3	14.6	14.3	
Min	18	1.6	60	18.6	
Max	48	1.8	98	30	

*Smoker: not more than three cigarettes/ day during sampling days, ten cigarettes/day during the washout period.

S2. Tables of laboratory value listing on-screening tables.

HEMATOLOGY ON-SCREENING							
	R.B.C 4.2 - 6.1 10 ¹² /L	Hemoglobin 14.0- 18.0 g/dL	Hematocrit 40.0 - 54.0 %	M.C.V 76.0 - 94.0 fL	M.C.H 26.0 - 31.0 pg	M.C.H.C 31.0 - 36.0 g/dL	W.B.C. 4.5 - 11.0 10 ⁹ /L
Mean	5.2	15.6	45.3	86.8	30.0	34.5	7.8
SD	0.45	0.96	2.5	4.4	1.7	0.62	1.7
Min	4.5	13.6	41.1	75.0	24.9	33.2	4.6
Max	6.1	17.4	50.4	93.7	32.3	35.4	11.7
DIFFERENTIAL LEUKOCYTES COUNT ON-SCREENING							
	Neutrophils 45 - 75 %	Lymphocytes 25 - 40 %	Monocytes 0 - 7 %	Eosinophils 0 - 4 %	Basophils 0 - 1 %	Platelets 150 - 450 × 10 ⁹ /L	
Mean	66	30	3	0.5	0.1	231	
SD	2.9	2.2	1	0.5	0.3	43	
Min	60	27	2	0	0	154	
Max	70	34	5	1	1	338	

*NA is not applicable.

S3. Table of laboratory value listing during the study periods of each subject.

URINANALYSIS ON-SCREENING													
PHYSICAL AND CHEMICAL EXAMINATION												Microscopic Examination	
	Color Yellow / clear	SP Gravity 1.003 - 1.030	pH 5.0 - 8.0	Nitrate Negative	Protein Negative	Ketones Negative	Glucose Negative	Bilirubin Negative	Urobilinogen Normal	Leukocytes /Epi Negative	Blood/Hb Negative	Leukocytes Up to 10/μL	Erythrocytes Up to 3/μL
Average	*NA	1.02	5.53	NA	NA	NA	NA	NA	NA	NA	NA	3.9	1.3
Everyone	Yellow	NA	NA	-ve	-ve	-ve	-ve	-ve	Nor	-ve	-ve	NA	NA

Serum Creatinine and Potassium Level Tests			
Subject No.	Post 8 hours from Drug administration in PI		Post 24 hours from Drug administration in PI
	Creatinine 0.60 - 1.30 mg/dL	Potassium 3.5 - 5.3 mmol/L	Creatinine 0.60 - 1.30 mg/dL
Mean	0.72	3.9	N/A
SD	0.076	0.32	N/A
Min	0.60	3.5	N/A
Max	0.87	4.6	N/A

Serum Creatinine and Potassium Level Tests					
Subject No.	Before Period II		Post 8 hours from Drug administration in PII		Post 24 hours from Drug administration in PII
	Creatinine 0.60 - 1.30 mg/dL	Potassium 3.5 - 5.3 mmol/L	Creatinine 0.60 - 1.30 mg/dL	Potassium 3.5 - 5.3 mmol/L	Creatinine 0.60 - 1.30 mg/dL
Mean	0.85	4.0	0.91	4.0	N/A
SD	0.13	0.30	0.12	0.24	N/A
Min	0.64	3.5	0.65	3.6	N/A
Max	1.21	4.8	1.16	4.7	N/A

IMMUNOLOGY ON SCREENING						
	HBs Ag Negative < 1.00 S/CO	HCV Ab Negative < 1.00 S/CO	HIV I and II Negative < 1.00 S/CO			
Every participant	Negative	Negative	Negative			
DIFFERENTIAL LEUKOCYTES COUNT ON FOLLOW-UP						
Subject No.	Neutrophils 45 - 75 %	Lymphocytes 25 - 40 %	Monocytes 0 - 7 %	Eosinophils 0 - 4 %	Basophils 0 - 1 %	Platelets 150 - 450 × 10 ⁹ /L
Mean	54	35	6	3	0.6	260
SD	4.6	3.5	0.70	1.2	0.50	56
Min	45	26	5	0	0	139
Max	67	40	7	4	1	393

S4. Table of laboratory value listing follow-up of each subject.

BIOCHEMISTRY ON-SCREENING									
Subject No.	Fasting Blood Sugar 70 - 115 mg/dL	Urea 10.0 - 50.0 mg/dL	Creatinine 0.60 - 1.30 mg/dL	Sodium 135 - 153 mmol/L	Potassium 3.5 - 5.3 mmol/L	GOT Up to 42 UNITS/L	GPT Up to 50 UNITS/L	ALK 40 - 150 UNITS/L	Bilirubin Total Up to 1.4 mg/dL
Mean	98	30.9	0.83	142	4.0	20	20	81	0.5
SD	6.8	6.5	0.12	3.1	0.32	5.9	9.7	21	0.4
Min	80	19.4	0.61	137	3.5	13	2	44	0.1
Max	112	47.0	1.07	147	4.9	39	45	132	1.4
Mean	88.01	28.7	0.95	143	4.2	21	24	81	0.6
SD	12.028	5.73	0.197	1.7	0.43	9.5	15.5	28.1	0.37
Min	65.00	19.1	0.56	139	3.6	13	8	35	0.2
Max	125.00	41.7	1.36	147	5.3	63	84	186	1.8

HEMATOLOGY ON FOLLOW-UP							
Subject No.	R.B.C 4.2 - 6.1 $\times 10^{12}/L$	Hemoglobin 14.0- 18.0 g/dL	Hematocrit 40.0 - 54.0 %	M.C.V 76.0 - 94.0 fL	M.C.H 26.0 - 31.0 pg	M.C.H.C 31.0 - 36.0 g/dL	W.B.C. 4.5 - 11.0 $\times 10^9/L$
Mean	5.1	15.0	44.2	86.9	29.4	33.8	7.8
SD	0.37	1.1	3.0	4.3	1.6	0.53	2.4
Min	4.3	13.1	38.7	75.5	24.6	32.7	4.1
Max	5.8	17.4	50.2	95.8	32.0	34.6	13.2