

Appendix 1-4 Body weights during quarantine period

Sex	Individual No.	Animal <sup>1)</sup> No.	Receipt day (Day 1)	Final day of quarantine (Day 5)	Body weight gain
Female	1	2305	103	136	33
	2	2401	103	128	25
	3	2105	106	133	27
	4	exc.	95	119	24
	5	2304	103	130	27
	6	2504	105	132	27
	7	2303	100	127	27
	8	2107	104	131	27
	9	2204	103	130	27
	10	2403	105	134	29
	11	exc.	92	120	28
	12	2203	102	133	31
	13	2301	102	129	27
	14	2205	100	127	27
	15	exc.	107	139	32
	16	2307	105	133	28
	17	2206	96	125	29
	18	2104	102	134	32
	19	2201	100	131	31
	20	2207	101	135	34
	21	2502	107	134	27
	22	2202	101	128	27
	23	2106	97	124	27
	24	exc.	106	139	33
	25	exc.	93	121	28
	26	2102	102	129	27
	27	2503	98	124	26
	28	2402	100	126	26
	29	exc.	82	125	43
	30	exc.	100	120	20
	31	2306	100	130	30
	32	exc.	94	119	25
	33	2404	100	131	31
	34	2302	99	125	26
	35	2501	101	129	28
	36	2101	98	127	29
	37	2103	95	126	31
	38	exc.	91	122	31
	39	exc.	102	138	36
	Mean		100	129	29
	SD		5	5	4

Unit: g.

Body weight gain = Body weight difference of allocation day and receipt day during 5 days.

1) Identification numbers after allocation to treatment groups (exc.: excluded from the study system).

Appendix 2-1 Clinical signs of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg) rapid (2min) infusion (1h)	Animal No.	Day Time	-1	1 pre admin. 1h	2 pre admin. 1h	3 pre admin. 1h	Necropsy day	
Male	Control (Saline)	0	1101	-	-	-	-	-	-	
			1102	-	-	-	-	-	-	
			1103	-	-	-	-	-	-	-
			1104	-	-	-	-	-	-	-
			1105	-	-	-	-	-	-	-
			1106	-	-	-	-	-	-	-
			1107	-	-	-	-	-	-	-
	AcPepA	10	1201	-	-	-	-	-	-	
			1202	-	-	-	-	-	-	
			1203	-	-	-	-	-	-	
			1204	-	-	-	-	-	-	
			1205	-	-	-	-	-	-	
			1206	-	-	-	-	-	-	
			1207	-	-	-	-	-	-	
		20	1301	-	-	-	-	-	-	
			1302	-	-	-	-	-	-	
			1303	-	-	-	-	-	-	
			1304	-	-	-	-	-	-	
			1305	-	-	-	-	-	-	
			1306	-	-	-	-	-	-	
			1307	-	-	-	-	-	-	

Time pre: pre-administration, admin.: during administration, 1h: from finish of administration to 1 hour after administration.  
-: No abnormalities.

Appendix 2-2 Clinical signs of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg) rapid (2min) infusion (Ih)	Animal No.	Day Time	-1	1 pre admin. Ih	2 pre admin. Ih	3 pre admin. Ih	Necropsy day	
Female	Control (Saline)	0	2101	-	-	-	-	-	-	
			2102	-	-	-	-	-	-	
			2103	-	-	-	-	-	-	
			2104	-	-	-	-	-	-	
			2105	-	-	-	-	-	-	
			2106	-	-	-	-	-	-	
			2107	-	-	-	-	-	-	
Female	AcPepA	10	30	2201	-	-	-	-	-	
				2202	-	-	-	-	-	
				2203	-	-	-	-	-	
				2204	-	-	-	-	-	
				2205	-	-	-	-	-	
				2206	-	-	-	-	-	
				2207	-	-	-	-	-	
		20	60	2301	-	-	-	-	-	-
				2302	-	-	-	-	-	
				2303	-	-	-	-	-	
				2304	-	-	-	-	-	
				2305	-	-	-	-	-	
				2306	-	-	-	-	-	
				2307	-	-	-	-	-	

Time pre: pre-administration, admin.: during administration, Ih: from finish of administration to 1 hour after administration.  
-: No abnormalities.

Appendix 2-3 Clinical signs of rats treated intravenously with AcPepA for 3 days - TK group

Sex	Test substance	Dose (mg/kg)		Animal No.	Day of treatment								
		rapid (2min)	infusion (1h)		-6	-5	-4	-3	-2	-1	1		
Male	AcPepA	10	30	1401	-	-	-	-	-	-	-	-	-
				1402	-	-	-	-	-	-	-	-	-
		1403	-	-	-	-	-	-	-	-	-	-	
		1404	-	-	-	-	-	-	-	-	-	-	
Female	AcPepA	20	60	1501	-	-	-	-	-	-	-	-	-
				1502	-	-	-	-	-	-	-	-	-
		1503	-	-	-	-	-	-	-	-	-	-	
		1504	-	-	-	-	-	-	-	-	-	-	
		10	30	2401	-	-	-	-	-	-	-	-	-
				2402	-	-	-	-	-	-	-	-	-
		2403	-	-	-	-	-	-	-	-	-	-	
		2404	-	-	-	-	-	-	-	-	-	-	
		20	60	2501	-	-	-	-	-	-	-	-	-
				2502	-	-	-	-	-	-	-	-	-
		2503	-	-	-	-	-	-	-	-	-	-	
		2504	-	-	-	-	-	-	-	-	-	-	

-: No abnormalities.

Appendix 3-1 Body weights of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Day of treatment			Necropsy			
		rapid (2min)	infusion (1h)		1	2	3				
Male	Control (Saline)	0	0	1101	188	195	201	170			
				1102	214	222	233	195			
				1103	212	212	223	189			
				1104	206	208	215	182			
				1105	183	187	189	163			
				1106	201	205	212	178			
				1107	208	213	217	184			
				Mean	202	206	213	180			
				SD	12	12	14	11			
				AcPepA	10	30	1201	208	215	218	185
							1202	199	207	214	181
							1203	189	193	197	172
							1204	213	212	215	187
							1205	204	207	212	179
	1206	198	201				206	178			
	1207	215	217				225	192			
	Mean	204	207				212	182			
	SD	9	8				9	7			
	AcPepA	20	60				1301	203	208	217	189
							1302	203	207	213	185
							1303	212	218	222	192
							1304	207	210	218	185
							1305	205	210	212	184
				1306	200	204	209	179			
				1307	189	193	202	173			
				Mean	203	207	213	184			
				SD	7	8	7	6			
				Female	Control (Saline)	0	0	2101	140	137	149
2102								151	148	157	132
2103								142	145	146	122
2104								154	149	156	135
2105								150	150	155	135
2106	140	139	136					125			
2107	148	143	147					130			
Mean	146	144	149					129			
SD	6	5	7					5			
AcPepA	10	30	2201					150	148	156	130
			2202					138	137	142	123
			2203					151	150	157	137
			2204					142	144	151	126
			2205					133	140	144	127
			2206		147	149	151	127			
			2207		152	155	157	136			
			Mean		145	146	151	129			
			SD		7	6	6	5			
			AcPepA		20	60	2301	149	148	153	131
							2302	140	141	142	121
							2303	144	149	154	129
							2304	149	146	149	134
							2305	155	161	163	137
2306	146	148					150	133			
2307	146	144					150	127			
Mean	147	148					152	130			
SD	5	6					6	5			

Unit: g.

Appendix 3-2 Body weights of rats treated intravenously with AcPepA for 3 days - TK group

Sex	Test substance	Dose (mg/kg)		Animal No.	Administration day		
		rapid (2min)	infusion (1h)				
Male	AcPepA	10	30	1401	247		
				1402	233		
				1403	223		
				1404	251		
				Mean	239		
				SD	13		
				20	60	1501	231
		1502	250				
		1503	240				
		1504	228				
		Mean	237				
		SD	10				
		Female	AcPepA	10	30	2401	160
						2402	156
2403	178						
2404	164						
Mean	165						
SD	10						
20	60					2501	159
2502	156						
2503	162						
2504	172						
Mean	162						
SD	7						

Unit: g.

Appendix 4 Food consumption of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Day of treatment			
		rapid (2min)	infusion (1h)		0-1	1-2	2-3	
Male	Control (Saline)	0	0	1101	23	24	23	
				1102	25	26	25	
				1103	25	20	25	
				1104	25	21	25	
				1105	19	18	17	
				1106	24	20	21	
				1107	24	22	23	
				Mean	23.6	21.6	22.7	
				SD	2.1	2.7	2.9	
	AcPepA	10	30	1201	26	24	24	
				1202	27	25	24	
				1203	23	20	21	
				1204	24	21	22	
				1205	23	22	21	
				1206	23	20	22	
				1207	26	23	25	
					Mean	24.6	22.1	22.7
					SD	1.7	2.0	1.6
		20	60	1301	22	22	24	
				1302	23	21	22	
				1303	24	24	22	
1304				27	22	25		
1305				22	21	19		
1306	25			22	23			
1307	22			20	22			
			Mean	23.6	21.7	22.4		
			SD	1.9	1.3	1.9		
Female	Control (Saline)	0	0	2101	16	13	18	
				2102	18	16	17	
				2103	18	15	15	
				2104	19	14	19	
				2105	18	15	17	
				2106	17	13	14	
				2107	17	13	14	
				Mean	17.6	14.1	16.3	
				SD	1.0	1.2	2.0	
	AcPepA	10	30	2201	18	15	17	
				2202	14	12	15	
				2203	18	16	19	
				2204	15	15	18	
				2205	13	16	16	
				2206	17	16	16	
				2207	19	15	17	
					Mean	16.3	15.0	16.9
					SD	2.3	1.4	1.3
		20	60	2301	18	14	18	
				2302	16	13	14	
				2303	17	18	18	
2304				19	16	18		
2305				20	19	20		
2306	17			14	15			
2307	16			13	17			
			Mean	17.6	15.3	17.1		
			SD	1.5	2.4	2.0		

Unit: g/day.

Appendix 5-1 Hematology in rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	RBC (10 <sup>6</sup> /μL)	WBC (10 <sup>2</sup> /μL)	Ht (%)	Hb (g/dL)	MCH (pg)	MCV (fL)	
		rapid (2min)	infusion (1h)								
Male	Control (Saline)	0	0	1101	736	68.5	44.9	15.3	20.8	61.0	
				1102	703	85.8	46.6	15.8	22.5	66.3	
				1103	685	82.0	43.8	14.9	21.8	63.9	
				1104	737	99.4	44.0	15.1	20.5	59.7	
				1105	743	56.7	45.3	15.5	20.9	61.0	
				1106	770	64.8	45.9	15.7	20.4	59.6	
				1107	739	85.2	45.9	15.6	21.1	62.1	
		Mean	730	77.5	45.2	15.4	21.1	61.9			
		SD	28	14.7	1.0	0.3	0.8	2.4			
		AcPepA	10	30	1201	695	53.2	41.8	14.3	20.6	60.1
					1202	729	62.0	43.4	15.0	20.6	59.5
					1203	738	71.0	42.7	14.7	19.9	57.9
					1204	741	62.5	44.0	15.1	20.4	59.4
					1205	766	58.8	43.9	15.1	19.7	57.3
	1206				776	58.8	44.4	15.7	20.2	57.2	
	1207				673	88.6	42.4	14.3	21.2	63.0	
	Mean		731	65.0	43.2	14.9	20.4	59.2			
	SD		37	11.7	1.0	0.5	0.5	2.0			
	AcPepA		20	60	1301	650	106.0	41.1	14.0	21.5	63.2
					1302	657	103.0	41.7	14.6	22.2	63.5
					1303	725	64.5	42.6	14.7	20.3	58.8
					1304	685	95.0	42.3	14.2	20.7	61.8
					1305	672	62.2	41.2	14.2	21.1	61.3
		1306			720	52.0	45.2	15.6	21.7	62.8	
		1307			716	80.2	44.2	14.9	20.8	61.7	
		Mean	689	80.4	42.6	14.6	21.2	61.9			
		SD	31	21.5	1.6	0.5	0.7	1.6			
		Female	Control (Saline)	0	0	2101	736	75.2	43.3	15.1	20.5
2102						717	64.2	42.0	14.5	20.2	58.6
2103						736	60.5	43.0	15.0	20.4	58.4
2104						743	74.5	44.6	15.7	21.1	60.0
2105						716	72.6	44.2	15.3	21.4	61.7
2106	684					69.4	41.3	14.6	21.3	60.4	
2107	743					85.9	44.0	15.6	21.0	59.2	
Mean	725			71.8	43.2	15.1	20.8	59.6			
SD	21			8.3	1.2	0.5	0.5	1.2			
AcPepA	10			30	2201	724	51.4	44.8	15.7	21.7	61.9
					2202	742	87.4	43.5	15.2	20.5	58.6
					2203	687	74.0	41.8	14.5	21.1	60.8
					2204	689	76.9	42.3	15.1	21.9	61.4
					2205	683	72.3	42.2	14.7	21.5	61.8
			2206		708	87.8	42.1	14.7	20.8	59.5	
			2207		673	95.0	42.9	15.0	22.3	63.7	
	Mean		701	77.8	42.8	15.0	21.4	61.1			
	SD		25	14.3	1.0	0.4	0.6	1.7			
	AcPepA		20	60	2301	731	67.3	42.3	14.7	20.1	57.9
					2302	719	83.3	42.9	15.0	20.9	59.7
					2303	728	59.6	43.9	15.1	20.7	60.3
					2304	662	74.7	41.3	14.6	22.1	62.4
					2305	723	64.2	43.9	15.4	21.3	60.7
2306					684	74.7	42.0	14.7	21.5	61.4	
2307					789	94.2	46.1	16.4	20.8	58.4	
Mean			719	74.0	43.2	15.1	21.1	60.1			
SD			40	11.9	1.6	0.6	0.6	1.6			

Appendix 5-2 Hematology in rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	MCHC (g/dL)	Ret		Plt ( $10^4/\mu\text{L}$ )	PT (sec)	APTT (sec)
		rapid (2min)	infusion (1h)			(%)	( $10^4/\mu\text{L}$ )			
Male	Control (Saline)	0	0	1101	34.1	10.04	73.89	120.7	13.2	20.1
				1102	33.9	10.43	73.32	106.2	12.8	20.7
				1103	34.0	10.01	68.57	126.5	13.2	17.6
				1104	34.3	10.04	73.99	127.2	13.8	18.8
				1105	34.2	9.80	72.81	123.7	13.6	20.7
				1106	34.2	8.04	61.91	104.6	12.9	19.1
				1107	34.0	9.35	69.10	112.2	13.5	21.3
				Mean	34.1	9.67	70.51	117.3	13.3	19.8
	SD	0.1	0.79	4.41	9.5	0.4	1.3			
	AcPepA	10	30	1201	34.2	9.37	65.12	143.6	14.4	20.8
				1202	34.6	12.69	92.51	142.7	12.7	19.5
				1203	34.4	10.60	78.23	125.7	13.4	18.0
				1204	34.3	10.40	77.06	120.4	14.0	19.0
				1205	34.4	8.37	64.11	159.2	13.1	21.0
				1206	35.4	7.51	58.28	119.0	12.4	18.5
				1207	33.7	11.92	80.22	110.2	12.5	19.8
		Mean	34.4	10.12	73.65	131.5	13.2	19.5		
		SD	0.5	1.85	11.77	17.3	0.8	1.1		
		20	60	1301	34.1	9.47	61.56	126.1	11.9	17.6
				1302	35.0	9.20	60.44	126.0	12.7	20.2
				1303	34.5	9.49	68.80	129.5	11.9	18.0
				1304	33.6	11.30	77.41	140.8	13.9	19.0
				1305	34.5	9.30	62.50	132.6	13.6	21.1
	1306			34.5	10.50	75.60	137.3	13.4	21.6	
	1307			33.7	10.76	77.04	132.5	13.4	20.2	
	Mean	34.3	10.00	69.05	132.1	13.0	19.7			
	SD	0.5	0.84	7.64	5.5	0.8	1.5			
	Female	Control (Saline)	0	0	2101	34.9	6.73	49.53	161.9	12.6
2102					34.5	8.32	59.65	142.2	12.2	15.9
2103					34.9	6.56	48.28	141.6	11.7	14.2
2104					35.2	7.30	54.24	116.0	12.3	16.3
2105					34.6	9.40	67.30	133.3	11.7	17.1
2106					35.4	9.06	61.97	128.1	12.2	17.1
2107					35.5	7.43	55.20	106.6	12.5	26.7
Mean					35.0	7.83	56.60	132.8	12.2	18.2
SD		0.4	1.12	6.82	18.3	0.4	4.1			
AcPepA		10	30	2201	35.0	7.98	57.78	133.1	11.4	14.9
				2202	34.9	6.66	49.42	128.5	11.9	17.2
				2203	34.7	7.81	53.65	210.2	12.2	15.0
				2204	35.7	8.01	55.19	145.0	11.9	17.6
				2205	34.8	8.32	56.83	123.1	12.2	16.9
				2206	34.9	9.34	66.13	154.7	12.2	14.7
				2207	35.0	8.71	58.62	124.5	12.2	17.8
		Mean	35.0	8.12	56.80	145.6	12.0	16.3		
		SD	0.3	0.83	5.14	30.7	0.3	1.4		
		20	60	2301	34.8	8.45	61.77	155.9	11.5	15.9
				2302	35.0	7.44	53.49	121.7	11.6	16.5
				2303	34.4	7.81	56.86	158.3	11.2	15.9
				2304	35.4	9.00	59.58	27.2 <sup>a)</sup>	11.8	17.0
				2305	35.1	8.95	64.71	138.4	11.9	17.2
2306				35.0	9.06	61.97	134.7	11.6	15.6	
2307				35.6	6.38	50.34	135.5	12.3	14.7	
Mean		35.0	8.16	58.39	124.5	11.7	16.1			
SD		0.4	1.00	5.11	44.8	0.3	0.9			

a) re-measured for low level and accepted this value (re-measurement:  $25.8 \times 10^4/\mu\text{L}$ ).

Appendix 5-3 Hematology in rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Differential leukocyte counts (%)					Differential leukocyte counts ( $10^2/\mu\text{L}$ )					
		rapid (2min)	infusion (1h)		Baso	Eosi	Neut	Lym	Mono	Baso	Eosi	Neut	Lym	Mono	
Male	Control (Saline)	0	0	1101	0.0	0.7	13.2	85.7	0.4	0.0	0.5	9.0	58.7	0.3	
				1102	0.0	1.7	25.7	70.6	2.0	0.0	1.5	22.0	60.6	1.7	
				1103	0.1	0.4	13.1	84.1	2.3	0.1	0.3	10.7	69.0	1.9	
				1104	0.1	0.8	9.8	86.2	3.1	0.1	0.8	9.7	85.7	3.1	
				1105	0.0	1.2	13.8	82.7	2.3	0.0	0.7	7.8	46.9	1.3	
				1106	0.2	1.1	14.8	81.0	2.9	0.1	0.7	9.6	52.5	1.9	
				1107	0.1	0.9	8.9	88.6	1.5	0.1	0.8	7.5	75.5	1.3	
		Mean	0.1	1.0	14.2	82.7	2.1	0.1	0.8	10.9	64.1	1.6			
		SD	0.1	0.4	5.5	5.9	0.9	0.1	0.4	5.0	13.5	0.8			
		AcPepA	10	30	1201	0.0	0.6	9.2	88.3	1.9	0.0	0.3	4.9	47.0	1.0
					1202	0.0	1.1	28.4	67.1	3.4	0.0	0.7	17.6	41.6	2.1
					1203	0.0	1.4	9.5	85.6	3.5	0.0	1.0	6.7	60.8	2.5
					1204	0.2	1.0	13.9	83.0	1.9	0.1	0.6	8.7	51.9	1.2
					1205	0.0	0.9	14.0	83.7	1.4	0.0	0.5	8.3	49.2	0.8
	1206				0.0	1.0	15.0	82.5	1.5	0.0	0.6	8.8	48.5	0.9	
	1207				0.0	0.9	20.8	75.1	3.2	0.0	0.8	18.5	66.5	2.8	
	Mean		0.0	1.0	15.8	80.8	2.4	0.0	0.6	10.5	52.2	1.6			
	SD		0.1	0.2	6.8	7.3	0.9	0.0	0.2	5.3	8.6	0.8			
	AcPepA		20	60	1301	0.1	1.0	7.6	89.9	1.4	0.1	1.1	8.0	95.3	1.5
					1302	0.1	1.6	18.0	76.6	3.7	0.1	1.6	18.6	78.9	3.8
					1303	0.0	1.1	13.9	82.2	2.8	0.0	0.7	9.0	53.0	1.8
					1304	0.0	0.8	11.3	85.4	2.5	0.0	0.8	10.7	81.1	2.4
					1305	0.0	1.1	10.5	86.8	1.6	0.0	0.7	6.5	54.0	1.0
		1306			0.0	0.6	22.5	74.2	2.7	0.0	0.3	11.7	38.6	1.4	
		1307			0.1	1.0	23.6	72.1	3.2	0.1	0.8	18.9	57.8	2.6	
		Mean	0.0	1.0	15.3	81.0	2.6	0.0	0.9	11.9	65.5	2.1			
		SD	0.1	0.3	6.2	6.8	0.8	0.1	0.4	5.0	19.9	0.9			
		Female	Control (Saline)	0	0	2101	0.3	0.3	7.5	90.4	1.5	0.2	0.2	5.7	68.0
2102						0.0	1.1	17.6	79.6	1.7	0.0	0.7	11.3	51.1	1.1
2103						0.0	0.7	9.9	87.6	1.8	0.0	0.4	6.0	53.0	1.1
2104						0.1	0.5	11.9	86.3	1.2	0.1	0.4	8.8	64.3	0.9
2105						0.0	1.0	15.2	82.0	1.8	0.0	0.7	11.1	59.5	1.3
2106	0.1					1.3	7.8	88.6	2.2	0.1	0.9	5.4	61.5	1.5	
2107	0.0					0.5	10.5	88.0	1.0	0.0	0.4	9.0	75.6	0.9	
Mean	0.1			0.8	11.5	86.1	1.6	0.1	0.5	8.2	61.9	1.1			
SD	0.1			0.4	3.7	3.9	0.4	0.1	0.2	2.5	8.5	0.2			
AcPepA	10			30	2201	0.0	1.2	17.5	79.4	1.9	0.0	0.6	9.0	40.8	1.0
					2202	0.0	0.5	10.0	87.4	2.1	0.0	0.4	8.8	76.4	1.8
					2203	0.1	2.0	15.4	80.9	1.6	0.1	1.5	11.3	59.9	1.2
					2204	0.1	1.0	7.0	90.9	1.0	0.1	0.8	5.3	69.9	0.8
					2205	0.1	1.2	9.9	86.9	1.9	0.1	0.9	7.1	62.8	1.4
			2206		0.1	0.7	6.7	90.8	1.7	0.1	0.6	5.9	79.7	1.5	
			2207		0.0	0.9	7.1	90.2	1.8	0.0	0.9	6.7	85.7	1.7	
	Mean		0.1	1.1	10.5	86.6	1.7	0.1	0.8	7.7	67.9	1.3			
	SD		0.1	0.5	4.3	4.7	0.4	0.1	0.4	2.1	15.0	0.4			
	AcPepA		20	60	2301	0.0	1.2	11.8	85.7	1.3	0.0	0.8	7.9	57.7	0.9
					2302	0.1	0.6	10.7	87.3	1.3	0.1	0.5	8.9	72.7	1.1
					2303	0.0	0.8	16.1	80.9	2.2	0.0	0.5	9.6	48.2	1.3
					2304	0.0	0.5	8.4	89.6	1.5	0.0	0.4	6.3	66.9	1.1
					2305	0.2	1.4	9.3	87.5	1.6	0.1	0.9	6.0	56.2	1.0
2306					0.1	0.9	9.2	87.4	2.4	0.1	0.7	6.8	65.3	1.8	
2307					0.0	0.6	7.7	90.1	1.6	0.0	0.6	7.2	84.9	1.5	
Mean			0.1	0.9	10.5	86.9	1.7	0.0	0.6	7.5	64.6	1.2			
SD			0.1	0.3	2.8	3.0	0.4	0.1	0.2	1.3	12.0	0.3			

Appendix 6-1 Blood chemistry in rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	LDH (IU/L)	γ-GTP (IU/L)	Glu. (mg/dL)	T.Cho. (mg/dL)
		rapid (2min)	infusion (1h)								
Male	Control (Saline)	0	0	1101	87.9	37.5	346.2	238.4	4.54	111	64
				1102	80.2	32.9	382.7	247.4	3.39	103	91
				1103	74.5	29.4	378.1	166.0	5.51	114	65
				1104	72.8	28.5	346.6	170.5	5.55	115	61
				1105	73.2	30.2	436.0	185.4	4.97	127	85
				1106	63.7	21.5	363.3	154.0	4.81	129	99
				1107	87.3	28.2	281.6	554.3	5.12	122	60
				Mean	77.1	29.7	362.1	245.1	4.84	117	75
	SD	8.7	4.9	46.8	141.0	0.74	9	16			
	AcPepA	10	30	1201	79.4	31.1	296.9	199.6	4.55	115	79
				1202	73.0	27.7	261.3	223.4	2.42	113	80
				1203	79.3	30.1	340.9	211.5	4.76	105	60
				1204	78.1	29.0	339.1	180.9	5.36	103	56
				1205	72.8	25.8	332.9	199.4	4.67	128	82
				1206	71.6	28.9	208.1	128.4	6.80	112	92
				1207	84.0	32.6	343.3	245.6	4.98	101	85
		Mean	76.9	29.3	303.2	198.4	4.79	111	76		
		SD	4.5	2.2	51.7	37.0	1.30	9	13		
		20	60	1301	79.1	32.0	312.8	214.9	4.38	129	114
				1302	74.2	27.2	214.3	223.4	4.69	110	75
				1303	87.0	39.3	323.2	186.4	6.44	102	77
				1304	84.3	29.4	400.0	205.1	5.58	121	111
				1305	83.3	30.5	215.0	199.1	5.37	95	70
	1306			79.2	27.4	374.5	201.0	5.55	134	68	
	1307			75.3	24.6	342.3	220.0	5.41	126	63	
	Mean	80.3	30.1	311.7	207.1	5.35	117	83			
	SD	4.7	4.7	72.6	13.1	0.67	15	21			
	Female	Control (Saline)	0	0	2101	91.9	29.0	157.3	283.6	5.61	117
2102					82.3	25.6	212.9	241.6	5.46	105	57
2103					102.8	25.4	239.4	1357.5	6.85	135	68
2104					69.9	20.9	152.0	136.7	5.06	119	35
2105					93.7	18.7	270.3	264.2	5.00	106	57
2106					79.3	25.5	159.1	231.2	6.03	130	59
2107					76.5	30.8	161.9	128.4	4.82	130	44
Mean					85.2	25.1	193.3	377.6	5.55	120	53
SD		11.4	4.2	47.6	436.3	0.71	12	11			
AcPepA		10	30	2201	86.5	24.5	268.2	218.9	5.36	122	52
				2202	90.7	32.0	222.8	332.1	5.45	122	53
				2203	72.7	23.0	204.9	194.3	6.35	109	67
				2204	69.8	22.3	153.9	202.8	5.01	147	57
				2205	72.5	28.2	112.4	114.7	6.25	107	67
				2206	72.4	25.6	133.7	239.2	4.82	107	54
				2207	79.6	27.2	192.6	142.9	5.52	116	62
		Mean	77.7	26.1	184.1	206.4	5.54	119	59		
		SD	8.1	3.3	54.3	70.3	0.58	14	6		
		20	60	2301	72.6	27.2	164.7	235.7	4.49	113	67
				2302	76.4	22.1	150.4	242.7	6.07	103	75
				2303	75.3	21.3	161.8	191.6	5.44	107	63
				2304	74.4	25.0	143.6	173.6	6.68	143	68
				2305	70.6	16.0	253.7	179.7	6.22	115	52
2306				72.4	24.9	141.1	135.4	6.17	116	73	
2307				83.1	26.8	281.5	151.4	5.63	132	42	
Mean		75.0	23.3	185.3	187.2	5.81	118	63			
SD		4.1	3.9	57.5	40.1	0.71	14	12			

Appendix 6-2 Blood chemistry in rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	TG (mg/dL)	PL (mg/dL)	TP (g/dL)	Alb. (g/dL)	A/G	BUN (mg/dL)	Crea. (mg/dL)		
		rapid (2min)	infusion (1h)										
Male	Control (Saline)	0	0	1101	35	99	5.0	2.2	0.79	14	0.31		
				1102	26	131	5.7	2.4	0.73	11	0.40		
				1103	25	103	5.5	2.4	0.77	18	0.44		
				1104	15	96	5.5	2.4	0.77	18	0.42		
				1105	27	117	5.5	2.5	0.83	16	0.40		
				1106	38	135	5.6	2.6	0.87	16	0.47		
				1107	21	97	5.5	2.4	0.77	16	0.28		
					Mean	26.7	111	5.5	2.4	0.79	15.6	0.39	
					SD	7.8	17	0.2	0.1	0.05	2.4	0.07	
		AcPepA	10	30	1201	25	119	5.3	2.3	0.77	14	0.32	
	1202				31	121	5.3	2.3	0.77	10	0.32		
	1203				19	96	5.3	2.4	0.83	17	0.40		
	1204				20	92	5.5	2.4	0.77	13	0.35		
	1205				21	119	5.7	2.7	0.90	15	0.26		
	1206				27	128	5.5	2.4	0.77	13	0.39		
	1207				23	126	5.5	2.5	0.83	14	0.42		
						Mean	23.7	114	5.4	2.4	0.81	13.7	0.35
						SD	4.3	14	0.2	0.1	0.05	2.1	0.06
				20	60	1301	24	154	5.0	2.3	0.85	15	0.35
	1302		42			119	5.6	2.5	0.81	18	0.31		
	1303		27			115	5.2	2.3	0.79	10	0.26		
	1304		29			160	5.6	2.5	0.81	18	0.45		
	1305		31			108	5.0	2.2	0.79	14	0.42		
	1306	13	103			5.8	2.4	0.71	17	0.36			
	1307	40	102			5.4	2.3	0.74	15	0.39			
					Mean	29.4	123	5.4	2.4	0.79	15.3	0.36	
					SD	9.8	24	0.3	0.1	0.05	2.8	0.06	
	Female	Control (Saline)	0	0	2101	14	89	5.8	2.3	0.66	20	0.57	
2102					<10 <sup>a)</sup>	87	5.4	2.4	0.80	21	0.47		
2103					20	101	5.6	2.5	0.81	21	0.40		
2104					11	67	5.4	2.5	0.86	21	0.28		
2105					22	97	5.3	2.4	0.83	20	0.60		
2106					14	94	5.4	2.4	0.80	16	0.35		
2107					10	73	5.3	2.3	0.77	23	0.51		
					Mean	14.4	87	5.5	2.4	0.79	20.3	0.45	
					SD	4.8	13	0.2	0.1	0.06	2.1	0.12	
		AcPepA	10	30	2201	13	82	5.5	2.4	0.77	19	0.37	
2202					12	84	5.2	2.4	0.86	20	0.19		
2203					23	102	5.4	2.5	0.86	18	0.38		
2204					13	92	5.7	2.6	0.84	22	0.43		
2205					13	106	5.7	2.6	0.84	18	0.35		
2206					16	83	5.2	2.4	0.86	21	0.31		
2207					17	97	5.6	2.5	0.81	18	0.37		
						Mean	15.3	92	5.5	2.5	0.83	19.4	0.34
						SD	3.9	10	0.2	0.1	0.03	1.6	0.08
				20	60	2301	23	110	5.5	2.4	0.77	19	0.51
2302			15			112	5.8	2.6	0.81	17	0.39		
2303			23			107	5.8	2.6	0.81	21	0.47		
2304			15			103	5.2	2.4	0.86	21	0.37		
2305			16			85	5.4	2.3	0.74	18	0.37		
2306		11	109			5.7	2.6	0.84	23	0.45			
2307		13	80			5.7	2.5	0.78	22	0.49			
					Mean	16.6	101	5.6	2.5	0.80	20.1	0.44	
					SD	4.7	13	0.2	0.1	0.04	2.2	0.06	

a) re-measured and confirmed less than lower limit of quantitation (10 mg/dL), calculated as 10 mg/dL.

Appendix 6-3 Blood chemistry in rats treated intravenously with AcPepA for 5 days

Sex	Test substance	Dose (mg/kg)		Animal No.	T.Bil. (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	P (mg/dL)	Ca (mg/dL)	
		rapid (2min)	infusion (1h)								
Male	Control (Saline)	0	0	1101	0.73	140	4.3	112	9.9	9.6	
				1102	0.45	140	4.4	113	7.9	10.0	
				1103	0.79	139	4.7	113	9.1	9.8	
				1104	0.54	142	4.5	112	9.4	9.3	
				1105	0.52	141	4.2	110	8.9	9.4	
				1106	0.32	139	4.5	107	9.5	9.9	
				1107	0.29	137	4.1	111	8.6	9.1	
		Mean	0.52	140	4.4	111	9.0	9.6			
		SD	0.19	2	0.2	2	0.7	0.3			
		AcPepA	10	30	1201	0.45	139	4.4	112	9.3	9.8
					1202	0.59	140	4.6	108	9.2	9.8
					1203	0.52	140	4.8	110	10.3	9.6
					1204	0.41	140	4.9	113	9.5	9.3
					1205	0.37	143	4.6	112	9.6	9.5
	1206				0.54	140	4.5	112	9.1	9.3	
	1207				0.57	139	4.5	110	9.3	9.2	
	Mean		0.49	140	4.6	111	9.5	9.5			
	SD		0.08	1	0.2	2	0.4	0.2			
	20		60	1301	0.40	139	4.4	109	9.0	9.8	
				1302	0.66	141	4.0	110	9.5	10.2	
				1303	0.46	139	5.2	111	8.8	9.9	
				1304	0.48	140	4.8	110	10.1	9.8	
				1305	0.50	141	4.8	110	10.7	9.2	
		1306		0.39	140	4.5	110	10.1	9.5		
		1307		0.46	139	4.5	110	9.3	9.3		
	Mean	0.48	140	4.6	110	9.6	9.7				
	SD	0.09	1	0.4	1	0.7	0.4				
	Female	Control (Saline)	0	0	2101	0.19	137	4.6	112	10.1	9.7
2102					0.44	140	5.0	114	8.9	9.3	
2103					0.59	141	4.7	110	9.8	9.8	
2104					0.44	139	4.3	110	9.6	9.4	
2105					0.40	138	4.5	110	9.7	9.7	
2106					0.48	138	4.5	111	9.1	9.4	
2107					0.45	139	4.7	110	8.7	9.4	
Mean			0.43	139	4.6	111	9.4	9.5			
SD			0.12	1	0.2	2	0.5	0.2			
AcPepA			10	30	2201	0.29	139	4.1	112	9.8	10.1
					2202	0.29	139	5.1	111	9.4	9.1
					2203	0.37	139	5.1	112	10.6	9.3
					2204	0.24	140	4.3	111	9.4	9.7
					2205	0.36	140	4.2	110	9.2	9.3
		2206			0.40	136	5.0	110	9.9	9.2	
		2207			0.36	138	4.9	110	9.7	9.9	
		Mean	0.33	139	4.7	111	9.7	9.5			
		SD	0.06	1	0.4	1	0.5	0.4			
		20	60	2301	0.36	140	4.2	110	9.5	9.5	
				2302	0.26	139	4.5	110	9.2	9.6	
				2303	0.36	138	4.6	111	8.7	9.9	
				2304	0.54	139	3.4 <sup>a)</sup>	112	7.8	9.6	
				2305	0.22	140	4.2	113	9.8	9.5	
2306				0.66	138	4.2	109	9.1	9.8		
2307				0.60	140	4.2	109	8.9	9.9		
Mean		0.43	139	4.2	111	9.0	9.7				
SD		0.17	1	0.4	2	0.6	0.2				

a) re-measured for low level and accepted this value (re-measurement: 3.5 mEq/L).

Appendix 7-1 Organ weights of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Brain (g)	Pituitary	Thyroid <sup>a)</sup>	Submandi- <sup>b)</sup>	Thymus (mg)	Heart (mg)	
		rapid (2min)	infusion (1h)			gland (mg)	glands (mg)	bular glands (mg)			
Male	Control (Saline)	0	0	1101	1.78	8.0	14.1	370	609	698	
				1102	1.86	9.9	14.8	470	494	923	
				1103	1.88	8.3	15.9	442	595	807	
				1104	1.78	7.4	10.9	424	560	770	
				1105	1.80	8.0	11.2	378	548	699	
				1106	1.90	9.6	14.3	305	468	748	
				1107	1.81	7.5	12.3	409	500	811	
		Mean	1.83	8.4	13.4	400	539	779			
		SD	0.05	1.0	1.9	54	53	78			
		AcPepA	10	30	1201	1.84	9.2	16.6	385	525	772
					1202	1.97	8.3	15.2	417	608	843
					1203	1.91	8.7	13.0	370	475	770
					1204	1.89	9.3	13.9	435	478	881
					1205	1.86	8.5	15.7	419	497	747
	1206				1.90	8.0	14.4	365	457	759	
	1207				1.81	9.1	13.2	462	700	820	
	Mean		1.88	8.7	14.6	408	534	799			
	SD		0.05	0.5	1.3	36	89	50			
	20		60	1301	1.86	9.1	13.7	387	436	810	
				1302	1.79	8.6	17.7	370	420	737	
				1303	1.83	9.4	13.1	413	620	791	
				1304	1.84	8.5	13.8	394	416	834	
				1305	1.87	8.4	15.3	428	735	801	
		1306		1.72	8.6	13.0	341	410	783		
		1307		1.69	8.3	15.0	403	547	780		
	Mean	1.80	8.7	14.5	391	512	791				
	SD	0.07	0.4	1.7	29	127	30				
	Female	Control (Saline)	0	0	2101	1.78	10.5	13.5	382	381	574
2102					1.81	10.5	13.2	336	583	611	
2103					1.71	8.9	15.0	310	513	582	
2104					1.72	8.9	12.5	314	524	595	
2105					1.65	8.5	14.1	297	583	586	
2106					1.58	8.3	15.2	268	436	555	
2107					1.74	8.9	13.7	340	457	581	
Mean			1.71	9.2	13.9	321	497	583			
SD			0.08	0.9	1.0	36	76	17			
AcPepA			10	30	2201	1.62	9.7	12.2	321	460	614
					2202	1.74	6.6	12.3	303	365	556
					2203	1.73	9.0	16.4	337	605	570
					2204	1.69	8.7	14.6	276	423	583
					2205	1.59	10.5	10.7	283	375	532
		2206			1.60	8.3	13.0	299	418	539	
		2207			1.64	10.1	13.2	304	478	558	
		Mean	1.66	9.0	13.2	303	446	565			
		SD	0.06	1.3	1.8	21	81	28			
		20	60	2301	1.65	10.4	14.2	302	472	622	
				2302	1.67	9.3	14.0	308	327	568	
				2303	1.68	9.0	14.3	273	437	582	
				2304	1.87	11.6	15.2	316	526	598	
				2305	1.67	9.7	15.6	297	562	596	
2306				1.71	10.4	12.8	300	453	563		
2307				1.73	8.1	11.2	267	444	553		
Mean		1.71	9.8	13.9	295	460	583				
SD		0.07	1.1	1.5	18	75	24				

a) with parathyroid gland.

b) with sublingual gland.

Appendix 7-2 Organ weights of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Lung <sup>a)</sup> (g)	Liver (g)	Spleen (mg)	Kidneys (g)	Adrenal glands (mg)	Testes (g)
		rapid (2min)	infusion (1h)							
Male	Control (Saline)	0	0	1101	0.86	5.56	373	1.65	44	1.67
				1102	0.91	6.51	573	1.76	40	2.09
				1103	1.04	6.10	592	1.78	37	2.14
				1104	0.94	5.91	438	1.62	52	1.99
				1105	0.88	5.25	421	1.57	41	1.94
				1106	0.85	5.99	532	1.81	60	1.77
				1107	0.88	5.98	495	1.70	38	1.57
				Mean	0.91	5.90	489	1.70	45	1.88
	SD	0.07	0.40	82	0.09	8	0.22			
	AcPepA	10	30	1201	0.96	6.22	360	1.69	49	2.08
				1202	0.96	6.06	550	1.89	36	2.08
				1203	0.82	5.41	444	1.52	42	1.96
				1204	0.94	6.02	433	1.77	44	1.98
				1205	0.88	5.56	398	1.67	50	2.68
				1206	0.86	5.81	409	1.67	44	1.97
				1207	0.97	6.44	550	1.68	45	2.30
		Mean	0.91	5.93	449	1.70	44	2.15		
		SD	0.06	0.36	74	0.11	5	0.26		
		20	60	1301	1.03	6.19	499	1.72	44	2.02
				1302	0.85	6.35	464	1.87	35	1.93
				1303	0.96	6.21	539	2.00	45	1.95
				1304	0.93	6.27	413	1.75	40	1.95
				1305	1.03	6.02	390	1.68	41	1.96
	1306			0.82	6.44	406	1.77	37	2.06	
	1307			0.89	5.70	439	1.68	52	1.99	
	Mean	0.93	6.17	450	1.78	42	1.98			
	SD	0.08	0.25	54	0.12	6	0.05			
	Female	Control (Saline)	0	0	2101	0.78	4.81	421	1.35	45
2102					0.68	4.68	372	1.39	36	
2103					0.72	4.47	272	1.21	36	
2104					0.79	4.50	293	1.43	46	
2105					0.82	4.94	403	1.25	45	
2106					0.69	4.34	249	1.10	34	
2107					0.71	4.37	281	1.27	52	
Mean					0.74	4.59	327	1.29	42	
SD		0.05	0.23	70	0.11	7				
AcPepA		10	30	2201	0.73	4.62	324	1.28	46	
				2202	0.69	4.17	248	1.28	39	
				2203	0.77	4.63	309	1.35	39	
				2204	0.72	4.40	274	1.21	46	
				2205	0.68	4.24	290	1.19	34	
				2206	0.71	4.29	345	1.30	41	
				2207	0.79	4.73	347	1.23	32	
		Mean	0.73	4.44	305	1.26	40			
		SD	0.04	0.22	37	0.06	5			
		20	60	2301	0.72	4.62	281	1.32	35	
				2302	0.68	4.21	271	1.24	32	
				2303	0.71	4.61	294	1.30	44	
				2304	0.78	4.82	330	1.30	42	
				2305	0.80	4.89	380	1.38	45	
2306				0.72	4.75	338	1.21	45		
2307				0.70	4.17	276	1.31	39		
Mean		0.73	4.58	310	1.29	40				
SD		0.04	0.29	41	0.06	5				

a) with bronchus.

Appendix 7-3 Organ weights of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Epididymides (mg)	Seminal vesicles (mg)	Prostate (mg)	Ovaries (mg)	Uterus (mg)		
		rapid (2min)	infusion (1h)								
Male	Control (Saline)	0	0	1101	278	135	172				
				1102	296	268	264				
				1103	288	206	258				
				1104	288	173	294				
				1105	250	96	183				
				1106	202	129	207				
				1107	293	214	172				
					Mean	271	174	221			
					SD	34	59	50			
	AcPepA	10	30	1201	334	169	238				
				1202	292	176	229				
				1203	247	148	237				
				1204	280	256	243				
				1205	331	310	237				
				1206	229	90	143				
				1207	289	140	246				
						Mean	286	184	225		
						SD	39	75	36		
			20	60	1301	336	242	249			
		1302			270	226	244				
		1303			336	294	195				
1304		279			172	224					
1305		263			202	246					
1306	296	240			267						
1307	307	230			287						
				Mean	298	229	245				
				SD	30	38	29				
Female	Control (Saline)	0	0	2101				82	209		
				2102				84	274		
				2103				74	219		
				2104				76	201		
				2105				82	311		
				2106				59	157		
				2107				86	244		
					Mean			78	231		
					SD			9	51		
	AcPepA	10	30	2201				81	362		
				2202				75	277		
				2203				68	184		
				2204				77	318		
				2205				60	346		
				2206				65	233		
				2207				81	198		
						Mean			72	274	
						SD			8	71	
			20	60	2301				72	223	
		2302						65	202		
		2303						61	180		
2304							91	393			
2305							76	348			
2306						77	304				
2307						72	213				
				Mean			73	266			
				SD			10	82			

Appendix 7-4 Relative organ weights of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Brain (g%)	Pituitary gland (mg%)	Thyroid <sup>a)</sup> glands (mg%)	Submandi- <sup>b)</sup> bular glands (mg%)	Thymus (mg%)	Heart (mg%)			
		rapid (2min)	infusion (1h)										
Male	Control (Saline)	0	0	1101	1.05	4.7	8.3	218	358	411			
				1102	0.95	5.1	7.6	241	253	473			
				1103	0.99	4.4	8.4	234	315	427			
				1104	0.98	4.1	6.0	233	308	423			
				1105	1.10	4.9	6.9	232	336	429			
				1106	1.07	5.4	8.0	171	263	420			
				1107	0.98	4.1	6.7	222	272	441			
				Mean	1.02	4.7	7.4	222	301	432			
	SD	0.06	0.5	0.9	24	39	20						
	AcPepA	10	30	1201	0.99	5.0	9.0	208	284	417			
				1202	1.09	4.6	8.4	230	336	466			
				1203	1.11	5.1	7.6	215	276	448			
				1204	1.01	5.0	7.4	233	256	471			
				1205	1.04	4.7	8.8	234	278	417			
				1206	1.07	4.5	8.1	205	257	426			
				1207	0.94	4.7	6.9	241	365	427			
				Mean	1.04	4.8	8.0	224	293	439			
		SD	0.06	0.2	0.8	14	41	23					
		20	60	1301	0.98	4.8	7.2	205	231	429			
				1302	0.97	4.6	9.6	200	227	398			
				1303	0.95	4.9	6.8	215	323	412			
				1304	0.99	4.6	7.5	213	225	451			
				1305	1.02	4.6	8.3	233	399	435			
				1306	0.96	4.8	7.3	191	229	437			
				1307	0.98	4.8	8.7	233	316	451			
				Mean	0.98	4.7	7.9	213	279	430			
				SD	0.02	0.1	1.0	16	68	20			
				Female	Control (Saline)	0	0	2101	1.40	8.3	10.6	301	300
2102								1.37	8.0	10.0	255	442	463
2103								1.40	7.3	12.3	254	420	477
2104		1.27	6.6					9.3	233	388	441		
2105		1.22	6.3					10.4	220	432	434		
2106		1.26	6.6					12.2	214	349	444		
2107		1.34	6.8					10.5	262	352	447		
Mean		1.32	7.1					10.8	248	383	451		
SD		0.07	0.8		1.1	30	52	15					
AcPepA		10	30		2201	1.25	7.5	9.4	247	354	472		
	2202				1.41	5.4	10.0	246	297	452			
	2203				1.26	6.6	12.0	246	442	416			
	2204				1.34	6.9	11.6	219	336	463			
	2205				1.25	8.3	8.4	223	295	419			
	2206				1.26	6.5	10.2	235	329	424			
	2207				1.21	7.4	9.7	224	351	410			
	Mean				1.28	6.9	10.2	234	343	437			
	SD	0.07	0.9		1.2	12	49	25					
	20	60	2301		1.26	7.9	10.8	231	360	475			
			2302		1.38	7.7	11.6	255	270	469			
			2303		1.30	7.0	11.1	212	339	451			
			2304		1.40	8.7	11.3	236	393	446			
			2305		1.22	7.1	11.4	217	410	435			
			2306		1.29	7.8	9.6	226	341	423			
			2307		1.36	6.4	8.8	210	350	435			
			Mean		1.32	7.5	10.7	227	352	448			
			SD		0.07	0.7	1.1	16	45	19			

Values are the percentage relative to the 100 g body weight.

a) with parathyroid gland. b) with sublingual gland.

Appendix 7-5 Relative organ weights of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Lung <sup>a)</sup> (g%)	Liver (g%)	Spleen (mg%)	Kidneys (g%)	Adrenal glands (mg%)	Testes (g%)			
		rapid (2min)	infusion (1h)										
Male	Control (Saline)	0	0	1101	0.51	3.27	219	0.97	25.9	0.98			
				1102	0.47	3.34	294	0.90	20.5	1.07			
				1103	0.55	3.23	313	0.94	19.6	1.13			
				1104	0.52	3.25	241	0.89	28.6	1.09			
				1105	0.54	3.22	258	0.96	25.2	1.19			
				1106	0.48	3.37	299	1.02	33.7	0.99			
				1107	0.48	3.25	269	0.92	20.7	0.85			
				Mean	0.51	3.28	270	0.94	24.9	1.04			
				SD	0.03	0.06	34	0.04	5.1	0.11			
				AcPepA	10	30	1201	0.52	3.36	195	0.91	26.5	1.12
							1202	0.53	3.35	304	1.04	19.9	1.15
							1203	0.48	3.15	258	0.88	24.4	1.14
							1204	0.50	3.22	232	0.95	23.5	1.06
							1205	0.49	3.11	222	0.93	27.9	1.50
	1206	0.48	3.26				230	0.94	24.7	1.11			
	1207	0.51	3.35				286	0.88	23.4	1.20			
	Mean	0.50	3.26		247	0.93	24.3	1.18					
	SD	0.02	0.10		38	0.05	2.5	0.15					
	20	60	1301		0.54	3.28	264	0.91	23.3	1.07			
			1302		0.46	3.43	251	1.01	18.9	1.04			
			1303		0.50	3.23	281	1.04	23.4	1.02			
			1304		0.50	3.39	223	0.95	21.6	1.05			
			1305		0.56	3.27	212	0.91	22.3	1.07			
			1306	0.46	3.60	227	0.99	20.7	1.15				
			1307	0.51	3.29	254	0.97	30.1	1.15				
	Mean	0.50	3.36	245	0.97	22.9	1.08						
	SD	0.04	0.13	25	0.05	3.5	0.05						
	Female	Control (Saline)	0	0	2101	0.61	3.79	331	1.06	35.4			
2102					0.52	3.55	282	1.05	27.3				
2103					0.59	3.66	223	0.99	29.5				
2104					0.59	3.33	217	1.06	34.1				
2105					0.61	3.66	299	0.93	33.3				
2106					0.55	3.47	199	0.88	27.2				
2107					0.55	3.36	216	0.98	40.0				
Mean					0.57	3.55	252	0.99	32.4				
SD					0.03	0.17	51	0.07	4.7				
AcPepA					10	30	2201	0.56	3.55	249	0.98	35.4	
							2202	0.56	3.39	202	1.04	31.7	
							2203	0.56	3.38	226	0.99	28.5	
							2204	0.57	3.49	217	0.96	36.5	
							2205	0.54	3.34	228	0.94	26.8	
		2206	0.56	3.38			272	1.02	32.3				
		2207	0.58	3.48			255	0.90	23.5				
		Mean	0.56	3.43	236	0.98	30.7						
		SD	0.01	0.08	24	0.05	4.7						
		20	60	2301	0.55	3.53	215	1.01	26.7				
				2302	0.56	3.48	224	1.02	26.4				
				2303	0.55	3.57	228	1.01	34.1				
				2304	0.58	3.60	246	0.97	31.3				
				2305	0.58	3.57	277	1.01	32.8				
2306				0.54	3.57	254	0.91	33.8					
2307				0.55	3.28	217	1.03	30.7					
Mean		0.56	3.51	237	0.99	30.8							
SD		0.02	0.11	23	0.04	3.2							

Values are the percentage relative to the 100 g body weight.

a) with bronchus.

Appendix 7-6 Relative organ weights of rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Dose (mg/kg)		Animal No.	Epididymides (mg%)	Seminal vesicles (mg%)	Prostate (mg%)	Ovaries (mg%)	Uterus (mg%)	Body weight (g)
		rapid (2min)	infusion (1h)							
Male	Control (Saline)	0	0	1101	164	79	101			170
				1102	152	137	135		195	
				1103	152	109	137		189	
				1104	158	95	162		182	
				1105	153	59	112		163	
				1106	113	72	116		178	
				1107	159	116	93		184	
				Mean	150	95	122		180	
	SD	17	27	24		11				
	AcPepA	10	30	1201	181	91	129			185
				1202	161	97	127		181	
				1203	144	86	138		172	
				1204	150	137	130		187	
				1205	185	173	132		179	
				1206	129	51	80		178	
				1207	151	73	128		192	
				Mean	157	101	123		182	
		SD	20	41	19		7			
		20	60	1301	178	128	132		189	
				1302	146	122	132		185	
				1303	175	153	102		192	
				1304	151	93	121		185	
				1305	143	110	134		184	
				1306	165	134	149		179	
1307				177	133	166		173		
Mean	162			125	134		184			
SD	15	19	20		6					
Female	Control (Saline)	0	0	2101				65	165	127
				2102				64	208	132
				2103				61	180	122
				2104				56	149	135
				2105				61	230	135
				2106				47	126	125
				2107				66	188	130
				Mean				60	178	129
	SD				7	35	5			
	AcPepA	10	30	2201				62	278	130
				2202				61	225	123
				2203				50	134	137
				2204				61	252	126
				2205				47	272	127
				2206				51	183	127
				2207				60	146	136
				Mean				56	213	129
		SD				6	59	5		
		20	60	2301				55	170	131
				2302				54	167	121
				2303				47	140	129
				2304				68	293	134
				2305				55	254	137
				2306				58	229	133
2307							57	168	127	
Mean						56	203	130		
SD				6	56	5				

Values are the percentage relative to the 100 g body weight.

## Appendix 8 Histopathological findings in rats treated intravenously with AcPepA for 3 days

Sex	Test substance	Control (Saline)	Male																					
			AcPepA (mg/kg) <sup>1)</sup>																					
			40 (10+30)							80 (20+60)														
Animal No.	No. 1101-1107						No. 1201-1207						No. 1301-1307											
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7			
Kidney																								
	Cyst, single, cortex		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	Fibrosis, cortex, focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0
	Cyst, single, medulla		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Testis																								
	Multinucleated giant cell formation		0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Epididymis																								
	Debris, duct		0	1	1	1	1	0	1	1	1	1	0	1	0	1	1	1	0	0	0	1	1	
	Mononuclear cell infiltration, interstitium		0	1	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0	1	0	0	1	
Prostate																								
	Mononuclear cell infiltration, interstitium		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Injection site																								
	Necrosis, focal, wall of injected vein		0	0	0	0	0	1	2	0	0	1	0	0	2	0	0	0	1	0	0	0	0	
	Hemorrhage, perivascular tissue		0	0	0	0	1	1	1	1	0	1	1	2	0	0	1	1	0	0	0	0	1	
	Inflammatory cell infiltration, perivascular tissue <sup>a)</sup>		0	1	1	1	1	1	1	1	0	2	1	2	1	1	1	1	1	1	1	1	1	
	Thrombus		0	0	2 <sup>b)</sup>	0	0	2 <sup>b)</sup>	1	0	0	2	0	0	0	0	0	0	1	0	0	0	0	
	Fibrinoid exudation, perivascular tissue		0	0	1	1	1	1	1	0	0	1	1	1	1	1	0	0	1	0	1	1	1	

0: No change, 1: Slight, 2: Moderate, 3: Marked.

a) neutrophil, mononuclear cell. b) with hair shaft.

No significant changes were detected: Cerebrum, Cerebellum, Medulla oblongata, Heart, Lung, Thymus, Spleen, Mesenteric lymph node, Submaxillary lymph node, Axillary lymph node, Submaxillary gland, Liver, Urinary bladder, Seminal vesicles, Pituitary gland, Thyroid gland, Parathyroid gland, Adrenal gland, Sternum and bone marrow.

1) AcPepA 40 mg/kg group: 10 mg/kg lipid (2min) dosing + 30 mg infusion (1h) dosing.

80 mg/kg group: 20 mg/kg lipid (2min) dosing + 60 mg infusion (1h) dosing.

Sex	Test substance	Control (Saline)	Female																				
			AcPepA (mg/kg) <sup>1)</sup>																				
			40 (10+30)							80 (20+60)													
Animal No.	No. 2101-2107						No. 2201-2207						No. 2301-2307										
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7		
Thymus																							
	Increased tingible macrophage		2	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
Kidney																							
	Tubular dilatation, cortex, focal		0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	Cyst, single, cortex		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	Fibrosis, cortex, focal		0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Ovary																							
	Cyst, oviduct		0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Injection site																							
	Necrosis, focal, wall of injected vein		0	0	0	0	3	0	0	1	0	2	0	0	0	0	0	0	0	0	0	1	0
	Hemorrhage, perivascular tissue		2	1	3	0	0	1	0	1	1	1	1	3	1	0	3	0	3	3	0	3	0
	Inflammatory cell infiltration, perivascular tissue <sup>a)</sup>		1	2	2	2	1	2	1	1	1	1	2	1	1	1	1	1	1	1	1	2	0
	Thrombus		0	0	0	0	2	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2	0
	Fibrinoid exudation, perivascular tissue		0	0	0	1	1	1	0	1	1	1	1	1	0	0	1	1	0	0	1	1	0

0: No change, 1: Slight, 2: Moderate, 3: Marked.

a) neutrophil, mononuclear cell.

No significant changes were detected: Cerebrum, Cerebellum, Medulla oblongata, Heart, Lung, Spleen, Mesenteric lymph node, Submaxillary lymph node, Axillary lymph node, Submaxillary gland, Liver, Urinary bladder, Uterus, Vagina, Pituitary gland, Thyroid gland, Parathyroid gland, Adrenal gland, Sternum and bone marrow.

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