

Table 5-1 Urinalysis in male rats

Group	Dose(mg/kg)	Day	Grade	Water for injection	CCA	CCA
Color		26	0	6	6	6
			1			
pH		26	5			
			5.5			
			6	1		
			6.5			
			7	1	1	2
			7.5	2	2	2
			8	1	4	2
			8.5	1	1	
			9			

Numerals represent the number of animals.  
 Not significantly different from Water for injection.

Table 5-2 Urinalysis in male rats

Group	Dose(mg/kg)	Day	Grade	Water for injection	CCA	CCA
Protein	26	0	1	1	1	1
		1	1	1	1	1
		2	4	3	4	4
		3	1	1	1	1
Glucose	26	0	6	6	6	6
		1	2	2	2	2
		3	3	3	3	3
		4	4	4	4	4

Numerals represent the number of animals.  
 Not significantly different from Water for injection.

Table 5-3 Urinalysis in male rats

Group	Dose (mg/kg)	Day	Grade	Water for injection	CCA	CCA
Ketone body		26	0	2	4	3
			1	3	1	3
			2	1		
			3			
			4			
Bilirubin		26	0	5	6	6
			1	1		
			2			
			3			

Numerals represent the number of animals.  
 Not significantly different from Water for injection.

Table 5-4 Urinalysis in male rats

Group	Dose(mg/kg)	Day	Grade	Water for injection	CCA	CCA
Occult blood	26	0	3	3	1	10
			1	1		
			2	1		
			3	1		
			4	1		
Urobilinogen	26	0	3	5	6	
			1	3	1	
			2			
			3			
			4			

Numerals represent the number of animals.  
 Not significantly different from Water for injection.

Table 5-5 Urinalysis in female rats

Group	Dose(mg/kg)	Day	Grade	Water for injection	CCA	CCA
Color		26	0	6		6
			1		1	10
pH		26	5			
			5.5			
			6			
			6.5	1		1
			7	1	2	
			7.5	3	3	2
			8	1		2
			8.5		1	1
			9			

Numerals represent the number of animals.  
 Not significantly different from Water for injection.

Table 5-6 Urinalysis in female rats

Group	Dose (mg/kg)	Day	Grade	Water for Injection	CCA	CCA
Protein	26		0	3	3	2
			1	2	1	2
			2	1	2	2
			3			
			4			
Glucose	26		0	6	6	6
			1			
			2			
			3			
			4			

Numerals represent the number of animals.  
 Not significantly different from Water for Injection.

Table 5-7 Urinalysis in female rats

Group	Dose(mg/kg)	Day	Grade	Water for injection	CCA	CCA
Ketone body		26	0	6	5	5
			1		1	1
			2			
			3			
			4			
Bilirubin		26	0	6	6	6
			1			
			2			
			3			

Numerals represent the number of animals.  
 Not significantly different from Water for injection.

Table 5-8 Urinalysis in female rats

Group	Dose (mg/kg)	Day	Grade	Water for injection	CCA	CCA
Occult blood	26		0	3	4	2
			1	1	1	2
			2	2	1	1
			3	3		1
			4	4		1
Urobilinogen	26		0	4	4	4
			1	2	2	2
			2			
			3			
			4			

Numerals represent the number of animals.  
 Not significantly different from Water for injection.



Hematology

RBC	( $10^6/\text{mm}^3$ )	Erythrocyte count
WBC	( $10^3/\text{mm}^3$ )	Leukocyte count
Ht	(%)	Hematocrit value
Hb	(g/dL)	Hemoglobin concentration
Plat.	( $10^3/\text{mm}^3$ )	Platelet count
MCV	(fL)	Mean corpuscular volume
MCH	(pg)	Mean corpuscular hemoglobin
MCHC	(g/dL)	Mean corpuscular hemoglobin concentration
Ret.	(%)	Reticulocyte ratio
Hemogram		
Eosino.	( $10^3/\text{mm}^3$ )	Eosinophil count
Eosino.	(%)	Eosinophil ratio
Baso.	( $10^3/\text{mm}^3$ )	Basophil count
Baso.	(%)	Basophil ratio
Mono.	( $10^3/\text{mm}^3$ )	Monocyte count
Mono.	(%)	Monocyte ratio
Lymph.	( $10^3/\text{mm}^3$ )	Lymphocyte count
Lymph.	(%)	Lymphocyte ratio
Neutro.	( $10^3/\text{mm}^3$ )	Neutrophil count
Neutro.	(%)	Neutrophil ratio
LUC	( $10^3/\text{mm}^3$ )	Large unstained cell count
LUC	(%)	Large unstained cell ratio
Blood coagulation test		
PT	(Sec)	Prothrombin time
APTT	(Sec)	Activated partial thromboplastin time

Table 6-1 Hematology in male rats

Group	Dose (mg/kg)	N	Water for Injection	CCA		CCA	
				1	6	10	6
RBC	(10 <sup>6</sup> /mm <sup>3</sup> )		8.258±0.344	8.378±0.345	8.200±0.254		
WBC	(10 <sup>3</sup> /mm <sup>3</sup> )		9.340±3.158	10.278±1.246	9.782±1.344		
Ht	(%)		46.32±1.68	47.45±0.93	46.13±0.85		
Hb	(g/dL)		16.62±0.66	17.20±0.31	16.63±0.39		
Plat.	(10 <sup>5</sup> /mm <sup>3</sup> )		1240.3±125.8	1153.2±130.5	1186.8±190.0		
MCV	(fL)		56.08±0.95	56.68±1.41	56.28±1.44		
MCH	(pg)		20.07±0.28	20.53±0.62	20.30±0.40		
MCHC	(g/dL)		35.82±0.34	36.22±0.32	36.07±0.40		
Ret.	(%)		2.20±0.38	2.02±0.34	2.32±0.18		
Eosino.	(10 <sup>3</sup> /mm <sup>3</sup> )		0.103±0.048	0.103±0.019	0.102±0.030		
Eosino.	(%)		1.22±0.56	1.05±0.19	1.08±0.39		
Baso.	(10 <sup>3</sup> /mm <sup>3</sup> )		0.030±0.018	0.028±0.010	0.027±0.005		
Baso.	(%)		0.30±0.09	0.28±0.10	0.30±0.06		
Mono.	(10 <sup>3</sup> /mm <sup>3</sup> )		0.185±0.046	0.180±0.069	0.212±0.088		
Mono.	(%)		2.10±0.61	1.73±0.64	2.23±1.21		
Lymph.	(10 <sup>3</sup> /mm <sup>3</sup> )		7.022±2.526	8.485±1.214	7.763±1.046		
Lymph.	(%)		75.12±4.61	82.42±4.14*	79.50±4.35		
Neutro.	(10 <sup>3</sup> /mm <sup>3</sup> )		1.942±0.720	1.355±0.305	1.578±0.609		
Neutro.	(%)		20.67±4.28	13.33±3.38*	15.88±5.01		
LUC	(10 <sup>3</sup> /mm <sup>3</sup> )		0.062±0.033	0.122±0.057	0.098±0.035		
LUC	(%)		0.65±0.32	1.16±0.55	1.00±0.32		
PT	(Sec)		14.43±1.83	14.37±3.25	15.37±3.00		
APTT	(Sec)		22.32±1.44	22.53±2.45	23.97±1.77		

Values are expressed as the mean ± S.D.  
 \* P<0.05 : Significantly different from Water for Injection.

Table 6-2 Hematology in female rats

Group	Dose (mg/kg)	N	Water for injection		CCA		CCA	
			6	6	1	6	10	6
RBC	(10 <sup>6</sup> /mm <sup>3</sup> )		7.488±0.302	8.120±0.293**		7.725±0.312		
WBC	(10 <sup>3</sup> /mm <sup>3</sup> )		5.992±2.322	9.475±1.939*		7.092±3.006		
Ht	(%)		42.18±0.98	44.82±1.43*		42.77±1.74		
Hb	(g/dL)		15.60±0.42	16.62±0.52*		15.92±0.76		
Plat.	(10 <sup>3</sup> /mm <sup>3</sup> )		1166.7±99.7	1191.0±84.7		1243.5±117.5		
MCV	(fL)		56.35±1.62	55.17±0.80		55.37±0.92		
MCH	(pg)		20.85±0.57	20.45±0.48		20.58±0.48		
MCHC	(g/dL)		37.03±0.26	37.07±0.38		37.18±0.34		
Ret.	(%)		1.70±0.21	2.03±0.15		2.45±0.37**		
Eosino.	(10 <sup>3</sup> /mm <sup>3</sup> )		0.162±0.192	0.155±0.126		0.127±0.056		
Eosino.	(%)		2.70±2.97	1.50±0.84		1.88±0.60		
Baso.	(10 <sup>3</sup> /mm <sup>3</sup> )		0.012±0.010	0.032±0.013*		0.015±0.014		
Baso.	(%)		0.17±0.08	0.32±0.10*		0.20±0.09		
Mono.	(10 <sup>3</sup> /mm <sup>3</sup> )		0.072±0.028	0.195±0.092**		0.160±0.095*		
Mono.	(%)		1.25±0.24	2.00±0.66		2.28±0.71*		
Lymph.	(10 <sup>3</sup> /mm <sup>3</sup> )		4.422±1.838	8.087±1.591*		5.720±2.408		
Lymph.	(%)		73.90±6.53	85.55±2.90**		80.52±5.33		
Neutro.	(10 <sup>3</sup> /mm <sup>3</sup> )		1.283±0.519	0.918±0.280		0.992±0.536		
Neutro.	(%)		21.35±4.43	9.72±2.54**		14.05±4.57*		
LUC	(10 <sup>3</sup> /mm <sup>3</sup> )		0.038±0.017	0.088±0.056		0.073±0.040		
LUC	(%)		0.65±0.23	0.93±0.55		1.03±0.50		
PT	(Sec)		7.72±0.19	7.50±0.31		7.38±0.17*		
APTT	(Sec)		17.02±0.20	16.93±0.54		16.03±0.49**		

Values are expressed as the mean ± S.D.  
 \* P<0.05, \*\* P<0.01 : Significantly different from Water for injection.

Blood Chemistry

ASAT	(IU/L)	Aspartate aminotransferase
ALAT	(IU/L)	Alanine aminotransferase
ALP	(IU/L)	Alkaline phosphatase
LDH	(IU/L)	Lactate dehydrogenase
CPK	(IU/L)	Creatine phosphokinase
T.Bil.	(mg/dL)	Total bilirubin
T.Prot.	(g/dL)	Total protein
Albumin	(g/dL)	Albumin
T.Chol.	(mg/dL)	Total cholesterol
TGL	(mg/dL)	Triglyceride
Glucose	(mg/dL)	Glucose
BUN	(mg/dL)	Blood urea nitrogen
Creat.	(mg/dL)	Creatinine
IP	(mg/dL)	Inorganic phosphorus
Ca	(mg/dL)	Calcium
Na	(mEq/L)	Sodium
K	(mEq/L)	Potassium
Cl	(mEq/L)	Chloride
Protein fraction		
Albumin	(%)	Albumin ratio
A1-glob.	(%)	Alpha-1 globulin ratio
A2-glob.	(%)	Alpha-2 globulin ratio
B-glob.	(%)	Beta globulin ratio
G-glob.	(%)	Gamma globulin ratio
A/G		Albumin / Globulin

Table 7-1 Blood chemistry in male rats

Group	Dose (mg/kg)	N	Water for injection		CCA		CCA	
			1	6	1	6	10	6
ASAT	(IU/L)		109.2±19.9		93.8±22.4		79.5±9.8*	
ALAT	(IU/L)		33.7±4.2		31.7±3.9		28.0±1.5*	
ALP	(IU/L)		743.3±103.7		583.8±40.2*		548.3±143.6**	
LDH	(IU/L)		1558.7±948.4		939.3±822.2		483.7±343.2*	
CPK	(IU/L)		574.7±252.1		372.7±245.1		259.5±123.4*	
T.Bil.	(mg/dL)		0.033±0.005		0.043±0.005*		0.042±0.008	
T.Prot.	(g/dL)		5.77±0.21		5.80±0.13		5.65±0.20	
Albumin	(g/dL)		4.38±0.16		4.27±0.19		4.13±0.15*	
T.Chol.	(mg/dL)		53.7±8.5		47.7±7.1		46.5±5.5	
TGL	(mg/dL)		22.5±15.3		22.8±9.1		27.0±11.3	
Glucose	(mg/dL)		146.3±14.2		148.5±16.1		142.7±8.0	
BUN	(mg/dL)		16.37±1.26		15.00±1.06		15.27±0.89	
Creat.	(mg/dL)		0.177±0.016		0.175±0.016		0.180±0.017	
IP	(mg/dL)		8.467±0.385		7.972±0.488		8.797±0.513	
Ca	(mEq/L)		9.82±0.20		9.73±0.14		9.97±0.29	
Na	(mEq/L)		142.2±0.8		141.3±1.0		142.3±0.5	
K	(mEq/L)		4.27±0.41		4.20±0.26		4.40±0.20	
Cl	(mEq/L)		103.2±1.5		101.5±1.6		103.7±1.4	
Albumin (%)	(%)		54.80±2.82		53.68±2.06		52.53±2.29	
Al-glob. (%)	(%)		18.08±2.72		20.23±1.01		18.55±2.56	
A2-glob. (%)	(%)		7.58±0.57		7.10±0.43		7.73±0.54	
B-glob. (%)	(%)		14.68±0.40		14.25±0.56		15.08±1.03	
G-glob. (%)	(%)		4.85±0.45		4.73±1.09		6.10±0.43*	
A/G			1.222±0.147		1.162±0.097		1.112±0.108	

Values are expressed as the mean ± S.D.

\* P&lt;0.05, \*\* P&lt;0.01 : Significantly different from Water for injection.

Table 7-2 Blood chemistry in female rats

Group	Dose (mg/kg)	N	Water for injection		CCA		CCA	
			1	6	1	6	10	6
ASAF (IU/L)			108.3±19.9		134.3±31.2		115.3±22.9	
ALAT (IU/L)			27.2±3.8		27.0±3.0		25.3±6.3	
ALP (IU/L)			329.7±42.0		349.8±66.1		374.0±110.1	
LDH (IU/L)			1926.8±676.2		3030.3±1272.8		2056.2±1102.0	
CPK (IU/L)			611.5±250.1		831.0±278.4		561.8±253.9	
T.Bil. (mg/dL)			0.048±0.012		0.048±0.012		0.043±0.015	
T.Prot. (g/dL)			5.55±0.22		5.80±0.31		5.48±0.36	
Albumin (g/dL)			4.30±0.20		4.40±0.21		4.08±0.24	
T.Chol. (mg/dL)			53.2±11.0		64.5±13.1		62.0±15.8	
TGL (mg/dL)			10.7±3.3		14.5±3.4		13.5±3.6	
Glucose (mg/dL)			125.8±5.7		130.7±9.9		131.8±6.3	
BUN (mg/dL)			17.70±2.22		19.32±1.41		19.00±4.02	
Creat. (mg/dL)			0.205±0.023		0.230±0.013		0.223±0.043	
IP (mg/dL)			7.697±0.972		7.717±0.509		8.022±0.563	
Ca (mEq/L)			9.87±0.12		10.02±0.33		9.75±0.30	
Na (mEq/L)			141.7±1.0		142.7±1.0		142.8±0.8	
K (mEq/L)			3.78±0.12		3.83±0.14		3.77±0.28	
Cl (mEq/L)			105.8±2.4		104.8±1.0		106.2±0.4	
Albumin (%)			56.88±1.59		56.33±2.25		55.10±2.13	
A1-glob. (%)			15.77±1.82		16.88±1.60		14.73±1.94	
A2-glob. (%)			6.12±0.48		6.30±0.41		6.80±0.90	
B-glob. (%)			15.07±0.90		14.82±1.08		17.67±0.55**	
G-glob. (%)			6.17±0.88		5.67±0.43		5.70±0.81	
A/G			1.322±0.085		1.297±0.122		1.230±0.105	

Values are expressed as the mean ± S.D.  
 \*\* P<0.01 : Significantly different from Water for injection.

Gross Pathological Findings

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Marked
- P : Non-graded changes

Table 8-1 Gross pathological findings in male rats

Findings	Group	Water for injection						CCA								
		Dose (mg/kg)		Grade		CCA		CCA		CCA		CCA				
Epididymis		0	1	2	3	P	0	1	2	3	P	0	1	2	3	P
White focus		6				0	5				1	6				0
Application site		6				0	6				0	5				1
Crust		6				0	6				0	2				4
Hemorrhage																

Numerals represent the number of animals.



Table 8-2 Gross pathological findings in female rats

Findings	Group	Water for injection			CCA			CCA						
		Dose(mg/kg)	Grade											
Application site Crust		0	1	2	3	0	1	2	3	0	1	2	3	P
Hemorrhage		6				0	6			0	3			3
		6				0	6			0	0			6

Numerals represent the number of animals.

Organ weight

Submand.	Submandibular gland
Epididy.	Epididymis
Sem. Vesic.	Seminal vesicles
-R	(Right)
-L	(Left)
-R&L	(Right and Left)

Table 9-1 Organ weight in male rats

Group	Dose (mg/kg)	N	Water for injection		CCA		CCA	
			6	6	1	6	10	6
Pituitary	(mg)		10.97±2.15	10.48±3.97			10.35±2.30	
Thyroid-R	(mg)		11.12±2.87	9.47±2.08			10.77±2.44	
Thyroid-L	(mg)		8.58±2.35	8.85±1.45			10.97±2.44	
Thyroid-R&L	(mg)		19.70±3.12	18.32±1.94			21.73±4.70	
Adrenal-R	(mg)		29.65±3.81	31.52±2.88			30.33±3.16	
Adrenal-L	(mg)		32.05±4.20	32.88±3.97			32.85±3.88	
Adrenal-R&L	(mg)		61.70±7.88	64.40±6.33			63.18±6.73	
Testis-R	(mg)		1562.2±119.2	1545.7±75.1			1564.7±204.0	
Testis-L	(mg)		1574.3±118.8	1565.7±79.7			1583.7±192.6	
Testis-R&L	(mg)		3136.5±236.7	3111.3±153.2			3148.3±394.7	
Thymus	(mg)		406.2±76.1	433.3±92.6			461.3±110.7	
Submand.-R	(mg)		313.7±41.1	319.0±25.1			308.3±35.2	
Submand.-L	(mg)		313.8±30.0	319.0±29.8			309.5±42.5	
Submand.-R&L	(mg)		627.5±68.9	638.0±53.9			617.8±76.5	
Spleen	(mg)		679.3±99.0	675.7±105.7			738.5±148.6	
Brain	(mg)		2021.3±39.0	2036.2±86.0			2021.7±139.1	
Heart	(mg)		1316.5±76.2	1265.3±139.5			1268.7±163.7	
Lung	(mg)		1157.7±95.6	1219.5±117.7			1182.2±111.9	
Liver	(g)		10.910±1.537	10.727±1.501			10.398±0.575	
Kidney-R	(mg)		1470.3±132.3	1451.3±136.3			1455.2±130.7	
Kidney-L	(mg)		1454.2±133.6	1471.8±144.9			1466.7±147.2	
Kidney-R&L	(mg)		2924.5±257.6	2923.2±273.4			2921.8±275.5	
Epidid.-R	(mg)		418.3±30.6	427.2±48.9			415.0±66.1	
Epidid.-L	(mg)		408.7±39.8	409.7±34.7			413.8±66.4	
Epidid.-R&L	(mg)		827.0±65.6	836.8±76.8			828.8±132.4	
Sem. Vesic.	(mg)		1089.7±90.1	1047.7±132.3			1145.3±161.3	
Prostate	(mg)		950.5±208.6	881.3±92.9			936.8±66.4	

Values are expressed as the mean ± S.D.  
Not significantly different from Water for injection.

Table 9-2 Organ weight in female rats

Group	Dose (mg/kg)	N	Water for injection		CCA		CCA	
			6	6	1	6	10	6
Pituitary	(mg)		12.58±2.40		14.10±2.18		13.77±2.23	
Thyroid-R	(mg)		8.07±2.34		7.42±1.32		7.35±1.73	
Thyroid-L	(mg)		7.07±1.18		7.15±1.16		6.53±1.39	
Thyroid-R&L	(mg)		15.13±2.87		14.57±2.42		13.88±2.99	
Adrenal-R	(mg)		36.48±1.79		34.68±2.66		36.90±3.18	
Adrenal-L	(mg)		37.85±3.18		37.03±3.45		41.42±5.02	
Adrenal-R&L	(mg)		74.33±4.38		71.72±5.74		78.32±8.16	
Ovary-R	(mg)		37.43±7.42		43.48±6.96		38.02±3.76	
Ovary-L	(mg)		42.87±8.18		42.08±7.49		37.93±6.73	
Ovary-R&L	(mg)		80.30±13.98		85.57±13.85		75.95±9.20	
Thymus	(mg)		417.7±69.4		376.2±52.1		367.3±91.2	
Submand.-R	(mg)		211.7±22.7		217.2±15.1		212.2±13.2	
Submand.-L	(mg)		203.5±17.3		213.5±9.4		205.7±11.6	
Submand.-R&L	(mg)		415.2±39.7		430.7±24.1		417.8±24.7	
Spleen	(mg)		509.0±86.5		486.2±67.6		453.3±44.0	
Brain	(mg)		1924.5±59.1		1876.7±48.3		1886.3±62.1	
Heart	(mg)		863.2±93.6		910.8±50.6		850.5±54.9	
Lung	(mg)		1038.7±83.6		1027.3±47.7		958.5±68.2	
Liver	(g)		6.832±0.647		6.995±0.623		6.597±0.527	
Kidney-R	(mg)		950.7±55.7		931.8±100.5		934.3±88.8	
Kidney-L	(mg)		938.8±61.1		913.7±105.8		910.3±63.5	
Kidney-R&L	(mg)		1889.5±100.7		1845.5±204.2		1844.7±147.3	
Uterus	(mg)		403.0±98.4		356.7±42.5		451.8±117.1	

Values are expressed as the mean ± S.D.  
Not significantly different from Water for injection.