

Table 7 - 1 Body weight - Group mean values in male rats

Dose (mg/kg/day)		Week					(g)
		0 ^a	1	2	3	4	
0	Mean	176	220	257	282	300	
	S.D.	5	7	8	13	17	
	N	10	10	10	10	10	
8	Mean	176	220	256	283	301	
	S.D.	5	8	11	12	16	
	N	10	10	10	10	10	
40	Mean	176	218	250	272	291	
	S.D.	5	8	14	17	18	
	N	10	10	10	10	10	
200/100	Mean	176	196 **	214 **	249 **	264 **	
	S.D.	5	10	41	20	30	
	N	10	8	7	6	6	

^a: Week before initiation of treatment.

S.D.: Standard deviation.

N: Number of animals examined.

Significantly different from control: *, $p \leq 0.05$; **, $p \leq 0.01$.

Table 7 - 2 Body weight - Group mean values in male rats
 Immunized group

Dose (mg/kg/day)		Week					(g)
		0 ^a	1	2	3	4	
0	Mean	175	222	262	290	309	
	S.D.	4	4	7	12	19	
	N	8	8	8	8	8	
8	Mean	175	221	263	290	308	
	S.D.	4	7	9	14	20	
	N	8	8	8	8	8	
40	Mean	175	214	250	278	297	
	S.D.	4	8	19	23	26	
	N	8	8	8	8	8	
200/100	Mean	175	199 *	244	268	283	
	S.D.	4	23	7	18	19	
	N	8	6	3	3	3	

^a: Week before initiation of treatment.

S.D.: Standard deviation.

N: Number of animals examined.

Significantly different from control: *, $p \leq 0.05$; **, $p \leq 0.01$.

Table 8 Body weight - Group mean values in female rats

Dose (mg/kg/day)		Week					(g)
		0 ^a	1	2	3	4	
0	Mean	132	150	164	175	188	
	S.D.	4	6	8	11	11	
	N	10	10	10	10	10	
8	Mean	132	150	167	180	190	
	S.D.	4	7	9	10	13	
	N	10	10	10	10	10	
40	Mean	132	151	168	177	190	
	S.D.	4	4	6	7	6	
	N	10	10	10	10	10	
100	Mean	132	150	167	181	193	
	S.D.	4	7	9	8	8	
	N	10	10	10	9	9	

^a: Week before initiation of treatment.

S.D.: Standard deviation.

N: Number of animals examined.

Table 9 Food consumption - Group mean values in male rats

Dose (mg/kg/day)		Week				Average
		1	2	3	4	
0	Mean	19.1	21.3	21.7	21.7	21.0
	S.D.	0.4	1.5	1.1	2.0	
	N	5	5	5	5	
8	Mean	18.9	20.9	20.8	21.0	20.4
	S.D.	1.1	0.8	1.3	1.1	
	N	5	5	5	5	
40	Mean	18.3	19.3	19.5	20.3	19.4
	S.D.	1.1	2.3	2.3	1.3	
	N	5	5	5	5	
200/100	Mean	12.0 **	14.0 *	18.4 **	19.6	16.0
	S.D.	3.3	5.0	0.3	2.5	
	N	5	5	4	4	

S.D.: Standard deviation.

N: Number of cage.

Significantly different from control: *, $p \leq 0.05$; **, $p \leq 0.01$.

Table 10 Food consumption - Group mean values in female rats

Dose (mg/kg/day)		Week				Average
		1	2	3	4	
0	Mean	14.6	15.2	15.3	16.9	15.5
	S.D.	0.3	0.7	0.6	0.7	
	N	5	5	5	5	
8	Mean	13.7	14.4	14.8	16.1	14.8
	S.D.	1.1	1.6	2.1	1.7	
	N	5	5	5	5	
40	Mean	13.6	14.3	15.5	15.7	14.8
	S.D.	0.4	0.8	1.3	1.4	
	N	5	5	5	5	
100	Mean	13.4	15.2	14.4	17.4	15.1
	S.D.	0.8	1.7	3.4	1.8	
	N	5	5	5	5	

S.D.: Standard deviation.

N: Number of cage.

Table 11 Food efficiency - Group mean values in male rats

Dose (mg/kg/day)	Week				(%)
	1	2	3	4	Average
0	32.9	24.8	16.5	11.8	21.5
8	33.3	24.6	18.5	12.2	22.2
40	32.8	23.7	16.1	13.4	21.5
200/100	23.8	18.4	27.2	10.9	20.1

Food efficiency = (mean body weight gain from previous week/mean food consumption x 7) x 100

Table 12 Food efficiency - Group mean values in female rats

Dose (mg/kg/day)	Week				(%)
	1	2	3	4	Average
0	17.6	13.2	10.3	11.0	13.0
8	18.8	16.9	12.5	8.9	14.3
40	20.0	17.0	8.3	11.8	14.3
100	19.2	16.0	13.9	9.9	14.8

Food efficiency = (mean body weight gain from previous week/mean food consumption x 7) x 100

Table 13 Ophthalmology - Incidence of findings in male rats

Site & Lesion	Dose (mg/kg/day)					
	0	4	8	40	200/100	
Week	0 ^a	4	0 ^a	0 ^a	0 ^a	4
Number of animals examined	10	10	10	10	10	6
No abnormalities detected	10	10	10	10	10	6

^a: Week before initiation of treatment.

Ophthalmology - Incidence of findings in female rats

Table 14

Site & Lesion	Dose (mg/kg/day)				Number of animals examined
	0	4	8	40	
Week	0 ^a	4	0 ^a	0 ^a	100
	10	10	10	10	10
	10	10	10	10	9

No abnormalities detected

^a: Week before initiation of treatment.

Key to Tables 15 and 16
Standard key to urinalysis data

Grades for glucose, bilirubin, ketones, occult blood, protein:

-	Negative
±	Trace
+	Slight
++	Moderate
+++	Severe
++++	Extreme

Urinary sediments:

Abnormal crystals Crystals of cholesterol, tyrosine, leucine, cystine or test substance, etc.

-	Nil
+	A few in some fields
++	A few in any field
+++	Many in any field

Appearance:

C	Colorless
PY	Pale yellow
Y	Yellow
YB	Yellow brown
B	Brown

Urinalysis - Summary data in male rats

Table 15 - 2

At 4 weeks of treatment

Dose (mg/kg/day)	No. of animals examined	Appearance				Urine volume (mL/day) Mean \pm S.D.	Urinary sediments			
		C	PY	Y	YB		B	Red blood cells		
						-	+	++	+++	
0	10			10		12.1 \pm 2.3	10			
8	10			10		13.4 \pm 1.8	9			1
40	10			10		11.3 \pm 1.5	10			
200/100	6			6		14.4 \pm 5.2	6			

	Urinary sediments											
	White blood cells			Epithelial cells			Casts			Abnormal crystals		
	-	+	++	+++	-	+	++	+++	-	+	++	+++
10					10				10			
10					10				10			
10					10				10			
6					6				6			

S.D.: Standard deviation.

Urinalysis - Summary data in female rats

Table 16 - 2

At 4 weeks of treatment

Dose (mg/kg/day)	No. of animals examined	Appearance				Urine volume (mL/day) Mean \pm S.D.	Urinary sediments		
		C	PY	Y	YB		B	Red blood cells	
						-	+	++	+++
0	10			10		10			
8	10			10		10			
40	10			10		10			
100	9			8	1	14.2 \pm 9.6			

	Urinary sediments											
	White blood cells			Epithelial cells			Casts			Abnormal crystals		
	-	+	++	+++	-	+	++	+++	-	+	++	+++
10												
10												
10												
10												
9												

S.D.: Standard deviation.

Table 17 - 1
Hematology - Group mean values in male rats
After 4 weeks of treatment

Dose (mg/kg/day)	No. of animals examined	Ht (%)	Hb (g/dL)	RBC ($10^6/\mu\text{L}$)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($10^3/\mu\text{L}$)	Retics ($10^9/\text{L}$)	PT (sec)	APTT (sec)
0	10	Mean	15.6	8.42	54.4	18.6	34.1	1150	169.6	18.2	25.0
		S.D.	0.4	0.33	1.8	0.6	0.5	82	23.1	1.7	2.3
8	10	Mean	16.0	8.47	55.2	19.0	34.4	1090	173.1	17.8	24.9
		S.D.	0.4	0.34	1.4	0.5	0.4	132	25.4	1.6	1.3
40	10	Mean	15.4	8.45	53.7	18.3	34.0	1152	205.1	18.5	24.8
		S.D.	0.6	0.28	1.3	0.4	0.3	134	26.8	2.0	1.5
200/100	6	Mean	14.6 **	8.11	53.7	18.0	33.5	1298 *	308.3 *	16.2 *	23.7
		S.D.	0.7	0.33	1.2	0.6	0.6	54	115.4	0.2	1.7

S.D. : Standard deviation.

Significantly different from control : *, $p \leq 0.05$; **, $p \leq 0.01$.

Table 17 - 2 Hematology - Group mean values in male rats
After 4 weeks of treatment

Dose (mg/kg/day)	No. of animals examined	WBC ($10^3/\mu\text{L}$)	Differential leukocyte count ($10^3/\mu\text{L}$)						
			L	N	M	E	B	LUC	
0	10	Mean	6.77	1.67	0.14	0.08	0.03	0.05	
		S.D.	0.98	0.29	0.06	0.03	0.01	0.02	
8	10	Mean	6.72	1.42	0.13	0.06	0.02	0.05	
		S.D.	1.06	0.49	0.04	0.02	0.01	0.01	
40	10	Mean	5.95	1.75	0.11	0.07	0.02	0.04	
		S.D.	2.08	0.85	0.05	0.05	0.01	0.03	
200/100	6	Mean	7.34	2.06	0.17	0.05	0.02	0.05	
		S.D.	1.44	1.12	0.06	0.03	0.01	0.02	

S.D. : Standard deviation.

Table 18 - 1
 Hematology - Group mean values in female rats
 After 4 weeks of treatment

Dose (mg/kg/day)	No. of animals examined	Ht (%)	Hb (g/dL)	RBC ($10^6/\mu\text{L}$)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($10^3/\mu\text{L}$)	Retics ($10^9/\text{L}$)	PT (sec)	APTT (sec)
0	10	Mean	14.7	7.82	54.9	18.8	34.3	1140	196.8	16.5	20.1
		S.D.	0.4	0.27	0.9	0.3	0.4	146	37.4	0.6	1.2
8	10	Mean	15.0	7.90	54.9	19.0	34.5	1256	191.1	16.5	19.9
		S.D.	0.4	0.27	1.7	0.6	0.5	122	45.5	0.8	1.3
40	10	Mean	14.8	7.85	54.6	18.9	34.7	1185	188.4	16.6	20.3
		S.D.	0.4	0.41	1.7	0.8	0.7	115	33.7	0.8	1.2
100	9	Mean	14.5	7.75	54.6	18.8	34.4	1241	213.3	16.5	19.6
		S.D.	0.5	0.38	1.8	0.7	0.8	146	49.3	0.6	1.5

S.D. : Standard deviation.

Table 18 - 2 Hematology - Group mean values in female rats
After 4 weeks of treatment

Dose (mg/kg/day)	No. of animals examined	WBC ($10^3/\mu\text{L}$)	Differential leukocyte count ($10^3/\mu\text{L}$)						
			L	N	M	E	B	LUC	
0	10	Mean	4.87	0.98	0.07	0.04	0.01	0.03	
		S.D.	1.05	0.28	0.02	0.02	0.00	0.02	
8	10	Mean	4.52	0.76	0.06	0.04	0.01	0.03	
		S.D.	1.27	0.23	0.03	0.02	0.01	0.02	
40	10	Mean	4.68	0.67 *	0.07	0.04	0.01	0.03	
		S.D.	0.83	0.18	0.02	0.02	0.00	0.01	
100	9	Mean	6.28	1.17	0.09	0.04	0.01	0.03	
		S.D.	1.91	0.48	0.04	0.01	0.01	0.01	

S.D. : Standard deviation.

Significantly different from control : *, $p \leq 0.05$; **, $p \leq 0.01$.

Table 19 - 1
Blood biochemistry - Group mean values in male rats
After 4 weeks of treatment

Dose (mg/kg/day)	No. of animals examined	ALP (U/L)	AST (U/L)	ALT (U/L)	GGTP (U/L)	Creat (mg/dL)	BUN (mg/dL)	TP (g/dL)	Alb (g/dL)	Glob (g/dL)	A/G ratio	Gluc (mg/dL)
0	10	Mean 461 S.D. 104	71 5	26 4	0 0	0.30 0.02	15.9 1.4	6.38 0.20	4.25 0.17	2.13 0.08	2.00 0.10	131 9
8	10	Mean 497 S.D. 140	70 8	27 4	0 0	0.32 0.04	17.5 1.8	6.30 0.22	4.19 0.14	2.11 0.13	1.99 0.11	138 13
40	10	Mean 418 S.D. 102	75 6	26 2	0 0	0.32 0.03	16.6 3.1	6.03 ** 0.24	4.08 * 0.15	1.96 ** 0.12	2.09 0.10	129 11
200/100	6	Mean 471 S.D. 250	84 ** 12	35 * 10	0 0	0.30 0.03	15.3 2.2	5.60 ** 0.21	3.89 ** 0.13	1.72 ** 0.09	2.27 ** 0.10	124 9

S.D. : Standard deviation.

Significantly different from control : *, $p \leq 0.05$; **, $p \leq 0.01$.

Table 19 - 2 Blood biochemistry - Group mean values in male rats
After 4 weeks of treatment

Dose (mg/kg/day)	No. of animals examined	T.Chol (mg/dL)	TG (mg/dL)	T.Bil (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	10	Mean	64	0.05	10.2	6.9	146.5	3.48	108.3
		S.D.	32	0.01	0.3	0.6	1.1	0.22	0.8
8	10	Mean	53	0.05	10.1	7.0	146.3	3.40	107.8
		S.D.	26	0.01	0.2	0.7	1.0	0.21	0.8
40	10	Mean	51	0.06	10.0	7.1	146.5	3.43	108.9
		S.D.	51	0.01	0.2	0.7	1.7	0.17	1.1
200/100	6	Mean	48	0.06	10.2	7.3	146.4	3.42	107.8
		S.D.	28	0.01	0.2	0.6	0.6	0.07	1.3

S.D. : Standard deviation.