

Table 3-2 Food consumption in females - Before mating (mean \pm S.D. , g/day)

Study No. : SBL75-31

Dose (mg/kg) Day	Control	2.5	25	250
(Administration period)				
0- 1	18.0 \pm 2.3 (15)	17.8 \pm 1.8 (10)	18.8 \pm 2.1 (10)	18.5 \pm 2.2 (15)
3- 4	19.0 \pm 2.2 (15)	19.6 \pm 3.9 (10)	19.8 \pm 1.9 (10)	19.9 \pm 3.3 (15)
7- 8	19.6 \pm 2.6 (15)	20.6 \pm 3.0 (10)	20.2 \pm 1.6 (10)	19.0 \pm 2.6 (15)
10-11	20.4 \pm 2.6 (15)	20.9 \pm 4.9 (10)	19.4 \pm 2.3 (10)	20.1 \pm 3.3 (15)
14-15	19.0 \pm 2.1 (15)	17.9 \pm 3.2 (10)	19.0 \pm 2.8 (10)	19.1 \pm 2.3 (15)
17-18	19.9 \pm 4.0 (15)	19.3 \pm 2.4 (10)	21.4 \pm 1.8 (10)	21.2 \pm 2.7 (15)
21-22	20.3 \pm 3.7 (15)	20.2 \pm 2.9 (10)	21.1 \pm 1.9 (10)	20.1 \pm 2.1 (15)
24-25	19.9 \pm 3.1 (15)	22.2 \pm 4.7 (10)	21.9 \pm 3.5 (10)	21.6 \pm 3.5 (15)
28-29	21.0 \pm 2.3 (5)	(0)	(0)	19.8 \pm 3.4 (5)
31-32	19.4 \pm 1.3 (5)	(0)	(0)	22.4 \pm 2.1* (5)
35-36	19.8 \pm 1.3 (5)	(0)	(0)	21.0 \pm 1.2 (5)
38-39	21.0 \pm 2.0 (5)	(0)	(0)	24.0 \pm 2.6 (5)
42-43	21.8 \pm 2.2 (5)	(0)	(0)	21.6 \pm 2.2 (5)
45-46	22.4 \pm 4.2 (5)	(0)	(0)	22.2 \pm 2.0 (5)
49-50	19.2 \pm 4.2 (5)	(0)	(0)	19.8 \pm 3.9 (5)
52-53	20.0 \pm 2.3 (5)	(0)	(0)	21.2 \pm 1.6 (5)
(Recovery period)				
56-57	21.0 \pm 1.9 (5)	(0)	(0)	23.8 \pm 2.4 (5)
59-60	22.6 \pm 2.6 (5)	(0)	(0)	22.0 \pm 2.5 (5)
63-64	22.4 \pm 2.5 (5)	(0)	(0)	23.4 \pm 2.1 (5)
66-67	22.4 \pm 2.5 (5)	(0)	(0)	23.0 \pm 1.2 (5)

() : No. of animals

* P<0.05 : Significantly different from the control group by Dunnet's type test / Dunnet's test.
Not significantly different from the control group by t-test.

Table 3-3 Food consumption in dams (F0) - Gestation period (mean \pm S.D. , g/day) Study No. : SBL75-31

Dose (mg/kg) Days of gestation	Control	2.5	25	250
0- 1	20.9 \pm 3.9 (9)	20.8 \pm 2.1 (9)	20.3 \pm 3.1 (10)	20.8 \pm 3.3 (10)
3- 4	22.6 \pm 5.3 (9)	24.6 \pm 3.8 (9)	24.8 \pm 2.7 (10)	26.1 \pm 2.5 (10)
6- 7	25.3 \pm 3.5 (9)	26.1 \pm 2.0 (9)	24.3 \pm 2.9 (10)	26.6 \pm 2.2 (10)
10-11	26.7 \pm 3.6 (9)	28.0 \pm 2.7 (9)	27.7 \pm 1.9 (10)	28.2 \pm 2.3 (10)
14-15	26.1 \pm 3.0 (9)	28.2 \pm 4.5 (9)	28.1 \pm 2.1 (10)	25.9 \pm 2.5 (10)
17-18	29.4 \pm 2.9 (9)	28.7 \pm 3.0 (9)	30.1 \pm 2.7 (10)	29.8 \pm 2.4 (10)
19-20	27.1 \pm 3.8 (9)	27.7 \pm 3.5 (9)	28.2 \pm 2.5 (10)	29.1 \pm 2.7 (10)

() : No. of dams
 Not significantly different from the control group by Dunnet's type test / Dunnet's test

Table 3-4 Food consumption in dams (F0) - Lactation period (mean \pm S.D. , g/day) Study No. : SBL75-31

Dose (mg/kg) Days after delivery	Control	2.5	25	250
0- 1	13.8 \pm 8.9 (9)	12.8 \pm 7.4 (10)	12.9 \pm 9.8 (10)	15.0 \pm 8.7 (10)
2- 3	38.1 \pm 5.2 (9)	33.7 \pm 4.2 (10)	35.5 \pm 8.6 (10)	34.2 \pm 4.4 (10)

() : No. of dams

Not significantly different from the control group by Dunnet's type test / Dunnet's test

Table 4 Mating performance

Study No. : SBL75-31

Dose : (mg/kg)		Control	2.5	25	250
No. of pairs used for mating	(a)	10	10	10	10
No. of pairs with successful copulation	(b)	9	10	10	10
Copulatory index (%)	(b/a)	90.0	100.0	100.0	100.0
Mean copulatory interval (days , mean±S.D.)		4.9±4.4	3.4±3.8	2.7±1.3	2.8±1.5
No. of fertile pairs	(c)	9	10	10	10
Fertility index (%)	(c/b)	100.0	100.0	100.0	100.0

Not significantly different from the control group by Dunnet's type test / Dunnet's test.
Not significantly different from the control group by Fisher's exact test.

Table 5 Abbreviations of hematology parameters

Hematology

RBC	($10^6/\text{mm}^3$)	Number of red blood cells
WBC	($10^3/\text{mm}^3$)	Number of white blood cells
Ht	(%)	Hematocrit value
Hb	(g/dL)	Hemoglobin concentration
Plat.	($10^3/\text{mm}^3$)	Number of blood platelets
MCV	(fL)	Mean corpuscular volume
MCH	(pg)	Mean corpuscular hemoglobin
MCHC	(g/dL)	Mean corpuscular hemoglobin concentration
Ret.(%)	(%)	Reticulocyte ratio
Hemogram		
Eosino.	($10^3/\text{mm}^3$)	Number of eosinophilic leukocytes
Eosino.	(%)	Eosinophilic leukocyte ratio
Baso.	($10^3/\text{mm}^3$)	Number of basophilic leukocytes
Baso.	(%)	Basophilic leukocyte ratio
Mono.	($10^3/\text{mm}^3$)	Number of monocytes
Mono.	(%)	Monocyte ratio
Lymph.	($10^3/\text{mm}^3$)	Number of lymphocytes
Lymph.	(%)	Lymphocyte ratio
Neutro.	($10^3/\text{mm}^3$)	Number of neutrophilic leukocytes
Neutro.	(%)	Neutrophilic leukocyte ratio
LUC	($10^3/\text{mm}^3$)	Number of large unstained cells
LUC	(%)	Large unstained cell ratio
Blood coagulation test		
PT	(Sec)	Prothrombin time
APTT	(Sec)	Activated partial thromboplastin time

Table 5-1

Hematology in males (End of drug administration)

Study No. : SBL75-31

Dose(mg/kg)		Control	2.5	25	250
N		5	5	5	5
RBC	($10^6/\text{mm}^3$)	8.184±0.323	7.946±0.307	8.068±0.304	7.634±0.364*
WBC	($10^3/\text{mm}^3$)	9.414±1.059	8.218±2.935	8.102±2.368	8.936±1.133
Ht	(%)	45.56±1.90	44.32±0.91	44.68±2.24	42.70±1.68
Hb	(g/dL)	15.24±0.38	14.86±0.54	15.12±0.86	14.22±0.70
Plat.	($10^3/\text{mm}^3$)	1063.2±109.9	1145.2±134.1	1201.8±119.3	1204.8±107.7
MCV	(fL)	55.70±2.34	55.84±1.45	55.36±0.86	55.94±0.72
MCH	(pg)	18.66±0.70	18.68±0.79	18.72±0.43	18.60±0.27
MCHC	(g/dL)	33.54±0.69	33.50±0.71	33.82±0.37	33.26±0.44
Ret.	(%)	2.60±0.34	2.74±0.57	3.00±0.40	3.02±0.44
Eosino.	($10^3/\text{mm}^3$)	0.102±0.036	0.118±0.024	0.072±0.028	0.106±0.032
Eosino.	(%)	1.08±0.42	1.62±0.70	0.88±0.13	1.22±0.38
Baso.	($10^3/\text{mm}^3$)	0.018±0.004	0.016±0.009	0.014±0.005	0.012±0.004
Baso.	(%)	0.18±0.04	0.16±0.09	0.16±0.05	0.12±0.04
Mono.	($10^3/\text{mm}^3$)	0.158±0.078	0.114±0.025	0.100±0.062	0.148±0.008
Mono.	(%)	1.64±0.61	1.58±0.73	1.20±0.35	1.68±0.30
Lymph.	($10^3/\text{mm}^3$)	8.064±0.827	6.770±2.978	6.486±2.114	7.050±1.135
Lymph.	(%)	85.78±2.26	80.58±7.34	79.64±3.66	78.64±4.29
Neutro.	($10^3/\text{mm}^3$)	0.990±0.238	1.124±0.345	1.360±0.299	1.512±0.277*
Neutro.	(%)	10.48±1.99	14.96±5.91	17.30±3.71	17.18±4.23
LUC	($10^3/\text{mm}^3$)	0.082±0.008	0.078±0.024	0.068±0.040	0.104±0.078
LUC	(%)	0.86±0.05	1.10±0.51	0.82±0.43	1.10±0.74
PT	(Sec)	8.52±0.42	9.50±0.97	9.20±0.57	8.50±0.58
APTT	(Sec)	20.10±0.77	20.94±0.65	18.34±0.98**	18.18±0.71**

Values are expressed as the mean + S.D.

* $p < 0.05$, ** $p < 0.01$: Significantly different from the control group by Dunnet's type test / Dunnet's test.

Table 5-2

Hematology in females (End of drug administration)

Study No. : SBL75-31

Dose (mg/kg)		Control	2.5	25	250
N		5	5	5	5
RBC	($10^6/\text{mm}^3$)	6.810±0.489	6.904±0.360	6.816±0.138	6.500±0.243
WBC	($10^3/\text{mm}^3$)	5.952±0.959	6.188±1.379	6.344±1.463	5.050±0.711
Ht	(%)	40.16±2.06	41.08±1.68	39.40±1.19	39.58±2.33
Hb	(g/dL)	13.38±0.66	13.98±0.75	13.14±0.36	13.36±0.77
Plat.	($10^3/\text{mm}^3$)	1468.0±237.3	1517.6±44.2	1496.0±207.7	1502.6±156.5
MCV	(fL)	59.08±2.35	59.58±1.84	57.80±2.12	60.90±1.46
MCH	(pg)	19.70±0.82	20.26±0.46	19.28±0.65	20.54±0.50
MCHC	(g/dL)	33.34±0.21	34.00±0.59	33.40±0.73	33.74±0.37
Ret.	(%)	6.48±2.55	4.88±1.04	4.48±1.28	6.28±2.55
Eosino.	($10^3/\text{mm}^3$)	0.068±0.019	0.048±0.019	0.038±0.016*	0.038±0.018*
Eosino.	(%)	1.10±0.31	0.82±0.32	0.62±0.24	0.74±0.35
Baso.	($10^3/\text{mm}^3$)	0.004±0.005	0.008±0.004	0.010±0.007	0.000±0.000
Baso.	(%)	0.08±0.04	0.10±0.07	0.10±0.07	0.08±0.04
Mono.	($10^3/\text{mm}^3$)	0.088±0.053	0.058±0.027	0.078±0.036	0.072±0.044
Mono.	(%)	1.44±0.78	0.96±0.32	1.18±0.30	1.38±0.86
Lymph.	($10^3/\text{mm}^3$)	3.702±0.766	4.614±1.065	4.634±1.454	3.408±0.151
Lymph.	(%)	61.98±4.94	74.58±6.18	71.96±8.38	68.72±11.35
Neutro.	($10^3/\text{mm}^3$)	2.052±0.302	1.432±0.505	1.546±0.352	1.500±0.766
Neutro.	(%)	34.74±4.38	23.08±5.78	25.52±8.49	28.50±11.13
LUC	($10^3/\text{mm}^3$)	0.038±0.015	0.030±0.007	0.036±0.015	0.032±0.013
LUC	(%)	0.66±0.24	0.50±0.12	0.60±0.23	0.58±0.23
PT	(Sec)	7.38±0.29	7.28±0.19	7.42±0.27	6.94±0.32
APTT	(Sec)	18.56±1.19	19.14±1.92	18.82±0.25	14.74±3.36

Values are expressed as the mean ± S.D.

* P<0.05 : Significantly different from the control group by Dunnet's type test / Dunnet's test.

Table 5-3

Hematology in males (End of recovery test)

Study No. : SBL75-31

Dose (mg/kg)		Control	2.5	25	250
N		5	0	0	5
RBC	($10^6/\text{mm}^3$)	8.866±0.544			8.342±0.406
WBC	($10^3/\text{mm}^3$)	8.506±1.532			9.516±1.568
Ht	(%)	47.26±2.39			45.66±1.12
Hb	(g/dL)	15.76±0.74			15.10±0.32
Plat.	($10^3/\text{mm}^3$)	1081.0±73.3			1406.4±218.2*
MCV	(fL)	53.36±1.25			54.86±3.31
MCH	(pg)	17.80±0.46			18.14±0.95
MCHC	(g/dL)	33.36±0.17			33.06±0.69
Ret.	(%)	2.44±0.38			2.80±0.16
Eosino.	($10^3/\text{mm}^3$)	0.100±0.052			0.092±0.031
Eosino.	(%)	1.16±0.55			0.98±0.45
Baso.	($10^3/\text{mm}^3$)	0.008±0.004			0.016±0.009
Baso.	(%)	0.10±0.07			0.18±0.08
Mono.	($10^3/\text{mm}^3$)	0.116±0.041			0.174±0.046
Mono.	(%)	1.40±0.56			1.82±0.39
Lymph.	($10^3/\text{mm}^3$)	7.398±1.397			7.982±1.372
Lymph.	(%)	86.86±1.17			83.78±1.86*
Neutro.	($10^3/\text{mm}^3$)	0.784±0.164			1.176±0.214*
Neutro.	(%)	9.26±1.49			12.42±1.86*
LUC	($10^3/\text{mm}^3$)	0.094±0.064			0.078±0.038
LUC	(%)	1.18±0.83			0.82±0.27
PT	(Sec)	14.84±3.34			15.70±2.71
APTT	(Sec)	23.98±1.48			25.48±1.23

Values are expressed as the mean + S.D.

* P<0.05 : Significantly different from the control group by t-test / Wilcoxon test.

Table 5-4

Hematology in females (End of recovery test)

Study No. : SBL75-31

Dose(mg/kg)		Control	2.5	25	250
N		5	0	0	5
RBC	($10^6/\text{mm}^3$)	8.074±0.449			8.112±0.157
WBC	($10^3/\text{mm}^3$)	3.446±0.317			3.514±0.780
Ht	(%)	45.00±1.78			44.54±0.58
Hb	(g/dL)	15.40±0.66			15.30±0.39
Plat.	($10^3/\text{mm}^3$)	1113.2±77.9			1037.4±91.2
MCV	(fL)	55.78±1.08			54.94±0.52
MCH	(pg)	19.10±0.37			18.82±0.16
MCHC	(g/dL)	34.20±0.35			34.28±0.52
Ret.	(%)	2.32±0.42			2.08±0.43
Eosino.	($10^3/\text{mm}^3$)	0.064±0.015			0.056±0.015
Eosino.	(%)	1.80±0.45			1.66±0.74
Baso.	($10^3/\text{mm}^3$)	0.000±0.000			0.000±0.000
Baso.	(%)	0.06±0.05			0.04±0.05
Mono.	($10^3/\text{mm}^3$)	0.066±0.017			0.062±0.019
Mono.	(%)	1.92±0.45			1.74±0.50
Lymph.	($10^3/\text{mm}^3$)	2.634±0.281			2.834±0.698
Lymph.	(%)	76.78±7.95			80.34±4.18
Neutro.	($10^3/\text{mm}^3$)	0.652±0.295			0.542±0.157
Neutro.	(%)	18.64±7.31			15.60±3.83
LUC	($10^3/\text{mm}^3$)	0.028±0.015			0.022±0.008
LUC	(%)	0.74±0.34			0.62±0.24
PT	(Sec)	7.70±0.38			7.36±0.09
APTT	(Sec)	18.04±0.86			17.58±0.19

Values are expressed as the mean + S.D.

Not significantly different from the control group by t-test / Wilcoxon test.

Table 6 Abbreviations of blood chemistry parameters

Study No.SBL75-31

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
TBA	(μ mol/L)	Total bile acid

Protein fraction

Albumin	(%)	Albumin
A1-glob.	(%)	Alpha-1 globulin
A2-glob.	(%)	Alpha-2 globulin
B-glob.	(%)	Beta globulin
G-glob.	(%)	Gamma globulin
A/G		Albumin / Globulin

Table 6-1 Blood chemistry in males (End of drug administration)

Study No. : SBL75-31

Dose(mg/kg)	Control	2.5	25	250.
N	5	5	5	5
ASAT (IU/L)	115.6+23.0	92.4+17.7	135.8+28.1	120.8+23.1
ALAT (IU/L)	38.8±3.7	39.2±2.9	58.2±25.5*	48.8±7.5
ALP (IU/L)	539.0±57.3	475.6±77.7	616.8±177.8	942.6±149.6**
LDH (IU/L)	2106.6±753.8	1235.8±824.0	2751.8±1313.4	2255.6±792.4
CPK (IU/L)	836.6±225.3	441.8±232.4	826.8±314.2	694.0±248.4
T.Bil. (mg/dL)	0.052±0.008	0.048±0.016	0.046±0.013	0.024±0.009**
T.Prot. (g/dL)	5.60±0.10	6.04±0.27	6.26±0.41**	5.92±0.34
Albumin (g/dL)	4.10±0.10	4.54±0.25	5.18±0.43**	5.00±0.24**
T.Chol. (mg/dL)	68.0±6.9	58.4±12.8	64.0±7.3	61.2±16.5
TGL (mg/dL)	51.0±16.0	36.2±10.1	45.0±14.8	57.2±11.5
Glucose (mg/dL)	186.2±14.0	173.2±14.3	190.4±14.6	198.2±27.1
BUN (mg/dL)	20.74±1.17	19.68±2.59	21.78±1.85	21.34±3.76
Creat. (mg/dL)	0.312±0.053	0.274±0.022	0.226±0.037**	0.248±0.022*
IP (mg/dL)	7.106±0.352	7.004±0.515	7.848±0.606	7.490±0.692
Ca (mg/dL)	8.94±0.26	9.28±0.16	9.58±0.20**	9.18±0.24
Na (mEq/L)	141.0±0.7	142.4±0.5	142.2±1.6	140.2±0.4
K (mEq/L)	4.46±0.17	4.40±0.41	4.54±0.27	4.62±0.18
Cl (mEq/L)	103.0±1.4	104.6±1.7	103.6±0.9	102.8±0.8
Albumin (%)	51.48±2.34	53.26±1.80	58.56±2.53**	61.00±1.66**
A1-glob. (%)	20.38±2.69	20.66±2.51	19.14±2.91	18.14±1.16
A2-glob. (%)	9.44±0.51	9.00±0.33	7.76±0.21**	7.60±0.37**
B-glob. (%)	14.52±0.92	12.88±1.02**	10.56±0.56**	9.02±0.30**
G-glob. (%)	4.18±1.03	4.20±0.31	3.98±0.76	4.24±0.80
A/G	1.058±0.098	1.142±0.086	1.418±0.141**	1.568±0.106**
TBA (μ. mol/L)	15.02±7.33	13.16±4.54	24.98±8.23	40.06±44.09

Values are expressed as the mean + S.D.

* P<0.05, ** P<0.01 : Significantly different from the control group by Dunnet's type test / Dunnet's test.

Table 6-2

Blood chemistry in females (End of drug administration)

Study No. : SBL75-31

Dose (mg/kg)	Control	2.5	25	250
N	5	5	5	5
ASAT (IU/L)	130.2±11.3	112.8±37.2	106.4±14.8	103.8±22.6
ALAT (IU/L)	59.0±9.1	42.8±7.8	49.4±9.9	60.2±15.3
ALP (IU/L)	214.8±29.4	185.4±70.5	184.4±56.4	193.8±59.4
LDH (IU/L)	2642.2±802.9	2198.2±1795.1	1632.2±600.4	1347.4±653.2
CPK (IU/L)	794.4±425.0	588.4±457.5	445.6±137.3	333.0±156.2
T.Bil. (mg/dL)	0.058±0.016	0.074±0.030	0.044±0.011	0.056±0.013
T.Prot. (g/dL)	5.74±0.31	5.60±0.27	5.54±0.36	5.50±0.22
Albumin (g/dL)	4.46±0.29	4.36±0.15	4.38±0.31	4.30±0.19
T.Chol. (mg/dL)	79.6±16.8	58.4±3.2*	57.6±13.3*	64.2±12.9
TGL (mg/dL)	25.4±6.9	23.0±15.0	21.2±15.1	17.8±13.8
Glucose (mg/dL)	109.0±15.8	108.6±13.2	119.8±6.7	115.0±24.1
BUN (mg/dL)	26.14±8.24	17.28±5.27	19.82±4.06	18.90±4.97
Creat. (mg/dL)	0.308±0.044	0.290±0.040	0.330±0.029	0.282±0.028
IP (mg/dL)	6.614±0.971	5.620±0.963	6.274±0.867	6.020±0.726
Ca (mg/dL)	8.94±0.67	8.88±0.47	9.02±0.24	9.16±0.54
Na (mEq/L)	140.2±0.8	139.6±1.1	140.2±1.1	139.8±1.9
K (mEq/L)	4.10±0.16	4.22±0.16	4.00±0.14	3.92±0.19
Cl (mEq/L)	101.2±2.4	100.4±1.5	101.4±2.5	101.0±1.6
Albumin (%)	55.02±1.84	54.22±2.05	55.48±0.75	55.44±1.82
A1-glob. (%)	17.82±2.14	19.20±1.42	17.78±2.24	17.56±1.30
A2-glob. (%)	8.76±1.21	8.84±0.90	7.92±0.75	8.34±0.32
B-glob. (%)	13.46±0.92	13.34±0.90	13.68±0.76	13.38±0.99
G-glob. (%)	4.94±1.20	4.40±0.42	5.14±0.46	5.28±0.41
A/G	1.226±0.090	1.188±0.104	1.246±0.036	1.246±0.092
TBA (μ mol/L)	43.04±41.60	25.78±12.77	23.02±8.12	17.00±8.51

Values are expressed as the mean ± S.D.

* p<0.05 : significantly different from the control group by Dunnet's type test / Dunnet's test.

Table 6-3 Blood chemistry in males (End of recovery test)

Study No. : SBL75-31

Dose(mg/kg)	Control	2.5	25	250
N	5	0	0	5
ASAT (IU/L)	87.4±10.8			107.8±25.3
ALAT (IU/L)	34.0±4.4			74.2±35.0
ALP (IU/L)	316.8±65.4			343.0±38.7
LDH (IU/L)	756.8±223.1			838.4±309.5
CPK (IU/L)	384.6±98.9			353.8±127.5
T.Bil. (mg/dL)	0.054±0.023			0.040±0.012
T.Prot. (g/dL)	5.94±0.09			6.50±0.14**
Albumin (g/dL)	4.28±0.13			4.96±0.29**
T.Chol. (mg/dL)	55.4±16.8			96.6±30.3*
TGL (mg/dL)	20.0±5.3			37.0±27.0
Glucose (mg/dL)	194.4±22.7			183.4±16.1
BUN (mg/dL)	20.96±1.59			22.50±2.21
Creat. (mg/dL)	0.412±0.038			0.340±0.044*
IP (mg/dL)	7.568±0.159			7.552±0.674
Ca (mg/dL)	9.24±0.15			9.38±0.13
Na (mEq/L)	140.6±1.1			140.6±0.9
K (mEq/L)	4.36±0.19			4.50±0.48
Cl (mEq/L)	103.2±1.9			104.2±1.3
Albumin (%)	51.94±1.36			53.58±3.75
A1-glob. (%)	20.66±2.46			20.86±3.46
A2-glob. (%)	9.22±0.49			8.30±0.45*
B-glob. (%)	13.60±0.84			12.96±0.69
G-glob. (%)	4.58±0.89			4.30±0.60
A/G	1.084±0.058			1.168±0.174
TBA (μ mol/L)	15.44±8.92			21.42±19.90

Values are expressed as the mean + S.D.

* P<0.05 , ** P<0.01 : Significantly different from the control group by t-test / Wilcoxon test.

Table 6-4

Blood chemistry in females (End of recovery test)

Study No. : SBL75-31

Dose(mg/kg)	Control	2.5	25	250
N	5	0	0	5
ASAT (IU/L)	84.4±9.2			74.8±14.3
ALAT (IU/L)	24.4±6.1			21.8±4.0
ALP (IU/L)	167.4±29.2			188.6±38.3
LDH (IU/L)	1178.2±667.1			967.8±514.9
CPK (IU/L)	342.6±174.9			303.0±109.5
T.Bil. (mg/dL)	0.062±0.004			0.084±0.026
T.Prot. (g/dL)	6.18±0.33			6.42±0.30
Albumin (g/dL)	4.98±0.20			5.26±0.30
T.Chol. (mg/dL)	69.2±4.1			60.2±8.1
TGL (mg/dL)	17.2±4.2			19.2±6.5
Glucose (mg/dL)	162.6±9.9			161.0±13.0
BUN (mg/dL)	21.70±2.61			21.20±4.48
Creat. (mg/dL)	0.382±0.034			0.366±0.025
IP (mg/dL)	4.682±0.515			4.638±1.243
Ca (mg/dL)	9.12±0.29			9.26±0.23
Na (mEq/L)	140.6±0.9			140.4±1.1
K (mEq/L)	3.92±0.24			3.92±0.22
Cl (mEq/L)	105.6±1.1			106.6±1.1
Albumin (%)	59.66±2.81			59.06±0.26
A1-glob. (%)	13.06±2.91			14.82±0.94
A2-glob. (%)	7.36±0.59			7.50±1.05
B-glob. (%)	13.80±1.00			13.68±0.88
G-glob. (%)	6.12±1.26			4.94±0.54
A/G	1.488±0.175			1.438±0.013
TBA (μ mol/L)	14.86±12.28			25.18±17.85

Values are expressed as the mean ± S.D.

Not significantly different from the control group by t-test / Wilcoxon test.

Table 7-1 Gross pathological findings in males (End of drug administration)

Study No. : SBL75-31

Dose (mg/kg)	Control	2.5	25	250
No. of animals	10	10	10	10
Normal	10	10	10	9
Lung: Red focus	0	0	0	1

Table 7-2 Gross pathological findings in females (End of drug administration)

Study No. : SBL75-31

Dose (mg/kg)	Control	2.5	25	250
No. of animals	10	10	10	10
No. of dams	9	10	10	10
Normal	9	10	10	10
No. of non-copulated animal	1	0	0	0
Normal	1	0	0	0

Table 7-3 Gross pathological findings in males (End of recovery test)

Study No. : SBL75-31

Dose (mg/kg)	Control	250
No. of animals	5	5
Normal	4	5
Lung : Red focus	1	0

Table 7-4 Gross pathological findings in females (End of recovery test)

Study No. : SBL75-31

Dose (mg/kg)	Control	250
No. of animals	5	5
Normal	5	5

Table 8 Abbreviations of organ weights

Study No. SBL75-31

Organ weight

Epididy. Sem. Vesic.	Epididymis Seminal vesicle
-R	(Right)
-L	(Left)
-R&L	(Right and Left)

Table 8-1

Organ weight in males (End of drug administration)

Study No. : SBL75-31

Dose (mg/kg)		Control	2.5	25	250
	N	5	5	5	5
Adrenal-R	(mg)	29.46±6.49	28.76±4.44	29.54±2.67	24.92±2.33
Adrenal-L	(mg)	31.74±3.86	33.34±5.37	31.94±4.54	25.84±1.62
Adrenal-R&L	(mg)	61.20±9.48	62.10±9.20	61.48±6.92	50.76±3.21
Testis-R	(mg)	1613.6±63.3	1685.0±64.1	1501.4±132.3	1494.4±108.4
Testis-L	(mg)	1615.6±82.5	1700.6±112.8	1512.8±150.9	1504.0±146.5
Testis-R&L	(mg)	3229.2±141.5	3385.6±174.1	3014.2±281.9	2998.4±253.2
Thymus	(mg)	391.2±90.3	401.2±104.4	411.8±173.7	396.2±87.6
Spleen	(mg)	852.8±81.9	957.4±204.7	908.0±218.0	790.0±61.5
Brain	(mg)	2069.4±70.2	2093.0±63.3	2061.4±109.4	2001.2±88.0
Heart	(mg)	1413.4±69.9	1524.8±108.5	1440.2±156.4	1418.8±108.1
Liver	(g)	14.812±1.426	16.456±1.701	20.110±3.759*	24.110±2.602**
Kidney-R	(mg)	1572.6±92.6	1765.2±166.8	1761.0±195.5	1643.6±116.9
Kidney-L	(mg)	1595.6±161.4	1725.4±145.2	1739.0±206.0	1691.4±69.1
Kidney-R&L	(mg)	3168.2±248.7	3490.6±308.6	3500.0±398.5	3335.0±182.2
Epididy.-R	(mg)	620.8±23.6	635.4±36.1	596.0±54.2	613.8±63.4
Epididy.-L	(mg)	640.6±43.9	633.0±31.8	636.4±84.2	627.6±73.0
Epididy.-R&L	(mg)	1261.4±65.7	1268.4±58.7	1232.4±137.8	1241.4±134.0
Sem. Vesic.	(mg)	1712.4±178.5	1686.4±140.3	1704.4±210.8	1599.8±115.5
Prostate	(mg)	1365.8±92.7	1250.0±96.6	1415.8±339.7	1394.4±191.4

Values are expressed as the mean + S.D.

* P<0.05 , ** P<0.01 : Significantly different from the control group by Dunnet's type test / Dunnet's test.

Table 8-2

Organ weight in females (End of drug administration)

Study No. : SBL75-31

Dose (mg/kg)		Control	2.5	25	250
N		5	5	5	5
Adrenal-R	(mg)	45.28±6.52	41.40±4.69	41.42±4.94	42.72±1.73
Adrenal-L	(mg)	50.44±9.02	43.64±6.14	43.84±5.39	46.74±2.61
Adrenal-R&L	(mg)	95.72±15.21	85.04±10.30	85.26±10.30	89.46±3.98
Ovary-R	(mg)	50.30±7.29	47.90±4.66	49.22±11.74	53.64±6.91
Ovary-L	(mg)	45.60±6.62	48.46±5.16	46.38±0.89	51.24±17.35
Ovary-R&L	(mg)	95.90±10.44	96.36±6.23	95.60±11.60	104.88±18.78
Thymus	(mg)	219.0±40.2	272.2±59.8	247.2±87.2	252.8±64.2
Spleen	(mg)	715.8±177.7	713.0±125.0	665.6±172.1	748.8±61.7
Brain	(mg)	1962.2±38.4	1963.0±61.0	1967.2±90.9	1939.6±61.2
Heart	(mg)	1059.6±142.1	1003.0±35.6	984.0±76.3	1011.0±98.0
Liver	(g)	9.892±1.644	8.992±0.665	9.158±0.692	9.686±0.542
Kidney-R	(mg)	1082.0±141.9	1040.4±69.2	984.8±106.5	1025.2±25.1
Kidney-L	(mg)	1082.0±138.8	1029.4±74.0	991.6±108.1	1008.2±19.9
Kidney-R&L	(mg)	2164.0±279.6	2069.8±140.5	1976.4±213.1	2033.4±28.6

Values are expressed as the mean ± S.D.

Not significantly different from the control group by Dunnet's type test / Dunnet's test.

Table 8-3

Organ weight in males (End of recovery test)

Study No. : SBL75-31

Dose(mg/kg)		Control	2.5	25	250
N		5	0	0	5
Adrenal-R (mg)		30.28±4.07			32.00±4.41
Adrenal-L (mg)		29.96±4.22			33.10±6.34
Adrenal-R&L (mg)		60.24±8.16			65.10±10.65
Testis-R (mg)		1497.8±362.4			1434.4±375.4
Testis-L (mg)		1480.0±341.0			1416.6±370.9
Testis-R&L (mg)		2977.8±700.1			2851.0±744.8
Thymus (mg)		370.6±70.6			333.8±49.2
Spleen (mg)		833.8±85.2			868.2±151.5
Brain (mg)		2104.8±32.3			2161.0±61.7
Heart (mg)		1471.2±77.7			1584.6±46.7*
Liver (g)		13.318±1.013			15.678±1.709*
Kidney-R (mg)		1643.0±131.0			1663.8±171.6
Kidney-L (mg)		1620.0±101.4			1706.4±207.6
Kidney-R&L (mg)		3263.0±225.1			3390.2±377.3
Epididy.-R (mg)		647.6±121.0			621.2±82.9
Epididy.-L (mg)		628.8±116.3			597.8±79.4
Epididy.-R&L (mg)		1276.4±235.5			1219.0±161.6
Sem. Vesic. (mg)		1650.0±231.7			1629.6±377.5
Prostate (mg)		1304.4±173.4			1219.6±257.2

Values are expressed as the mean ± S.D.

* P<0.05 : Significantly different from the control group by t-test / Wilcoxon test.

Table 8-4 Organ weight in females (End of recovery test)

Study No. : SBL75-31

Dose (mg/kg)		Control	2.5	25	250
N		5	0	0	5
Adrenal-R (mg)		32.40±1.24			35.26±7.28
Adrenal-L (mg)		34.46±1.62			36.46±6.40
Adrenal-R&L (mg)		66.86±2.13			71.72±13.67
Ovary-R (mg)		42.58±4.16			45.66±5.97
Ovary-L (mg)		41.18±6.73			47.36±16.14
Ovary-R&L (mg)		83.76±8.16			93.02±19.94
Thymus (mg)		323.0±55.0			508.6±384.1
Spleen (mg)		489.6±47.5			511.6±89.6
Brain (mg)		1934.6±111.8			1894.8±86.8
Heart (mg)		906.6±99.7			928.8±85.5
Liver (g)		7.096±0.549			7.544±0.500
Kidney-R (mg)		944.2±78.3			941.0±26.4
Kidney-L (mg)		931.6±83.0			924.6±15.9
Kidney-R&L (mg)		1875.8±153.6			1865.6±26.0

Values are expressed as the mean ± S.D.

Not significantly different from the control group by t-test / Wilcoxon test.

Table 8-5

Relative organ weight in males (End of drug administration)

Study No. : SBL75-31

Dose(mg/kg) N	Control 5	2.5 5	25 5	250 5
Body weight (g)	450.8±34.6	463.4±26.2	454.4±36.7	437.0±10.9
Adrenal-R (mg/100gBW)	6.60±1.56	6.22±0.98	6.56±1.05	5.70±0.46
Adrenal-L (mg/100gBW)	7.08±0.87	7.20±1.21	7.08±1.25	5.90±0.34
Adrenal-R&L (mg/100gBW)	13.64±2.29	13.42±2.06	13.62±2.20	11.60±0.62
Testis-R (mg/100gBW)	359.8±30.0	364.4±21.2	331.6±33.0	341.8±24.9
Testis-L (mg/100gBW)	360.2±32.8	368.0±30.9	334.4±39.8	344.0±33.7
Testis-R&L (mg/100gBW)	719.8±62.3	732.2±51.3	666.0±72.7	686.2±58.2
Thymus (mg/100gBW)	87.4±22.7	86.2±18.6	89.4±31.5	90.8±20.5
Spleen (mg/100gBW)	189.8±19.4	206.0±37.6	198.8±35.3	181.2±17.3
Brain (mg/100gBW)	461.0±34.3	453.0±34.0	457.4±61.2	458.6±30.0
Heart (mg/100gBW)	314.2±11.1	329.4±18.4	316.6±18.2	324.8±23.8
Liver (g/100gBW)	3.284±0.127	3.544±0.198	4.408±0.548*	5.524±0.658**
Kidney-R (mg/100gBW)	350.8±39.4	380.8±24.8	387.2±22.4	376.2±27.9
Kidney-L (mg/100gBW)	355.6±44.2	372.8±27.0	382.4±23.5	387.6±18.7
Kidney-R&L (mg/100gBW)	706.4±81.9	753.2±50.6	769.4±44.6	763.4±45.2
Epididy.-R (mg/100gBW)	138.4±12.3	137.0±4.5	131.4±7.5	140.0±12.6
Epididy.-L (mg/100gBW)	142.8±14.7	136.6±7.9	139.8±11.3	143.6±15.7
Epididy.-R&L (mg/100gBW)	281.2±26.5	274.2±10.4	271.2±17.9	284.0±28.0
Sem. Vesic. (mg/100gBW)	382.6±60.3	365.2±40.4	375.6±40.3	366.2±26.8
Prostate (mg/100gBW)	304.6±35.2	270.4±24.5	309.2±57.1	318.6±38.1

Values are expressed as the mean + S.D.

* P<0.05 , ** P<0.01 : Significantly different from the control group by Dunnet's type test / Dunnet's test.

Table 8-6

Relative organ weight in females (End of drug administration)

Study No. : SBL75-31

Dose (mg/kg) N	Control 5	2.5 5	25 5	250 5
Body weight (g)	281.6±32.8	290.4±13.6	276.0±14.5	283.0±20.9
Adrenal-R (mg/100gBW)	16.20±2.75	14.28±1.66	15.02±1.60	15.14±0.76
Adrenal-L (mg/100gBW)	17.96±2.71	15.04±2.10	15.88±1.72	16.56±1.02
Adrenal-R&L (mg/100gBW)	34.14±5.23	29.34±3.59	30.90±3.31	31.70±1.60
Ovary-R (mg/100gBW)	18.10±3.61	16.54±2.06	17.84±4.11	18.96±1.85
Ovary-L (mg/100gBW)	16.42±3.19	16.66±1.07	16.84±0.71	17.96±5.11
Ovary-R&L (mg/100gBW)	34.54±5.90	33.20±1.89	34.68±4.16	36.94±4.45
Thymus (mg/100gBW)	77.6±7.8	93.6±18.6	90.2±32.9	90.2±26.5
Spleen (mg/100gBW)	252.0±44.0	246.0±46.5	239.8±51.6	264.6±15.5
Brain (mg/100gBW)	705.6±97.9	677.2±43.8	715.6±67.6	688.4±57.5
Heart (mg/100gBW)	376.2±18.5	345.6±11.9	356.6±21.7	358.0±35.1
Liver (g/100gBW)	3.506±0.365	3.098±0.185*	3.318±0.099	3.432±0.203
Kidney-R (mg/100gBW)	385.0±30.7	358.0±13.3	356.4±27.6	363.8±27.8
Kidney-L (mg/100gBW)	385.2±37.0	354.4±20.4	359.0±30.4	357.8±22.4
Kidney-R&L (mg/100gBW)	770.2±67.4	712.8±32.5	715.2±57.2	721.4±48.8

Values are expressed as the mean + S.D.

* P<0.05 : Significantly different from the control group by Dunnet's type test / Dunnet's test.

Table 8-7 Relative organ weight in males (End of recovery test)

Study No. : SBL75-31

Dose(mg/kg)	Control	2.5	25	250
N	5	0	0	5
Body weight (g)	474.2±22.8			457.0±25.2
Adrenal-R (mg/100gBW)	6.38±0.75			7.00±0.96
Adrenal-L (mg/100gBW)	6.30±0.81			7.26±1.37
Adrenal-R&L (mg/100gBW)	12.70±1.52			14.24±2.37
Testis-R (mg/100gBW)	317.6±82.5			311.8±70.5
Testis-L (mg/100gBW)	313.8±78.6			307.8±70.0
Testis-R&L (mg/100gBW)	631.4±160.4			619.2±140.6
Thymus (mg/100gBW)	79.0±18.3			73.2±11.9
Spleen (mg/100gBW)	176.2±20.8			189.8±29.8
Brain (mg/100gBW)	444.4±18.2			473.8±22.4
Heart (mg/100gBW)	310.0±1.9			347.2±9.3**
Liver (g/100gBW)	2.810±0.188			3.434±0.360**
Kidney-R (mg/100gBW)	346.8±27.1			368.0±26.7
Kidney-L (mg/100gBW)	342.0±24.0			373.0±32.9
Kidney-R&L (mg/100gBW)	689.0±49.5			741.0±58.7
Epididym.-R (mg/100gBW)	137.0±28.3			135.8±16.0
Epididym.-L (mg/100gBW)	133.0±26.3			130.8±14.6
Epididym.-R&L (mg/100gBW)	270.2±54.2			266.6±30.9
Sem. Vesic. (mg/100gBW)	348.0±43.8			357.6±89.0
Prostate (mg/100gBW)	275.6±40.9			267.6±62.3

Values are expressed as the mean + S.D.

* P<0.01 : Significantly different from the control group by t-test / Wilcoxon test.

Table 8-8

Relative organ weight in females (End of recovery test)

Study No. : SBL75-31

Dose(mg/kg)	Control	2.5	25	250
N	5	0	0	5
Body weight (g)	268.2±21.4			283.0±17.5
Adrenal-R (mg/100gBW)	12.12±0.90			12.46±2.47
Adrenal-L (mg/100gBW)	12.94±1.17			12.90±2.18
Adrenal-R&L (mg/100gBW)	25.04±1.99			25.36±4.64
Ovary-R (mg/100gBW)	15.98±2.33			16.22±2.50
Ovary-L (mg/100gBW)	15.32±1.93			16.88±6.32
Ovary-R&L (mg/100gBW)	31.32±3.15			33.12±8.11
Thymus (mg/100gBW)	120.0±12.3			174.2±115.9
Spleen (mg/100gBW)	183.6±22.6			180.8±30.5
Brain (mg/100gBW)	724.2±57.3			670.2±25.4
Heart (mg/100gBW)	338.0±21.6			328.4±30.9
Liver (g/100gBW)	2.652±0.184			2.664±0.107
Kidney-R (mg/100gBW)	354.2±44.9			333.0±12.9
Kidney-L (mg/100gBW)	349.0±39.4			327.8±22.4
Kidney-R&L (mg/100gBW)	703.2±82.6			660.8±34.6

Values are expressed as the mean + S.D.

Not significantly different from the control group by t-test / Wilcoxon test.

Table 9-1 Histopathological findings in males [H.E. staining] (End of drug administration)

Study No.: SBL75-31

Dose (mg/kg)	Control	250
No. of animals	5	5
Normal	0	0
Adrenal (Left)		
Vacuolation, zona fasciculata cell	2	2
Adrenal (Right)		
Vacuolation, zona fasciculata cell	2	2
Heart		
Fibrosis, myocardium, left ventricle	1	1
Mononuclear cell infiltration, myocardium, left ventricle	0	2
Mononuclear cell infiltration, myocardium, right ventricle	1	0
Kidney (Left)		
Basophilia, tubule	3	3
Hyaline cast, tubular lumen	1	0
Mineralization, cortex	1	0
Mononuclear cell infiltration, cortex	1	0
Vacuolation, tubular epithelium	1	0

Table 9-1 (Continued)

Study No.: SBL75-31

Dose (mg/kg)	Control	250
No. of animals	5	5
Kidney (Right)		
Basophilia, tubule	1	2
Mononuclear cell infiltration, cortex	1	0
Lung (Including bronchus, left)		
Foam cell accumulation, alveolus	2	1
Osseous metaplasia	1	0
Lung (Including bronchus, right)		
Foam cell accumulation, alveolus	1	2
Mineralization, arterial wall	2	0
Mononuclear cell infiltration, alveolus	1	0
Lung (Gross abnormal site, right)		
Inflammatory cell infiltration, alveolus, focal	0	1

Table 9-2 Histopathological findings in females [H.E. staining] (End of drug administration)

Study No.: SBL75-31

Dose (mg/kg)	Control	250
No. of animals	5	5
Normal	1	0
Kindney (Left)		
Basophilia, tubule	3	0
Mineralization, cortico-medullary junction	0	1
Mononuclear cell infiltration, cortex	1	0
Kindney (Right)		
Eosinophil infiltration, transitional epithelium, pelvis	1	0
Foreign material, pelvic lumen	1	0
Mineralization, cortico-medullary junction	0	1
Mononuclear cell infiltration, cortex	1	0

Table 9-2 (Continued)

Study No.: SBL75-31

Dose (mg/kg)	Control	250
No. of animals	5	5
Lung (Including bronchus, left)		
Foam cell accumulation, alveolus	1	1
Inflammatory cell infiltration, perivasular	1	0
Proliferation, alveolar epithelium	1	0
Lung (Including bronchus, right)		
Foam cell accumulation, alveolus	1	2
Granuloma	1	0
Mineralization, arterial wall	0	3
Lymph node (Mesenteric)		
Increase, dendritic cell-like cell	0	1
Trachea		
Squamous metaplasia, ciliated epithelium	1	0

Table 9-3 Histopathological findings in males [Testis, PAS-Hematoxylin staining] (End of drug administration)

Study No.: SBL75-31

Dose (mg/kg)	Control	250
No. of animals	5	5
Normal	5	5

Table 9-4 Histopathological findings in animals [Liver, H.E. staining] (End of drug administration) Study No.: SBL75-31

Male

Dose (mg/kg)	Control	2.5	25	250
No. of animals	5	5	5	5
Liver				
Normal	1	3	3	3
Bile duct proliferation, focal	0	0	0	1
Mononuclear cell infiltration	2	2	2	1
Vacuolation, hepatocyte	2	0	0	0

Female

Dose (mg/kg)	Control	2.5	25	250
No. of animals	5	5	5	5
Liver				
Normal	3	3	3	5
Mononuclear cell infiltration	1	1	2	0
Vacuolation, hepatocyte	1	1	0	0

Table 10-1 Clinical signs in pups (F1) - Lactation period

Study No. : SBL75-31

Group	Control	2.5	25	250
Dose (mg/kg)				
No. of dams	9	10	10	10
No. of live pups at birth	126	139	128	139
No. of live pups at day 4	126	137	125	136
Clinical signs				
No. of pups(No. of dams)				
Normal	126 (9)	139 (10)	128 (10)	139 (10)
Death(No. of dams with total litter loss)	0 (0)	0 (0)	0 (0)	0 (0)

Table 10-2 External findings at birth (F1)

Study No. : SBL75-31

Group Dose (mg/kg)	Control	2.5	25	250
No. of dams	9	10	10	10
No. of pups	126	139	128	139
External findings in pups				
Malformations (%)	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]

(%) : Litter - basis analysis
[]:No. of pups with malformations
Not significantly different from control.

Table 11 Development of pups (F1) up to Day 4 after birth

Study No. : SBL75-31

Dose (mg/kg)	Control	2.5	25	250
Pregnant animal	9	10	10	10
Duration of gestation (day)	21.89 ± 0.42	21.94 ± 0.30	21.95 ± 0.37	22.00 ± 0.24
Delivery animal	9	10	10	10
Gestation index (%)	100.0	100.0	100.0	100.0
No. of corpora lutea	16.1 ± 1.9	15.7 ± 1.8	15.3 ± 1.5	16.0 ± 1.9
No. of implantations	15.3 ± 1.7	14.8 ± 1.5	14.1 ± 1.2	14.2 ± 3.2
Implantation index (%) a)	95.36 ± 5.02	94.91 ± 10.81	92.54 ± 6.97	90.72 ± 16.91
At birth				
No. of born	14.1 ± 2.2	14.0 ± 1.9	12.8 ± 2.0	14.0 ± 3.1
No. of live	14.0 ± 2.2	13.9 ± 1.9	12.8 ± 2.0	13.9 ± 2.9
Live birth index (%) b)	91.07 ± 7.23	93.80 ± 7.00	91.01 ± 13.84	96.45 ± 5.69
Viability index (%) c)	99.21 ± 2.37	99.29 ± 2.25	98.82 ± 3.73	98.80 ± 2.55
Sex ratio (Female/Total)	0.53 ± 0.09	0.50 ± 0.15	0.53 ± 0.09	0.61 ± 0.16
At 4 days				
No. of live	14.0 ± 2.2	13.7 ± 1.6	12.5 ± 2.1	13.6 ± 3.0
Viability index (%) d)	100.00 ± 0.00	98.79 ± 2.55	97.55 ± 3.96	97.73 ± 3.67
Sex ratio (Female/Total)	0.53 ± 0.09	0.49 ± 0.14	0.54 ± 0.10	0.61 ± 0.15

a) Implantation index : (No. of implantations / No. of corpora lutea) × 100

b) Live birth index : (No. of live at birth / No. of implantations) × 100

c) Viability index Day 0 : (No. of live at birth / No. of born at birth) × 100

d) Viability index Day 4 : (No. of live at 4 days / No. of live at birth) × 100

Not significantly different from the control group by Dunnet's test / Dunnet's type test.

Not significantly different from the control group by Fisher's exact test.

Table 12

Body weight of pups (F1) - Lactation period (mean \pm S.D. , g)

Study No. : SBL75-31

Dose (mg/kg)	Control	2.5	25	250
No. of dams	9	10	10	10
Postnatal day				
0 : Male	6.5 \pm 0.5 (58)	6.5 \pm 0.5 (70)	6.8 \pm 0.3 (60)	6.5 \pm 0.4 (58)
Female	6.0 \pm 0.4 (58)	6.2 \pm 0.5 (69)	6.3 \pm 0.4 (68)	6.1 \pm 0.4 (81)
4 : Male	9.3 \pm 1.1 (58)	9.4 \pm 0.9 (70)	10.2 \pm 0.7 (58)	9.6 \pm 1.4 (56)
Female	8.9 \pm 1.0 (58)	9.0 \pm 0.8 (67)	9.7 \pm 0.7 (67)	9.1 \pm 1.5 (80)

() : No. of pups (F1)

Not significantly different from the control group by Dunnet's type test / Dunnet's test

Table 13 Gross pathological findings in pups (F1) at Day 4 after birth

Study No. : SBL75-31

Dose (mg/kg)	Control	2.5	25	250
No. of dams (F0)	9	10	10	10
No. of pups (F1)	126	137	125	136
External findings				
Malformations				
Mean frequencies (%)	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]
Visceral findings				
Malformations				
Mean frequencies (%)	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]

(*) : Litter - basis analysis

[]:No. of pups with malformations

Not significantly different from control.

18-3. 2,4-ジ-tert-ブチル-6-(5-クロロ-2H-1,2,3-ベンゾトリアゾール-2-イル)フェノールの催奇形性試験

Title: Evaluation of Developmental Toxicity of Ultraviolet Absorber

2-(3',5'-Di-tert-butyl-2'-hydroxyphenyl)-5-chlorobenzotriazole in Rats

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Keywords Developmental toxicity, UV absorber, Benzotriazole, Rat

Running head: *Developmental Toxicity of UV Absorber*

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ABSTRACT

2-(3',5'-Di-tert-butyl-2'-hydroxyphenyl)-5-chlorobenzotriazole (DBHCB) is widely used as a UV absorber. In this study, the developmental toxicity of DBHCB was evaluated in rats. Pregnant rats were given DBHCB at 0, 62.5, 250 or 1000 mg/kg/day by gavage on days 5-19 of pregnancy. No deaths were observed in the pregnant rats of any group. No effect of DBHCB on the general conditions, body weight gain or feed consumption was observed in the pregnant rats. There were no changes in the ovarian weight, gravid uterine weight or necropsy findings in the maternal rats of the DBHCB-treated groups. No significant effects of DBHCB were found in the number of corpora lutea, implantations, live fetuses, resorptions or dead fetuses, incidence of pre- or postimplantation embryonic loss, viability of fetuses, fetal weight, or sex ratio of live fetuses. No significant difference in the incidence of fetuses with malformations or variations or degree of ossification was detected between the DBHCB-treated and control groups.

INTRODUCTION

2-(3',5'-Di-tert-butyl-2'-hydroxyphenyl)-5-chlorobenzotriazole (CAS No. 3864 99-1; DBHCB) is slightly yellowish powder, stable under ordinary conditions and insoluble in water. Its melting point is 154-158 °C, and its specific gravity is 1.26. This chemical provides effective light stabilization and prevents the yellowing and degradation of polymers such as polypropylene, high density polyethylene, unsaturated polyester, styrene-based thermoplastics elastomer, polyamide and impact polystyrene and is used as UV absorber (Chemical Land21, 2005). The finished polymers, which contained only at levels not to exceed 0.5% by weight of polyethylene phthalate polymers complying with 21 CFR 177.1630 (FDA, 2005a), may be used in contact with some food types and used under certain conditions as described in 21 CFR 176.170 (FDA, 2000; 2005b). UV absorbers are used in food packages as plastic