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EFFECTS OF PIROCTONE OLAMINE SUBCUTANEOUSLY GIVEN DURING THE LAST THIRD OF GESTATION AND THE PERIOD OF LACTATION IN THE RATS

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Subcutaneous Administration of Piroctone Olamine to Rats during the Last Third of Gestation and the Period of Lactation

Summary

Piroctone Olamine (PO) was administered subcutaneously to rats (Sprague-Dawley) at daily doses of 500, 100 and 20 mg/kg (vehicle: 0.5 % CMC) during the last third of gestation and the period of lactation (from 17th day of gestation until 21st day after delivery) to study the effects on growth of new born pups, and the following results were obtained:

1. All administration groups and the control group showed signs of pain at each time of administration and minor swelling at the site of administration (dorsal area).

2. Regarding the body weights of dams, the weight increase of the 500 mg/kg group was slightly retarded, and the body weight gains of all administration groups were depressed during pregnancy. No effect was observed during the lactation period.

   The feed intake decreased in each administration group at the end of pregnancy, but no change was observed during lactation.

3. No effect of the compound was observed on: body weights of dams at the weaning period, the pups at the delivery, the feed-intake and body weight of new-born pups, the general differenciation, the function test, the open field test and the learning test.

4. Regarding the organ weights of 8 weeks old F_1 pups, the weights of the heart, the lung, the liver, the kidneys and the adrenal in the 500 mg/kg male group and those of the heart, the lung, the liver and the kidneys in the 500 mg/kg female group respectively decreased.

5. No effect of the compound was observed in the following: skeleton examination of 8 weeks old pups, the generative test, the weights of pregnant rats, the feed-intake, the findings in F_1 dams and F_2 pups, the weights of organs at laparotomy and the organ weights of 18 weeks old males.

Summary

Effects of Piroctone Olamine Subcutaneously Given during the Last Third of Gestation and the Period of Lactation in the Rat

Piroctone Olamine (PO) was subcutaneously given at 500, 100 and 20 mg/kg/day to female rats during the last third of gestation and lactation period, and its effects on the dams and offspring were investigated.

(1) Dams: The animals in all the groups including the control showed a sign of pain at each time of administration, and those in the treated groups had a protrusive injection site. At each treatment level, body weight gains were depressed during gestation but not affected during lactation and food consumption was normal during the study except that it was decreased at near term. No changes attributable to PO occurred in the weights of organs examined.

(2) Offspring: There were no PO-related abnormalities in the following: various parameters examined at birth, general differentiation, functions, open field behavious and learning ability. At 500 mg/kg/day the following organs from 8-week-old rats weighed less: the heart, lung, liver, kidney and adrenal in the males and the first 4 organs in the females. No PO-related changes were observed in the skeletons. Examinations of the F_1 offspring for their fertility revealed no abnormalities attributable to PO; normal were the copulation and conception rates, body weight, food consumption and organ weight of the F_1 dams, and various maternal (F_1) and fetal (F_2) parameters examined at cesarean section.

Subcutaneous Administration of Piroctone Olamine to Rats

during the Last Third of Gestation and the Period of Lactation

I. Abstract

Piroctone Olamine was subcutaneously administered to rats at the daily doses of 500, 100 and 20 mg/kg during the last third of gestation and the period lactation to study the effects on growth of new born pups, and the following results were obtained.

1) All administration groups and the control group were in pain at the time of administration and showed minor swelling at the site of administration.

2) Regarding the body weights of dams, the weight increase of the 500 mg/kg group was slightly controlled, and the body weights of all administration groups decreased during pregnancy. No effect was observed during lactation.

   The volume of feed intake decreased in each administration group at the end of pregnancy, but no change was observed during lactation.

3) No effect of the compound was observed in the following; body weights of dams at the weaning period, the pups at the delivery at the delivery, the feed-intake and body weight of new-born pups, the general differenciation, the function test, the open field test and the learning test.

4) Regarding the organ weights of 8 weeks old F_1 pups, the weights of the heart, the lung, the liver, the kidneys and the adrenals in the 500 mg/kg male group and those of the heart, the lung, the liver and the kidneys in the 500 mg/kg female group respectively decreased.

5) No effect of the compound was ovserved in the following; skeleton examination of 8 weeks old pups, the generative test, the weights of pregnant rats, the feed-intake, the findings in F_1 dams and F_2 pups, the weights of organs at laparotomy and the organ weights of 18 weeks old males.

SEGMENT III

図 1 Body weight changes of F_0 Females

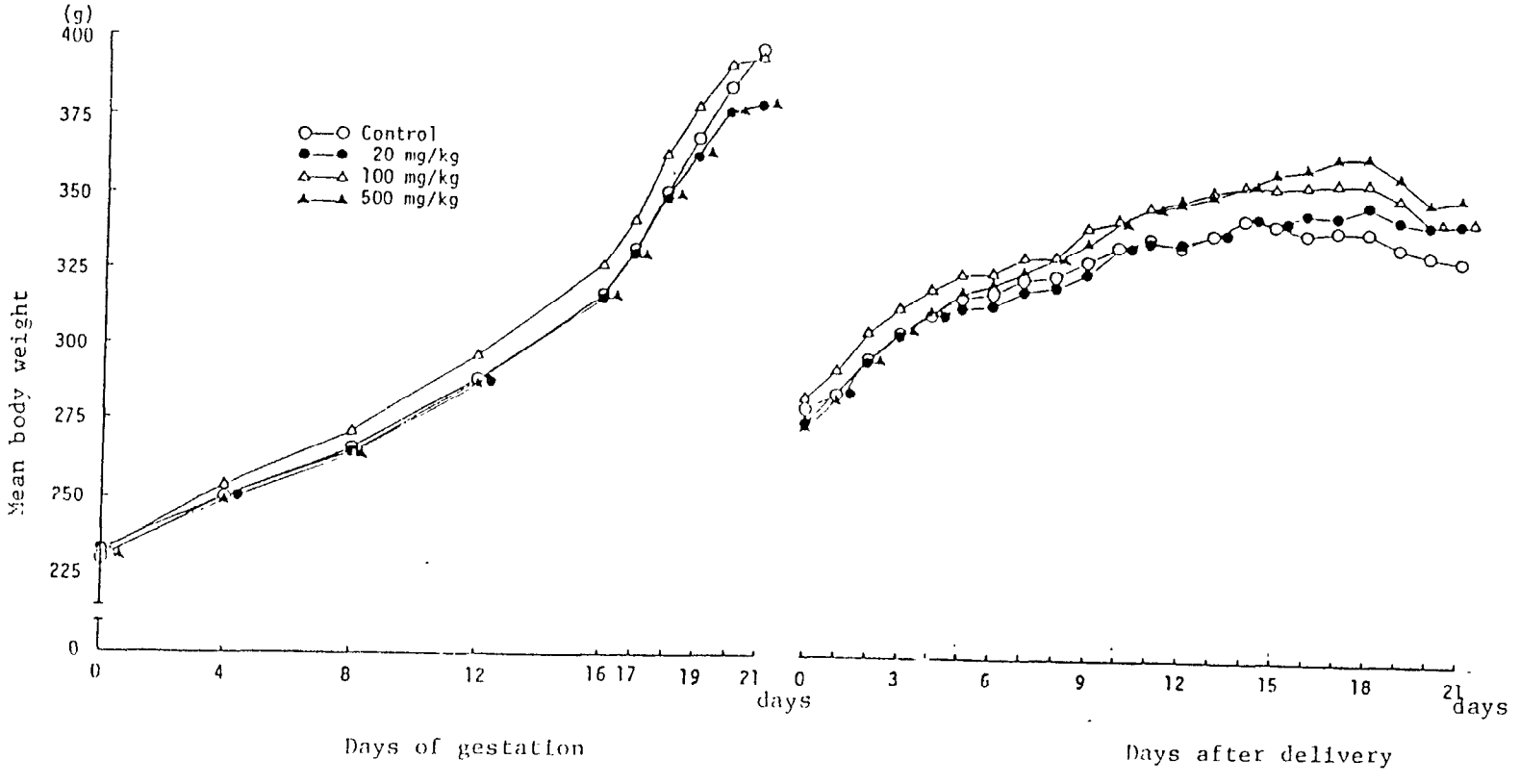


図 2　Food consumption of Fo Females

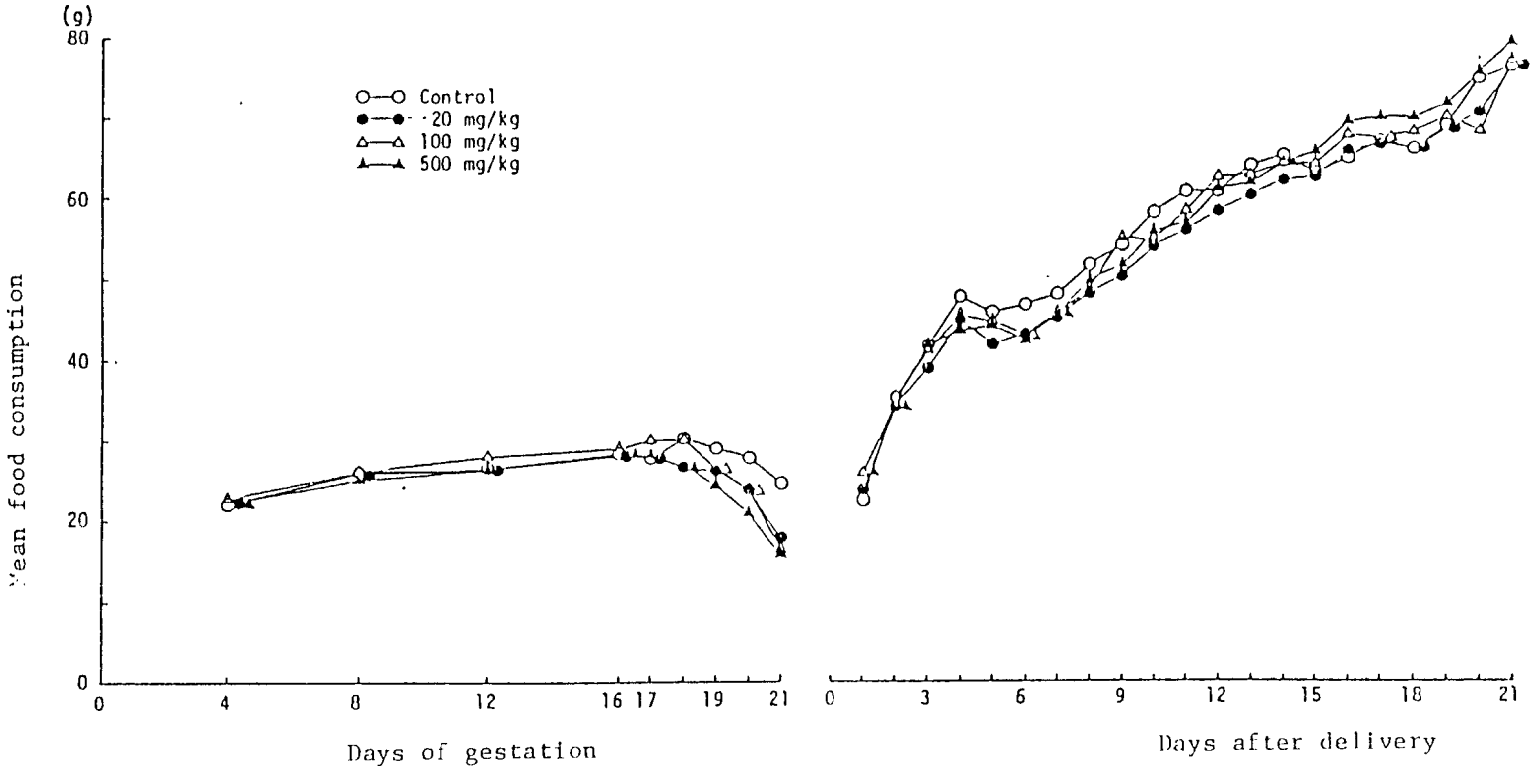


図 3　Body weight changes of F_1 male offspring

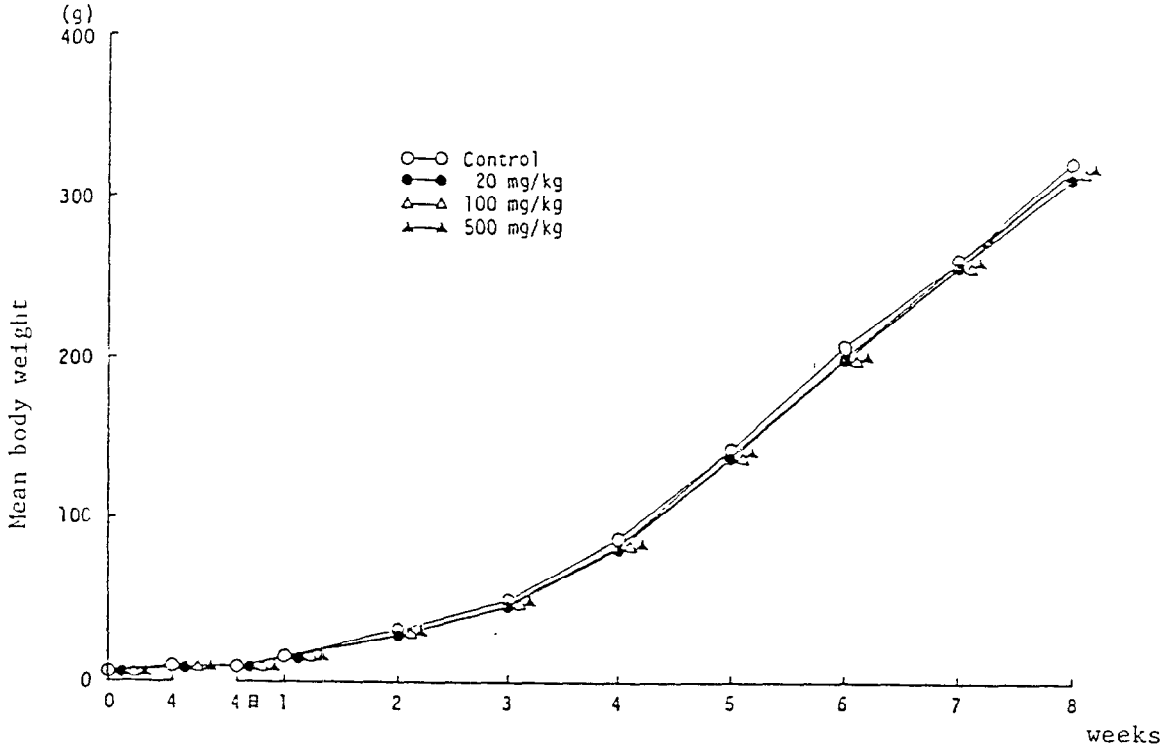


図 4　Body weight changes of F_1 female offspring

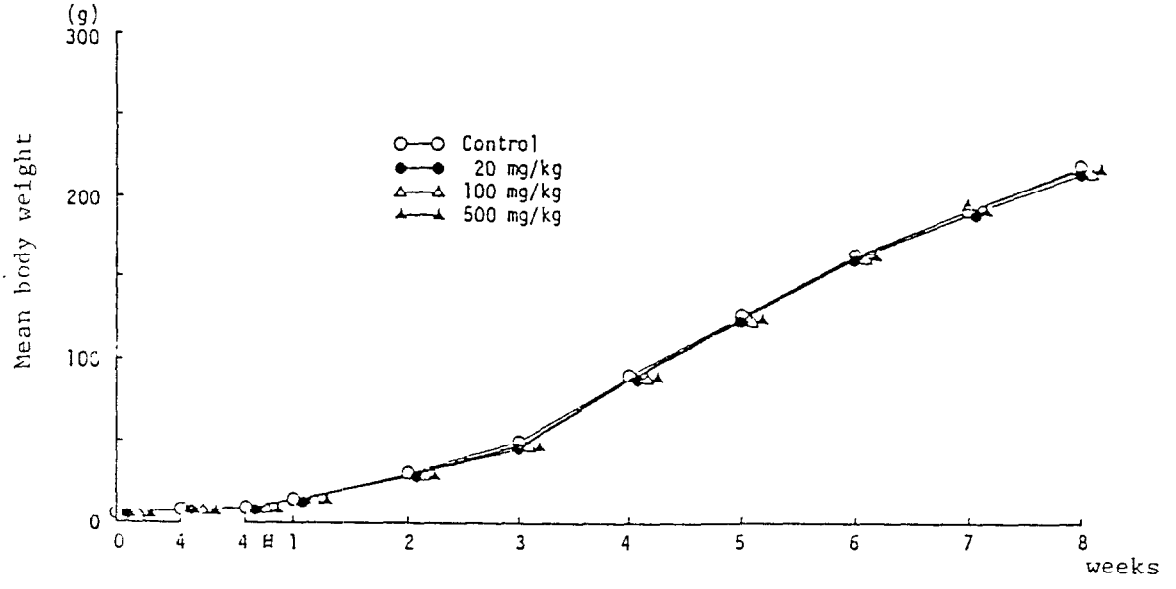


図 5　Food consumption of F_1 offspring

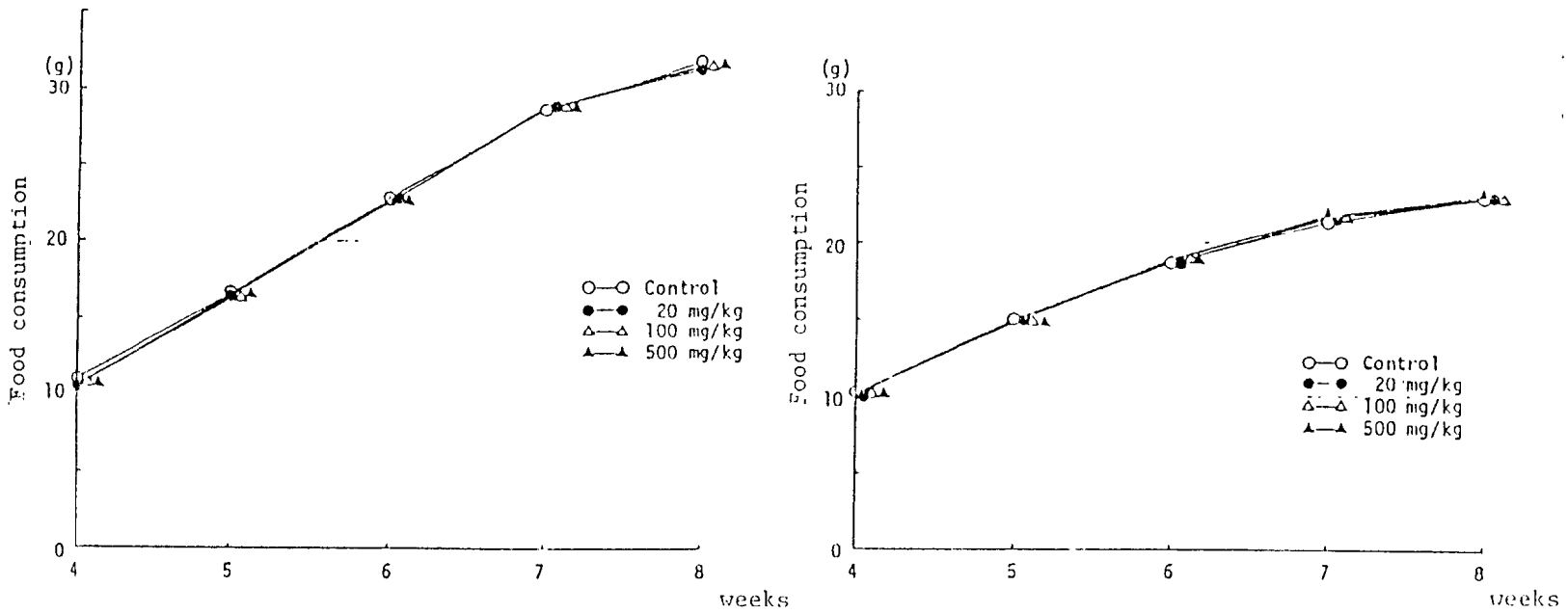
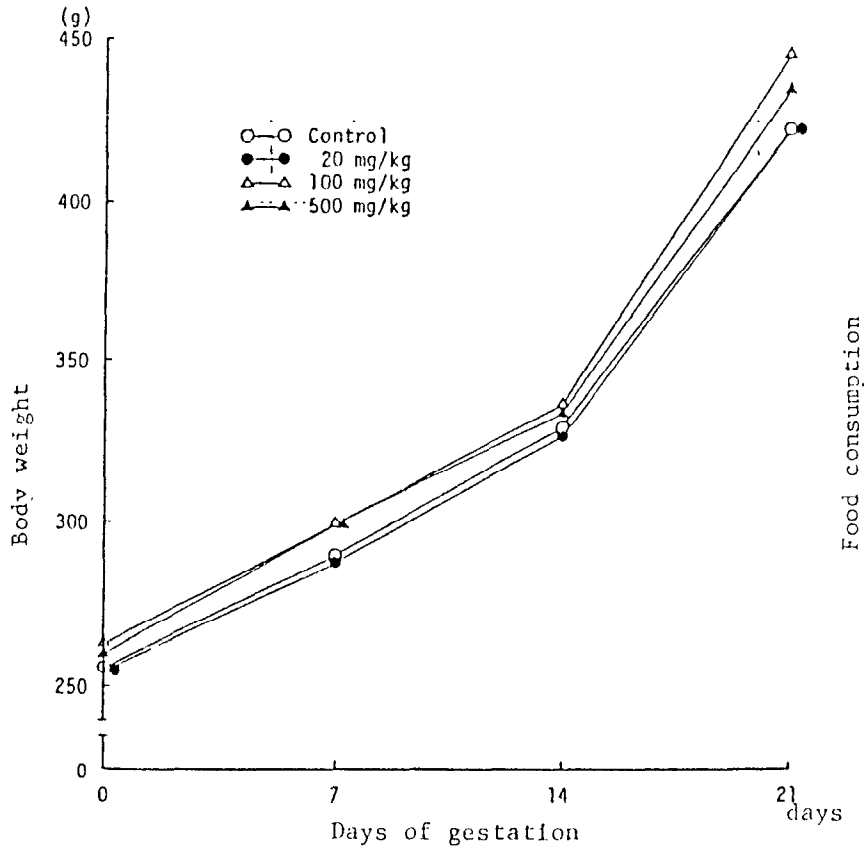


図 6　Body weight changes and food consumption of F_1 dams



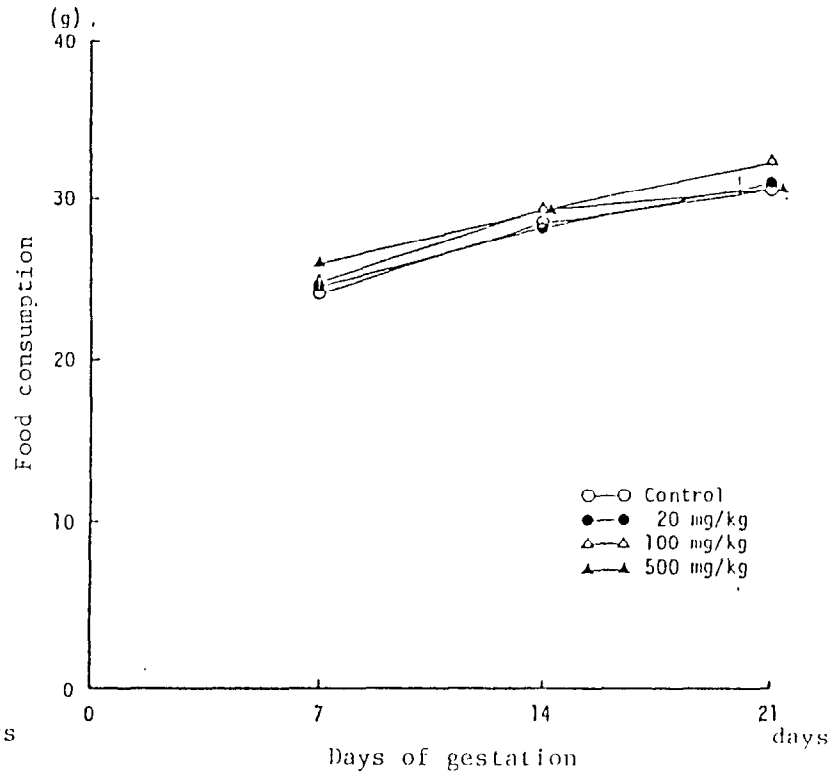


表 1　Body weight changes of F_0 pregnant females

Group	No. of Females	0	4	8	12	16	17	18	19	20	21 日	Gain of body weights 21-0	Gain of body weights 21-17
		days											
Control	22	229.8 ±3.16	250.1 ±3.40	266.0 ±3.16	287.9 ±3.62	317.4 ±3.76	332.5 ±4.13	351.4 ±4.07	368.5 ±4.62	384.9 ±4.58	397.1 ±5.03	167.3 ±4.17	64.6 ±2.08
20 mg/kg	23	232.8 ±3.57	250.2 ±3.83	264.5 ±3.83	287.5 ±4.30	316.3 ±4.63	331.0 ±4.77	349.0 ±5.10	362.8 ±5.39	377.2 ±6.01	379.7 ±7.08	** 147.0 ±5.72	*** 48.8 ±3.35
100 mg/kg	24	231.7 ±4.64	253.5 ±4.48	271.3 ±4.52	296.9 ±4.68	327.2 ±5.16	342.1 ±5.44	363.2 ±5.71	378.3 ±6.15	392.2 ±6.60	394.0 ±6.46	162.3 ±3.83	*** 51.9 ±2.03
500 mg/kg	24	230.4 ±2.80	248.5 ±2.57	263.4 ±2.71	286.9 ±3.07	316.7 ±3.76	330.5 ±4.10	350.4 ±4.51	364.1 ±5.01	377.8 ±5.41	* 380.0 ±5.30	** 149.6 ±4.08	*** 49.5 ±2.62

Mean(g) ±S.E.　　* P<0.05　　** P<0.01　　*** P<0.001

表 2　Food consumption of F_0 pregnant females

Group	No. of females	4	8	12	16	17	18	19	20	21 days
Control	22	22.11 ±0.59	25.91 ±0.42	26.55 ±0.46	28.36 ±0.57	27.5 ±1.25	30.3 ±0.76	28.9 ±1.09	27.4 ±0.71	24.5 ±0.93
20 mg/kg	23	22.30 ±0.49	25.52 ±0.59	26.30 ±0.62	27.89 ±0.61	27.7 ±0.76	** 26.5 ±0.87	* 26.1 ±0.85	** 23.6 ±1.13	*** 17.7 ±1.28
100 mg/kg	24	22.77 ±0.37	26.10 ±0.47	27.81 ±0.46	28.94 ±0.48	29.8 ±0.93	29.8 ±1.16	* 26.3 ±0.74	*** 23.4 ±0.74	*** 16.5 ±1.23
500 mg/kg	24	22.08 ±0.41	25.15 ±0.34	26.31 ±0.42	28.23 ±0.46	28.1 ±0.78	** 26.6 ±0.93	*** 24.2 ±0.79	*** 21.0 ±0.72	*** 15.8 ±1.35

Mean(g/day) ±S.E.　　* P<0.05　　** P<0.01　　*** P<0.001

表 3　Body weight changes during lactation

Group	No.of Females	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15 days
Control	22	279.9 ±4.76	284.9 ±4.60	297.0 ±3.97	305.5 ±4.41	311.3 ±4.67	316.9 ±4.46	318.8 ±4.46	323.0 ±4.45	324.8 ±4.37	329.7 ±4.54	334.7 ±4.17	337.4 ±4.33	334.7 ±4.38	338.7 ±4.85	343.7 ±4.99	342.1 ±4.74
20 mg/kg	23	275.3 ±5.11	285.0 ±4.95	295.7 ±4.82	304.2 ±5.18	310.4 ±4.99	313.5 ±4.87	314.2 ±4.68	319.0 ±4.67	321.0 ±4.12	325.5 ±4.31	334.0 ±4.86	336.0 ±5.09	335.9 ±4.41	339.1 ±4.90	344.2 ±4.53	343.0 ±4.82
100 mg/kg	24	282.9 ±5.14	292.6 ±5.02	305.8 ±5.15	313.1 ±4.85	319.2 ±4.80	324.5 ±5.18	325.7 ±4.84	330.3 ±5.38	331.2 ±5.23	340.9 ±4.89	343.1 ±5.08	347.6 ±5.17	350.5* ±4.93	353.3 ±5.66	355.2 ±5.88	354.8 ±6.43
500 mg/kg	24	274.0 ±2.35	282.7 ±3.19	296.7 ±3.36	306.3 ±3.85	311.9 ±3.95	318.8 ±4.13	322.1 ±3.76	326.6 ±4.05	330.1 ±4.20	335.8 ±4.60	342.5 ±4.32	347.3 ±4.31	348.8* ±4.42	352.4 ±4.90	355.2 ±5.59	359.3* ±5.00

Group	16	17	18	19	20	21 days	Gain of body weights 21-0 days
Control	339.2 ±5.42	340.5 ±4.88	340.2 ±5.12	335.4 ±5.33	332.7 ±4.56	331.4 ±5.23	51.5 ±3.54
20 mg/kg	345.8 ±4.57	345.2 ±4.84	348.6 ±4.33	343.9 ±4.35	342.8 ±4.36	343.5 ±4.23	68.2** ±4.79
100 mg/kg	355.9 ±6.24	356.7 ±6.33	356.8* ±5.98	351.8* ±5.89	343.8 ±5.14	344.4 ±5.03	61.5* ±3.48
500 mg/kg	360.9** ±4.42	364.2*** ±4.32	364.7** ±4.73	358.3** ±4.57	350.1* ±4.70	352.1** ±4.63	78.1*** ±4.05

Mean(g) ±S.E.　　* P<0.05　** P<0.01　*** P<0.001

表4　Food consumption during lactation

Group	No.of Females	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19 days
Control	22	22.5 ±0.97	35.2 ±1.03	41.5 ±1.35	47.5 ±1.45	45.6 ±1.31	46.6 ±1.07	47.9 ±1.16	51.5 ±1.32	54.0 ±1.33	58.0 ±1.25	60.5 ±1.13	60.6 ±0.92	63.6 ±1.29	64.9 ±1.69	62.7 ±1.51	64.7 ±1.64	66.8 ±1.63	65.7 ±1.15	68.7 ±0.97
20 mg/kg	23	23.6 ±0.96	34.2 ±1.29	38.9 ±1.64	44.7 ±1.62	41.7* ±1.01	42.9* ±1.09	45.0 ±1.41	48.0 ±1.65	51.1 ±1.60	53.7* ±1.66	55.7* ±1.85	58.3 ±1.77	60.1 ±2.09	61.8 ±1.88	62.4 ±1.93	65.5 ±1.79	66.4 ±1.97	65.9 ±2.18	68.5 ±2.37
100 mg/kg	24	25.5* ±0.84	35.4 ±0.92	41.0 ±1.14	45.4 ±1.15	44.5 ±1.38	42.8* ±0.99	45.7 ±1.23	48.7 ±1.37	54.9 ±1.33	54.7 ±1.54	58.2 ±1.71	62.3 ±1.57	62.5 ±1.53	63.9 ±1.13	63.7 ±1.99	67.6 ±1.84	67.2 ±1.15	68.0 ±1.58	69.8 ±1.46
500 mg/kg	24	25.7 ±1.72	34.3 ±1.24	41.5 ±1.14	43.4 ±1.58	43.8 ±1.19	42.3 ±1.15	45.4 ±0.86	49.7 ±1.50	51.5 ±1.62	55.7 ±1.60	56.8 ±1.38	60.8 ±1.73	61.5 ±1.42	63.9 ±1.81	65.4 ±1.56	69.3* ±1.38	69.9 ±1.24	69.8* ±1.43	71.6 ±1.60

20	21 days
74.8 ±1.70	76.4 ±1.63
70.5 ±2.20	76.4 ±2.59
68.0* ±1.86	77.1 ±1.97
75.6 ±1.46	79.4 ±1.85

Mean(g/day) ±S.E.

* P<0.05

表5 Weight of organs of dams after lactation

Group	No.of Females	Final body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney(g) right	Kidney(g) left	Adrenal(mg) right	Adrenal(mg) left	Ovary (mg) right	Ovary (mg) left	Uterus (g)	Bladder (g)
Control	22	331.4 ±5.23	1.86 ±0.02	16.0 ±0.64	20.0 ±1.32	168.7 ±9.29	1.11 ±0.03	1.39 ±0.05	17.93 ±0.33	0.63 ±0.03	0.75 ±0.03	1.25 ±0.03	1.21 ±0.03	43.6 ±2.22	49.8 ±2.52	50.6 ±2.71	55.0 ±3.01	0.39 ±0.03	0.13 ±0.004
20 mg/kg	23	343.5 ±4.23	1.84 ±0.02	17.1 ±0.56	20.7 ±1.26	* 132.0 ±10.97	1.12 ±0.03	1.42 ±0.03	18.84 ±0.32	*** 0.82 ±0.04	0.75 ±0.03	1.32 ±0.02	1.26 ±0.03	46.0 ±1.17	50.3 ±1.20	53.4 ±2.14	51.9 ±3.01	0.37 ±0.02	0.13 ±0.004
100 mg/kg	24	344.4 ±5.03	1.87 ±0.02	* 17.9 ±0.50	21.8 ±1.35	157.0 ±7.87	1.13 ±0.02	* 1.52 ±0.03	18.38 ±0.31	*** 0.83 ±0.03	0.73 ±0.04	* 1.36 ±0.03	1.32 ±0.05	47.1 ±1.21	52.1 ±1.55	** 63.8 ±3.77	56.4 ±2.85	0.41 ±0.02	0.20 ±0.04
500 mg/kg	24	** 352.1 ±4.63	1.88 ±0.02	17.5 ±0.63	21.9 ±0.90	148.0 ±10.05	1.15 ±0.02	1.50 ±0.03	18.88 ±0.38	* 0.72 ±0.02	0.76 ±0.03	1.32 ±0.02	* 1.30 ±0.02	48.4 ±1.06	54.0 ±1.64	56.8 ±2.56	52.3 ±2.79	0.38 ±0.03	** 0.15 ±0.004
			(g%)	(mg%)	(mg%)	(mg%)	(g%)	(g%)	(g%)	(g%)	(g%)	(g%)	(g%)	(mg%)	(mg%)	(mg%)	(mg%)	(g%)	(g%)
			0.56 ±0.01	4.85 ±0.18	6.05 ±0.39	51.17 ±2.96	0.34 ±0.01	0.42 ±0.01	5.41 ±0.06	0.19 ±0.01	0.22 ±0.01	0.38 ±0.01	0.36 ±0.01	13.20 ±0.66	15.02 ±0.71	15.30 ±0.82	16.55 ±0.83	0.12 ±0.01	0.04 ±0.001
			* 0.54 ±0.01	4.98 ±0.15	6.05 ±0.41	** 38.46 ±3.19	0.33 ±0.01	0.41 ±0.01	5.49 ±0.08	*** 0.24 ±0.01	0.22 ±0.01	0.39 ±0.01	0.37 ±0.01	13.40 ±0.34	14.64 ±0.32	15.64 ±0.68	15.15 ±0.89	0.11 ±0.01	0.04 ±0.002
			0.54 ±0.01	5.22 ±0.15	6.33 ±0.39	45.67 ±2.33	0.33 ±0.01	0.44 ±0.01	5.35 ±0.08	*** 0.24 ±0.01	0.22 ±0.01	0.40 ±0.01	0.39 ±0.02	13.72 ±0.37	15.18 ±0.46	* 18.39 ±0.98	16.34 ±0.77	0.12 ±0.01	0.06 ±0.01
			* 0.54 ±0.01	4.99 ±0.18	6.23 ±0.24	* 40.61 ±2.85	0.33 ±0.01	0.43 ±0.01	5.38 ±0.11	0.20 ±0.01	0.22 ±0.01	0.38 ±0.01	0.37 ±0.01	13.83 ±0.39	15.40 ±0.51	16.16 ±0.75	14.85 ±0.78	0.11 ±0.01	0.04 ±0.001

Mean ±S.E. * P<0.05 ** P<0.01 *** P<0.001

表6 Summary of delivery

Group	Control	20 mg/kg	100 mg/kg	500 mg/kg
No. of Dams	22	23	24	24
No. of Dams Delivered	22	23	24	24
Duration of Gestation Mean ± S.E.	22.0 ± 0	22.0 ± 0	22.0 ± 0	22.0 ± 0
Total No. of Implantation	348	351	392	381
Mean ± S.E.	15.8 ± 0.38	15.3 ± 0.37	16.3 ± 0.44	15.9 ± 0.37
No. of Pups Delivered	324(93.1%)	335(95.4%)	359(91.6%)	351(92.1%)
Mean ± S.E.	14.7 ± 0.51	14.6 ± 0.35	15.0 ± 0.59	14.6 ± 0.54
No. of Live-born	316(97.5%)	332(99.1%)	352(98.1%)	350(99.7%)
Mean ± S.E.	14.4 ± 0.51	14.4 ± 0.37	14.7 ± 0.64	14.6 ± 0.54
No. of Male Living Pups	142(44.9%)	172(51.8%)	179(50.9%)	179(51.1%)
Mean ± S.E.	6.5 ± 0.41	7.5 ± 0.29	7.5 ± 0.52	7.5 ± 0.50
No. of Female Living Pups	174(55.1%)	160(48.2%)	173(49.1%)	171(48.9%)
Mean ± S.E.	7.9 ± 0.36	7.0 ± 0.37	7.2 ± 0.38	7.1 ± 0.57
No. of Still-born	8(2.5%)	3(0.9%)	7(1.9%)	1(0.3%)
No. of Pups with External Abnormality	0	0	0	0
Body Weight of Living Pups				
Male Mean ± S.E.	5.80 ± 0.07	5.59 ± 0.09	5.70 ± 0.08	5.77 ± 0.07
Female Mean ± S.E.	5.55 ± 0.05	5.33 ± 0.10	5.43 ± 0.09	5.41 ± 0.05

表7　No. of live-born

Group	No. of offspring	0	1	2	3	Before thinning 4 days	After thinning 4 days	5	6	7	8	9	10	11	12	13	14 days
Control	a	316	311	309	308	308	176	176	176	176	176	176	176	175	175	175	175
	b	-	98.4	97.8	97.5	97.5	-	100.0	100.0	100.0	100.0	100.0	100.0	99.4	99.4	99.4	99.4
	c	14.4	14.1	14.0	14.0	14.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
	d	±0.51	±0.51	±0.50	±0.50	±0.50	±0	±0	±0	±0	±0	±0	±0	±0.05	±0.05	±0.05	±0.05
20 mg/kg	a	332	326	321	316	315	178	178	177	177	177	177	177	177	177	176	176
	b	-	98.2	96.7	95.2	94.9	-	100.0	99.4	99.4	99.4	99.4	99.4	99.4	99.4	98.9	98.9
	c	14.4	14.2	14.0	13.7	13.7	7.7	7.7	7.7	7.7	7.7	7.7	7.7	7.7	7.7	7.7	7.7
	d	±0.37	±0.43	±0.50	±0.59	±0.63	±0.26	±0.26	±0.26	±0.26	±0.26	±0.26	±0.26	±0.26	±0.26	±0.26	±0.26
100 mg/kg	a	352	350	343	337	334	190	190	190	190	190	190	190	190	190	190	190
	b	-	99.4	97.4	95.7	94.9	-	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	c	14.7	14.6	14.3	14.0	13.9	7.9	7.9	7.9	7.9	7.9	7.9	7.9	7.9	7.9	7.9	7.9
	d	±0.64	±0.63	±0.66	±0.64	±0.65	±0.06	±0.06	±0.06	±0.06	±0.06	±0.06	±0.06	±0.06	±0.06	±0.06	±0.06
500 mg/kg	a	350	346	343	340	338	190	190	190	190	189	189	187	187	186	186	186
	b	-	98.9	98.0	97.1	96.6	-	100.0	100.0	100.0	99.5	99.5	98.4	98.4	97.9	97.9	97.9
	c	14.6	14.4	14.3	14.2	14.1	7.9	7.9	7.9	7.9	7.9	7.9	7.8	7.8	7.8	7.8	7.8
	d	±0.54	±0.54	±0.55	±0.53	±0.51	±0.08	±0.08	±0.08	±0.08	±0.09	±0.09	±0.12	±0.12	±0.12	±0.12	±0.12

a: Total No. of live-born　　b: Rate of live-born　　c: Mean　　d: ± S.E.

15	16	17	18	19	20	21 days	4	5	6	7	8 weeks
175 99.4 8.0 ±0.05	175 99.4 8.0 ±0.05	175 99.4 8.0 ±0.05	175 99.4 8.0 ±0.05	175 99.4 8.0 ±0.05	175 99.4 8.0 ±0.05	175 99.4 8.0 ±0.05	175 99.4 8.0 ±0.05	175 99.4 8.0 ±0.05	174 98.9 7.9 ±0.06	174 98.9 7.9 ±0.06	174 98.9 7.9 ±0.06
176 98.9 7.7 ±0.26	176 98.9 7.7 ±0.26	176 98.9 7.7 ±0.26	176 98.9 7.7 ±0.26	176 98.9 7.7 ±0.26	176 98.9 7.7 ±0.26	176 98.9 7.7 ±0.26	174 97.8 7.9 ±0.06	174 97.8 7.9 ±0.06	174 97.8 7.9 ±0.06	174 97.8 7.9 ±0.06	174 97.8 7.9 ±0.06
190 100.0 7.9 ±0.06	190 100.0 7.9 ±0.06	190 100.0 7.9 ±0.06	190 100.0 7.9 ±0.06	190 100.0 7.9 ±0.06	190 100.0 7.9 ±0.06	190 100.0 7.9 ±0.06	190 100.0 7.9 ±0.06	189 99.5 7.9 ±0.07	189 99.5 7.9 ±0.07	189 99.5 7.9 ±0.07	189 99.5 7.9 ±0.07
186 97.9 7.8 ±0.12	186 97.9 7.8 ±0.12	186 97.9 7.8 ±0.12	186 97.9 7.8 ±0.12	186 97.9 7.8 ±0.12	186 97.9 7.8 ±0.12	186 97.9 7.8 ±0.12	185 97.4 7.7 ±0.14	184 96.8 7.7 ±0.14	184 96.8 7.7 ±0.14	184 96.8 7.7 ±0.14	184 96.8 7.7 ±0.14

表 8　Gain of body weight of male pups

Group	No. of male	0	4	4	1	2	3	4	5	6	7	8 (weeks)	Gain of body weight 8-3 (weeks)	Gain of body weight 3-0 (weeks)
Control	22	5.80 ±0.07	9.13 ±0.22	9.33 ±0.23	15.51 ± 0.41	32.03 ±0.60	50.33 ±1.05	87.39 ±1.91	143.35 ±3.06	205.96 ±3.92	261.69 ±3.77	320.54 ±4.59	270.20 ±3.79	44.53 ±1.00
20mg/kg	23	5.59 ±0.09	8.67 ±0.19	9.09 ±0.22	14.48 ±0.40	28.88** ±0.82	46.28* ±1.10	81.90* ±1.43	137.23 ±2.08	197.75 ±2.72	255.42 ±3.09	310.23 ±4.00	263.11 ±3.52	40.69 ±1.03
100mg/kg	24	5.70 ±0.08	8.96 ±0.25	9.21 ±0.25	14.84 ±0.38	29.51** ±0.66	46.96* ±1.03	83.04 ±1.82	136.83 ±2.81	196.58 ±3.15	255.83 ±3.72	313.42 ±3.80	266.46 ±3.31	41.25* ±1.00
500mg/kg	24	5.77 ±0.07	9.02 ±0.19	9.28 ±0.19	15.16 ±0.29	30.64 ±0.49	48.89 ±0.77	84.33 ±1.43	140.18 ±2.35	198.76 ±3.48	258.60 ±3.61	317.25 ±4.26	268.36 ±3.99	43.12 ±0.75

Mean(g)
±S.E.

* P<0.05　　** P<0.01

表 9　Gain body weight of female pups

Group	No. of females	0	4	4	1	2	3	4	5	6	7	8 weeks	Gain of body weight 8-3	3-0 weeks
Control	22	5.55 ±0.05	8.62 ±0.22	9.06 ±0.18	14.98 ±0.31	31.30 ±0.48	49.23 ±0.88	81.62 ±1.57	127.04 ±1.77	164.06 ±1.98	191.77 ±1.41	217.93 ±1.56	168.70 ±1.44	43.68 ±0.86
20mg/kg	23	5.33 ±0.10	8.17 ±0.26	8.54 ±0.27	13.91 ±0.47	27.96** ±0.98	45.18* ±1.37	75.84* ±1.59	123.45 ±2.25	160.34 ±2.35	188.02 ±2.29	213.42 ±2.49	167.09 ±2.10	39.85* ±1.29
100mg/kg	24	5.43 ±0.09	8.55 ±0.27	8.79 ±0.26	14.23 ±0.36	28.47** ±0.76	46.23* ±0.94	77.69 ±1.42	122.69 ±2.27	161.43 ±2.20	189.96 ±2.66	213.50 ±2.32	167.27 ±1.83	40.80* ±0.90
500mg/kg	24	5.41 ±0.05	8.40 ±0.16	8.64 ±0.17	14.31 ±0.30	28.90*** ±0.47	47.05 ±0.79	78.99 ±1.28	125.05 ±1.64	162.53 ±1.87	190.35 ±2.23	216.50 ±2.98	169.45 ±2.52	41.62 ±0.80

Mean(g)
±S.E.

* P<0.05　　** P<0.01　　*** P<0.001

表10　Food consumption of pups

Group	No. of pups	weeks 4	5	6	7	8	weeks 4	5	6	7	8
Control	22	11.00 ±0.23	16.68 ±0.36	22.81 ±0.46	28.70 ±0.39	31.99 ±0.44	10.29 ±0.19	15.10 ±0.22	18.65 ±0.28	21.40 ±0.27	22.82 ±0.35
20 mg/kg	22	10.46 ±0.20	16.41 ±0.29	22.75 ±0.38	28.95 ±0.37	31.38 ±0.37	9.88 ±0.22	14.96 ±0.28	18.61 ±0.28	21.64 ±0.35	22.96 ±0.30
100 mg/kg	24	10.67 ±0.23	16.28 ±0.29	22.55 ±0.35	28.83 ±0.37	31.58 ±0.37	10.19 ±0.18	14.95 ±0.25	18.93 ±0.27	21.66 ±0.32	22.88 ±0.37
500 mg/kg	24	10.60 ±0.22	16.54 ±0.22	22.67 ±0.41	28.82 ±0.35	31.64 ±0.45	10.20 ±0.18	14.89 ±0.21	18.81 ±0.23	21.91 ±0.27	23.15 ±0.33

Mean(g)
±S.E.

表11 Summary of postnatal development of F_1 offspring after weaning

Group	Date of Examination	Control	20 mg/kg	100 mg/kg	500 mg/kg
Opening of ear auricles	5日	176(100.0%)	176(100.0%)	190(100.0%)	190(100.0%)
Emergence of abdominal hair	10日	176(100.0%)	176(99.4%)	190(100.0%)	187(100.0%)
	11日		177(100.0%)		
Eruption of upper incisors	15日	175(100.0%)	175(99.4%)	190(100.0%)	186(100.0%)
	16日		176(100.0%)		
Opening of eyelids	15日	175(100.0%)	174(98.9%)	190(100.0%)	186(100.0%)
	16日		175(99.4)		
	17日		176(100.0%)		
Descent of testis	21日	85(100.0%)	89(98.9%)	94(100.0%)	95(100.0%)
			89(100.0%)		
Ocening of vagina	35日	90(100.0%)	85(100.0%)	95(100.0%)	91(100.0%)

表12 Summary of abnormalities in function

Group	Control	20 mg/kg	100 mg/kg	500 mg/kg
No. of offspring examined	175	176	190	186
No. of offspring with abnormality	0	2	0	0
Spontaneous activity	0	0	0	0
Gait	0	1(0.6%)	0	0
Posture	0	0	0	0
Pinna reflex	0	1(0.6%)	0	0
Corneal reflex	0	0	0	0
Righting reflex	0	0	0	0
Pain reflex	0	0	0	0

表13　Open-field behaviour of F_1 offspring

Male Pups

Group	Control	20 mg/kg	100 mg/kg	500 mg/kg
No. of F_1	22	22	24	24
Ambulation				
Mean ± S.E.	46.6 ± 4.81	58.6 ± 4.04	53.0 ± 4.05	51.6 ± 3.43
Rearing				
平均値 ± 標準誤差	4.6 ± 0.85	4.9 ± 0.63	4.9 ± 0.74	4.0 ± 0.61
Grooming				
平均値 ± 標準誤差	2.0 ± 0.25	1.0 ± 0.19	1.8 ± 0.35	1.9 ± 0.21
Urination				
平均値 ± 標準誤差	0.5 ± 0.13	0.7 ± 0.22	0.4 ± 0.18	0.3 ± 0.09
Defecation				
平均値 ± 標準誤差	0.8 ± 0.25	1.5 ± 0.40	0.8 ± 0.30	1.1 ± 0.37

Female Pups

Group	Control	20 mg/kg	100 mg/kg	500 mg/kg
No. of F_1	22	22	24	24
Ambulation				
平均値 ± 標準誤差	56.7 ± 4.38	65.0 ± 3.90	56.0 ± 2.90	50.7 ± 4.35
Rearing				
平均値 ± 標準誤差	6.3 ± 1.02	5.1 ± 0.87	4.8 ± 0.76	4.6 ± 0.78
Grooming				
平均値 ± 標準誤差	1.6 ± 0.24	1.5 ± 0.25	1.4 ± 0.19	1.6 ± 0.22
Urination				
平均値 ± 標準誤差	0.4 ± 0.12	0.6 ± 0.14	0.5 ± 0.10	0.3 ± 0.09
Defecation				
平均値 ± 標準誤差	0.2 ± 0.13	1.3 ± 0.37	0.3 ± 0.13	0.6 ± 0.29

表14　Water T-maze performance of F_1 offspring

Male pups

Group		Control	20 mg/kg	100 mg/kg	500 mg/kg
No. of F_1		22	22	24	24
1 day					
No. of errors	Mean ± S.E.	17.9 ± 3.09	15.5 ± 3.37	16.5 ± 2.02	19.5 ± 3.72
Time required (minutes)	平均値 ± 標準誤差	100.19 ± 14.76	99.82 ± 20.67	93.56 ± 12.24	102.33 ± 15.38
2 days					
No. of errors	平均値 ± 標準誤差	16.7 ± 2.88	15.9 ± 3.95	15.3 ± 2.38	14.8 ± 3.66
Time required (minutes)	平均値 ± 標準誤差	84.71 ± 10.67	107.08 ± 29.64	85.03 ± 11.11	73.72 ± 15.16
3 days					
No. of errors	平均値 ± 標準誤差	15.7 ± 3.05	12.2 ± 2.07	14.4 ± 2.13	10.4 ± 1.80
Time required (minutes)	平均値 ± 標準誤差	78.61 ± 16.49	77.36 ± 13.08	77.16 ± 8.60	59.42 ± 7.77

Female pups

Group		Control	20 mg/kg	100 mg/kg	500 mg/kg
No. of F_1		22	22	24	24
1 day					
No. of errors	Mean ± S.E.	19.2 ± 2.77	21.7 ± 3.48	14.7 ± 1.95	20.7 ± 2.75
Time required (minutes)	平均値 ± 標準誤差	102.36 ± 11.16	166.21 ± 44.51	87.41 ± 10.88	124.54 ± 19.52
2 days					
No. of errors	平均値 ± 標準誤差	13.4 ± 2.73	16.8 ± 3.10	10.5 ± 1.71	25.3 ± 6.12
Time required (minutes)	平均値 ± 標準誤差	79.72 ± 12.61	136.82 ± 44.12	56.45 ± 6.04	126.84 ± 26.44
3 days					
No. of errors	平均値 ± 標準誤差	10.6 ± 2.05	11.9 ± 2.43	12.1 ± 1.58	8.2 ± 1.36
Time required (minutes)	平均値 ± 標準誤差	59.16 ± 8.75	74.48 ± 14.14	66.94 ± 6.96	58.22 ± 8.96

表15 Weight of organs - 8 weeks' F_1 male rats

Group	No. of females	Final body weight (g)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) right	Kidney (g) left	Adrenal (mg) right	Adrenal (mg) left	Spermary (g) right	Spermary (g) left	Prostate (mg)	Seminal vesicle (g)	Bladder (g)
Control	41	319.5 ±4.33	21.1 ±0.82	679.9 ±20.98	1.11 ±0.02	1.55 ±0.03	19.13 ±0.42	0.83 ±0.02	0.62 ±0.02	1.45 ±0.02	1.42 ±0.02	28.3 ±0.88	28.7 ±0.70	1.50 ±0.03	1.49 ±0.02	0.34 ±0.01	0.55 ±0.02	0.11 ±0.003
20 mg/kg	45	309.4 ±3.22	19.7 ±0.64	639.8 ±16.59	1.11 ±0.02	* 1.46 ±0.02	18.33 ±0.29	0.86 ±0.02	0.64 ±0.02	* 1.38 ±0.02	1.36 ±0.02	27.1 ±0.78	28.0 ±0.76	1.45 ±0.03	* 1.43 ±0.01	0.33 ±0.01	0.55 ±0.02	0.10 ±0.003
100 mg/kg	46	* 305.7 ±3.93	20.5 ±0.72	639.5 ±17.09	1.10 ±0.02	* 1.45 ±0.02	** 17.51 ±0.40	0.84 ±0.02	0.64 ±0.02	** 1.35 ±0.03	** 1.33 ±0.03	26.5 ±0.89	27.9 ±0.79	1.44 ±0.02	1.43 ±0.02	0.32 ±0.02	0.55 ±0.02	* 0.10 ±0.002
500 mg/kg	45	318.9 ±3.46	20.7 ±0.69	653.3 ±21.95	* 1.06 ±0.01	** 1.44 ±0.02	18.21 ±0.28	0.80 ±0.02	0.61 ±0.01	** 1.36 ±0.02	1.35 ±0.02	25.5 ±0.84	27.0 ±0.77	1.44 ±0.02	* 1.43 ±0.02	0.33 ±0.01	0.53 ±0.02	0.11 ±0.003
			(mg%)	(mg%)	(g%)	(g%)	(g%)	(g%)	(g%)	(g%)	(g%)	(mg%)	(mg%)	(g%)	(g%)	(mg%)	(g%)	(g%)
			6.66 ±0.27	213.80 ±6.85	0.35 ±0.004	0.48 ±0.01	5.98 ±0.10	0.26 ±0.01	0.20 ±0.01	0.46 ±0.01	0.44 ±0.01	8.91 ±0.29	9.01 ±0.22	0.47 ±0.01	0.47 ±0.01	0.11 ±0.004	0.17 ±0.01	0.03 ±0.001
			6.40 ±0.21	207.74 ±5.75	0.36 ±0.005	0.47 ±0.01	5.92 ±0.06	* 0.28 ±0.005	0.21 ±0.01	0.45 ±0.01	0.44 ±0.01	8.78 ±0.24	9.07 ±0.24	0.47 ±0.01	0.46 ±0.01	0.11 ±0.004	0.18 ±0.01	0.03 ±0.001
			6.71 ±0.21	210.81 ±6.42	0.36 ±0.01	0.48 ±0.01	5.73 ±0.10	0.28 ±0.01	* 0.21 ±0.01	0.44 ±0.01	0.43 ±0.01	8.65 ±0.26	9.06 ±0.21	0.47 ±0.01	0.47 ±0.01	0.10 ±0.005	0.18 ±0.01	0.03 ±0.001
			6.52 ±0.23	205.15 ±6.91	* 0.33 ±0.005	** 0.45 ±0.01	* 5.72 ±0.07	0.25 ±0.01	0.19 ±0.005	** 0.43 ±0.01	0.42 ±0.01	* 8.01 ±0.26	8.52 ±0.26	0.45 ±0.01	0.45 ±0.01	0.11 ±0.004	0.17 ±0.01	0.04 ±0.001

Mean ±S.E. * $P<0.05$ ** $P<0.01$

表16 Weight of organs - 8 weeks' F_1 female rats

Group	No. of females	Final body weight (g)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) right	Kidney (g) left	Adrenal (mg) right	Adrenal (mg) left	Ovary (mg) right	Ovary (mg) left	Uterus (g)	Gladder (g)
Control	45	215.6 ±2.22	17.1 ±0.79	511.4 ±13.99	0.81 ±0.01	1.19 ±0.02	12.26 ±0.20	0.57 ±0.01	0.57 ±0.02	1.03 ±0.02	1.00 ±0.02	31.8 ±1.05	34.0 ±0.94	50.4 ±1.73	52.4 ±1.58	0.42 ±0.02	0.11 ±0.02
20 mg/kg	41	214.0 ±2.21	16.6 ±0.83	542.1 ±15.60	0.82 ±0.01	1.15 ±0.02	11.93 ±0.20	0.60 ±0.01	0.55 ±0.02	0.98 ±0.02	0.95 ±0.02	32.7 ±0.86	34.4 ±0.79	* 56.6 ±1.54	53.4 ±2.02	0.43 ±0.02	0.09 ±0.002
100 mg/kg	47	211.1 ±2.35	17.5 ±0.81	490.8 ±14.57	0.79 ±0.01	1.15 ±0.02	11.69 ±0.22	0.60 ±0.02	0.54 ±0.01	0.99 ±0.02	0.96 ±0.02	34.6 ±1.06	* 36.8 ±0.95	** 59.2 ±1.87	** 60.6 ±1.96	0.43 ±0.01	0.09 ±0.002
500 mg/kg	43	214.4 ±2.45	17.2 ±0.79	501.1 ±16.43	* 0.77 ±0.01	* 1.14 ±0.02	11.76 ±0.17	0.55 ±0.01	0.52 ±0.02	** 0.95 ±0.01	** 0.92 ±0.01	31.8 ±0.76	35.0 ±0.96	50.0 ±1.75	53.9 ±1.85	0.41 ±0.02	0.08 ±0.002
			(mg%)	(mg%)	(g%)	(g%)	(g%)	(g%)	(g%)	(g%)	(g%)	(mg%)	(mg%)	(mg%)	(mg%)	(g%)	(g%)
			7.89 ±0.34	236.79 ±5.60	0.38 ±0.01	0.55 ±0.01	5.69 ±0.08	0.26 ±0.01	0.26 ±0.01	0.48 ±0.01	0.46 ±0.01	14.78 ±0.49	15.79 ±0.45	23.47 ±0.82	24.37 ±0.76	0.20 ±0.01	0.05 ±0.01
			7.79 ±0.39	253.68 ±7.39	0.38 ±0.004	0.54 ±0.01	5.58 ±0.08	* 0.28 ±0.005	0.26 ±0.01	0.46 ±0.01	0.44 ±0.01	15.28 ±0.38	16.10 ±0.36	** 26.49 ±0.72	25.00 ±0.96	0.20 ±0.01	0.04 ±0.001
			8.34 ±0.40	234.01 ±7.69	0.38 ±0.004	0.54 ±0.01	5.53 ±0.07	* 0.29 ±0.01	0.26 ±0.01	0.47 ±0.01	0.46 ±0.01	* 16.44 ±0.52	** 17.50 ±0.45	*** 28.17 ±0.92	*** 28.81 ±0.95	0.20 ±0.01	0.04 ±0.001
			8.08 ±0.39	233.52 ±7.03	* 0.36 ±0.01	* 0.53 ±0.01	* 5.49 ±0.05	0.26 ±0.004	0.24 ±0.01	** 0.44 ±0.01	** 0.43 ±0.01	14.87 ±0.37	16.37 ±0.43	23.45 ±0.86	25.33 ±0.97	0.19 ±0.01	0.04 ±0.001

Mean ±S.E.

* P<0.05 ** P<0.01 *** P<0.001

表17 Summary of skeletal examination on 8 weeks' F_1 pups

Group	Control	20 mg/kg	100 mg/kg	500 mg/kg
No. of dams examined	22	22	24	24
No. of pups examined	86	86	93	88
No. of dams with fetuses with skeletal variations	9(40.9%)	8(36.4%)	16(66.7%)	14(58.33%)
No. of fetuses with skeletal variations	12(14.0%)	10(11.6%)	22(23.7%)	21(23.9%)
Unilateral lumbar ribs	0	7(8.1%)	3(3.2%)	6(6.8%)
Bilateral lumbar ribs	3(3.5%)	0	5(5.4%)	5(5.7%)
Total lumbar ribs	3(3.5%)	7(8.1%)	8(8.6%)	11(12.5%)
Accessory sternebrae	11(12.8%)	6(7.0%)	18(19.4%)	17(19.3%)
No. of fetuses with skeletal abnormalities	0	0	0	0

表18 Fertility findings

Group		Control	20 mg/kg	100 mg/kg	500 mg/kg
	male	44	44	48	48
	female	44	44	48	48
1st mating					
animals with verified fertility	male	42	39	46	45
	female	42	39	46	45
animals with unverified fertility	male	2	5	2	3
	female	2	5	2	3
copulation rate		44/44(100%)	44/44(100%)	48/48(100%)	48/48(100%)
conception rate		42/44(95.5%)	39/44(88.6%)	46/48(95.8%)	45/48(93.8%)
2nd mating					
animals with verified fertility	male	2	5	2	3
	female	2	5	2	3
animals with unverified fertility	male	0	0	0	0
	female	0	0	0	0
total		44	44	48	48
		44	44	48	48
copulation rate		2/2(100%)	5/5(100%)	2/2(100%)	3/3(100%)
conception rate		2/2(100%)	5/5(100%)	2/2(100%)	3/3(100%)

表19 Gain of body weight and food consumption of F_1 female rats during the period of pregnancy

		0	7	14	21 H	21-0	7	14	21
Control	44	255.7 ±2.44	289.9 ±3.23	329.1 ±3.01	422.6 ±5.50	166.9 ±4.76	24.21 ±0.28	28.56 ±0.36	30.55 ±0.41
20 mg/kg	44	254.5 ±4.01	287.5 ±3.96	326.8 ±4.43	422.5 ±7.53	167.9 ±5.45	24.55 ±0.38	28.26 ±0.41	31.03 ±0.49
100 mg/kg	48	263.0 ±3.65	299.4 ±3.67	336.8 ±4.17	** 446.0 ±6.00	** 182.9 ±3.37	25.00 ±0.36	29.41 ±0.40	** 32.45 ±0.45
500 mg/kg	48	259.8 ±3.06	* 298.9 ±3.04	333.8 ±3.29	434.7 ±4.99	175.0 ±3.88	*** 26.02 ±0.33	29.30 ±0.34	30.64 ±0.38

Mean(g) ±S.E.

* P<0.05 ** P<0.01 *** P<0.001

表20　Summary of fertility findings

Group	Control	20 mg/kg	100 mg/kg	500 mg/kg
No. of dams	44	44	48	48
No. of corpora lutea	650	650	753	726
Mean	14.8	14.8	15.7	15.1
± S.E.	±0.41	±0.35	±0.34	±0.42
Total No. of implantation	640(98.5%)	625(96.2%)	748(99.3%)	718(98.9%)
平均	14.5	14.2	15.6	15.0
±標準誤差	±0.47	±0.50	±0.35	±0.46
No. of living fetuses	621(97.0%)	617(98.7%)	723(96.7%)	685(95.4%)
平均	14.1	14.0	15.1	14.3
±標準誤差	±0.53	±0.51	±0.42	±0.57
No. of male living fetuses	327(52.7%)	306(49.6%)	371(51.3%)	350(51.1%)
平均	7.6	7.0	7.7	7.4
±標準誤差	±0.36	±0.39	±0.28	±0.36
No. of female living fetuses	294(47.3%)	311(50.4%)	352(48.7%)	335(48.9%)
平均	6.7	7.2	7.3	7.1
±標準誤差	±0.37	±0.38	±0.37	±0.33
No. of unnatured fetuses	0	0	1(0.1%)	1(0.1%)
No. of dead fetuses	0	0	0	0
No. of resorption				
implantation	3(0.5%)	0	0	6(0.8%)
placental remnant	16(2.5%)	8(1.3%)	25(3.3%)	25(3.5%)
early resorption	0	0	0	2(0.3%)
late resorption	0	0	0	0
macerated fetuse	0	0	0	0
No. of fetuses with external abnormalities	0	0	0	0
Body weight of living fetuses male 平均	5.63	5.63	5.63	5.54
±標準誤差	±0.05	±0.05	±0.03	±0.05
female 平均	5.33	5.29	5.27	5.28
±標準誤差	±0.06	±0.05	±0.03	±0.06

表21 Fertility findings on F_1 animals/organ weights

Group	No. of animals examined	Final body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) right	Kidney (g) left	Adrenal (mg) right	Adrenal (mg) left	Ovary (mg) right	Ovary (mg) left	Uterus (g)	Bladder (g)
Control	44	422.6 ±5.50	1.85 ±0.01	14.2 ±0.54	19.3 ±0.63	306.2 ±12.95	1.10 ±0.03	1.47 ±0.02	16.17 ±0.33	0.76 ±0.02	0.72 ±0.02	1.17 ±0.04	1.14 ±0.04	33.1 ±0.87	36.0 ±0.88	76.8 ±3.18	78.1 ±3.81	4.94 ±0.16	0.14 ±0.004
20 mg/kg	44	422.5 ±7.53	1.81* ±0.01	15.0 ±0.42	18.7 ±0.67	265.7* ±11.47	1.10 ±0.03	1.40* ±0.02	15.89 ±0.35	0.79 ±0.03	0.67 ±0.02	1.09 ±0.02	1.07 ±0.02	36.5* ±1.05	38.8 ±1.34	74.4 ±3.14	69.7 ±2.39	5.06 ±0.18	0.15 ±0.01
100 mg/kg	48	446.0** ±6.00	1.83 ±0.01	14.3 ±0.42	18.6 ±0.73	284.3 ±8.41	1.11 ±0.02	1.41 ±0.02	17.10* ±0.28	0.81 ±0.02	0.74 ±0.03	1.12 ±0.02	1.09 ±0.02	35.9 ±1.19	37.5 ±1.13	80.6 ±3.10	77.5 ±3.02	5.28 ±0.14	0.14 ±0.004
500 mg/kg	48	434.7 ±4.99	1.81 ±0.01	14.7 ±0.54	17.7 ±0.80	273.2 ±11.59	1.07 ±0.02	1.40* ±0.02	16.30 ±0.30	0.77 ±0.02	0.67 ±0.02	1.11 ±0.02	1.09 ±0.02	32.6 ±1.08	35.0 ±0.94	73.3 ±2.90	69.0* ±2.33	4.87 ±0.19	0.13 ±0.003

Mean ±S.E.

* $P<0.05$ ** $P<0.01$

表 22　8 weeks' F_1 males/organ weights

Group	No. of males	Final body weight (g)	Brain (g)	Pituitary (mg)	Thyroid (mg)	Thymus (mg)	Heart (g)	Lung (g)	Liver (g)	Spleen (g)	Pancreas (g)	Kidney (g) right	Kidney (g) left	Adrenal (mg) right	Adrenal (mg) left	Spermary (g) right	Spermary (g) left	Prostate (mg)	Seminal vesicle (g)	Bladder (g)
Control	44	562.8 ±7.71	1.93 ±0.03	12.8 ±0.42	22.5 ±0.75	441.1 ±14.31	1.49 ±0.03	1.87 ±0.03	24.99 ±0.53	0.95 ±0.02	0.77 ±0.02	1.91 ±0.03	1.89 ±0.03	27.8 ±1.02	30.7 ±1.03	1.84 ±0.02	1.84 ±0.03	645.2 ±29.80	0.84 ±0.03	0.14 ±0.003
20 mg/kg	44	543.5 ±9.72	1.97 ±0.01	13.4 ±0.43	21.8 ±0.81	419.8 ±18.95	1.51 ±0.03	1.76* ±0.03	23.70 ±0.59	0.96 ±0.03	0.79 ±0.03	1.89 ±0.04	1.88 ±0.04	27.0 ±0.87	29.5 ±0.83	1.82 ±0.02	1.83 ±0.02	569.0 ±27.93	0.82 ±0.03	0.14 ±0.004
100 mg/kg	48	565.7 ±7.31	2.00 ±0.02	13.2 ±0.29	22.5 ±0.73	406.2 ±15.49	1.54 ±0.03	1.81 ±0.03	25.11 ±0.52	0.99 ±0.03	0.76 ±0.02	1.91 ±0.04	1.91 ±0.03	28.7 ±0.92	29.8 ±0.69	1.85 ±0.02	1.86 ±0.02	622.0 ±28.32	0.84 ±0.02	0.14 ±0.004
500 mg/kg	48	552.9 ±6.87	1.97 ±0.02	12.3 ±0.40	22.3 ±0.71	392.6* ±16.28	1.51 ±0.03	1.84 ±0.03	24.10 ±0.56	0.91 ±0.02	0.73 ±0.02	1.88 ±0.03	1.86 ±0.04	25.8 ±0.80	29.9 ±0.94	1.80 ±0.03	1.83 ±0.03	636.1 ±29.74	0.81 ±0.02	0.14 ±0.003
			(g%)	(mg%)	(mg%)	(mg%)	(g%)	(g%)	(g%)	(g%)	(g%)	(g%)	(g%)	(mg%)	(mg%)	(g%)	(g%)	(mg%)	(g%)	(g%)
			0.35 ±0.01	2.27 ±0.07	4.01 ±0.13	78.80 ±2.67	0.27 ±0.004	0.33 ±0.01	4.43 ±0.06	0.17 ±0.004	0.14 ±0.003	0.34 ±0.004	0.34 ±0.004	4.94 ±0.17	5.46 ±0.18	0.33 ±0.01	0.33 ±0.01	115.14 ±5.43	0.15 ±0.01	0.03 ±0.001
			0.37* ±0.01	2.49 ±0.09	4.02 ±0.13	76.58 ±2.79	0.28* ±0.004	0.33 ±0.01	4.35 ±0.07	0.18 ±0.004	0.15 ±0.01	0.35 ±0.005	0.35 ±0.01	5.02 ±0.18	5.48 ±0.17	0.34 ±0.01	0.34 ±0.01	105.76 ±5.49	0.15 ±0.01	0.03 ±0.001
			0.35 ±0.01	2.35 ±0.06	4.00 ±0.14	72.03 ±2.67	0.27 ±0.004	0.32 ±0.004	4.43 ±0.06	0.18 ±0.01	0.14 ±0.003	0.34 ±0.005	0.34 ±0.004	5.13 ±0.19	5.31 ±0.15	0.33 ±0.005	0.33 ±0.01	108.87 ±4.71	0.15 ±0.005	0.02 ±0.001
			0.36 ±0.01	2.24 ±0.07	4.03 ±0.12	71.22 ±2.95	0.27 ±0.004	0.33 ±0.005	4.34 ±0.07	0.16 ±0.003	0.13 ±0.004	0.34 ±0.005	0.34 ±0.01	4.68 ±0.14	5.41 ±0.17	0.33 ±0.01	0.33 ±0.01	116.19 ±5.82	0.15 ±0.004	0.03 ±0.001

Mean ±S.E.　　* $P<0.05$