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ONE-YEAR CHRONIC PERCUTANEOUS TOXICITY OF PIROCTONE OLAMINE IN RATS

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One-Year Chronic Percutaneous Toxicity of Piroctone Olamine (PO) in Rats

Abstract

1. Symptoms

Just after the start of application of the test material (0 %, 0.5 % and 1.0 % PO), a bran-like change and some scratches were found at the application area of the skin in both male and female rats of each treated group except the control group, and their degrees and the number of cases were correlative with the concentrations of PO. A transient tendency to recover from these changes was noted from 3 to 7 months after the start of application, but the number of the cases gradually increased thereafter; these cases were slightly severe, accompanied with erythema, incrustation, and detachment of crusts in some females of the 0.5 % PO group and in some animals of both sexes of the 1.0 % PO group. In females of the 1.0 % PO group, hemorrhage was also found.

At the end of application, wounds and erythema were observed in one or 2 cases of the control group, about half of the 0.5 % PO group, and 7 cases of the 1.0 % PO group.

The recovery from the changes appeared to be rapid; the wounds disappeared within 2 weeks after the end of application even in males and females of the 1.0 % PO group.

The other symptom observed was bedsore of the hindlimbs in males about 6 months after initial application and in females about 7 months after the start of application, and these cases gradually increased thereafter.

2. Autopsy and Histopathological Findings

At the end of application, dark red spots, black spots and fat in the adrenal, hematoma and hypertrophy in the pituitary, and follicular cysts in the ovary were found in some cases of each group by autopsy. The histopathological findings included hyaline casts in the tubules and interstitial cell infiltration in the kidney in some male and female cases of each group; congestion and cysts in the adrenal in some female cases of each group; and thickening and necrosis of the epidermis and proliferation in the deep part of the epidermis in males and females of the PO groups.

Autopsy at the end of the recovery period revealed depression in the kidney, fat in the adrenal, hematoma and hypertrophy in the pituitary in some cases of each group. As the histopathological findings, hyaline casts in the renal tubules, cysts and interstitial cell infiltration in the kidney, and cysts in the adrenal were found in some cases of each group. Thickening and necrosis of the epidermis and proliferation in the deep part of the epidermis were observed only in one male and one female of the 1.0 % PO group.

3. Others

No remarkable change was observed in the body weight, the feed efficiency, the eyeground, the urine, blood, or biochemical values, the wet organ weights, or the bone marrow.

4. Dead Cases

One male died each in the control group (PG) and the 1 % PO group during treatment period; two males died in the 0.5 % PO group during the recovery period; these animals showed slight changes in the liver, kidney, and lung by autopsy and histopathological examination.

Discussion

1. Changes

The gross changes observed at the application area of PO disappeared within 2 weeks after the end of application, and the histopathological examination after the recovery period showed only the findings indicative of healing of the lesions. Therefore, the changes noted after the PO application are considered not to be significant since the acute signs caused by the PO application could rapidly disappear even in the cases of repeated application, and furthermore the PO application caused no cumulative or potentially malignant effects.
No other changes possibly caused by the toxicity of PO were observed in the autopsy or histopathological findings, and the dead cases showed no effects caused by the application. The increase in the body weight noted in the females of the control group was considered to occur spontaneously.

2. Safety

The PG solutions containing 0 %, 0.5 % and 1.0 % PO were applied to the skin of rats successively for 12 months, but only reversible changes were observed at the application area of males and females. No systemic toxicity considered to be related to the PO application was noted. Therefore, the long-term external application of a formula of shampoo or rinse containing about 1 % PO is considered to be safe.

Mean body weight
(Table 1)

Table - 1

Mean body weight

Piroctone Olamine
ﾋﾟﾛｸﾄﾝ ｵﾗﾐﾝ

(g:mean.sd)

Sex	Dose	Weeks 0	1	2	3	4	5
Male	Control	143.0 ± 6.5	201.4 ± 8.9	255.5 ± 10.5	302.4 ± 17.0	338.5 ± 20.9	366.6 ± 26.9
	PG	143.6 ± 6.0	204.6 ± 7.0	265.0* ± 10.3	315.0* ± 14.7	353.1 ± 17.0	385.8* ± 19.2
	0.5%PO	143.1 ± 6.7	201.7 ± 11.2	259.0 ± 16.6	309.4 ± 20.8	347.0 ± 24.9	377.0 ± 29.4
	1.0%PO	143.3 ± 7.2	206.0 ± 11.8	261.8 ± 19.7	310.9 ± 23.3	351.4 ± 24.3	379.2 ± 27.5
Female	Control	108.9 ± 4.1	147.1 ± 8.6	171.4 ± 11.7	199.1 ± 14.5	218.2 ± 17.4	231.5 ± 16.5
	PG	108.8 ± 4.2	143.9 ± 7.5	165.6 ± 8.1	195.1 ± 8.8	211.6 ± 11.5	226.8 ± 15.3
	0.5%PO	109.1 ± 5.4	147.1 ± 8.1	171.0 ± 12.8	197.2 ± 15.3	215.4 ± 17.7	231.1 ± 19.8
	1.0%PO	108.9 ± 5.5	144.9 ± 10.8	168.1 ± 12.6	194.6 ± 17.1	213.9 ± 23.1	230.0 ± 21.8

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight　　ﾋﾟﾛｸﾄﾝ ｵﾗﾙﾁﾝ　　(g:mean.sd)

Sex	Dose	Weeks 0	6	7	8	9	10
Male	Control	143.0 ± 6.5	392.8 ± 31.3	409.4 ± 34.0	426.1 ± 34.7	439.6 ± 36.9	451.7 ± 39.0
	PG	143.6 ± 6.0	409.2 ± 19.4	431.1 ± 21.3	447.6 ± 25.4	464.7 ± 28.8	477.7 ± 30.7
	0.5%PO	143.1 ± 6.7	400.7 ± 35.5	422.2 ± 35.2	444.6 ± 38.1	457.8 ± 42.7	470.3 ± 44.7
	1.0%PO	143.3 ± 7.2	404.6 ± 31.7	426.3 ± 31.9	444.4 ± 33.2	454.9 ± 36.9	471.7 ± 39.2
Female	Control	108.9 ± 4.1	248.6 ± 20.8	257.3 ± 23.0	260.4 ± 25.3	268.6 ± 21.2	275.3 ± 19.8
	PG	108.8 ± 4.2	241.0 ± 14.6	251.9 ± 15.7	255.5 ± 17.0	262.5 ± 18.3	269.1 ± 18.4
	0.5%PO	109.1 ± 5.4	244.4 ± 23.1	256.6 ± 25.6	262.3 ± 21.7	269.9 ± 24.3	275.4 ± 23.8
	1.0%PO	108.9 ± 5.5	243.0 ± 23.4	252.4 ± 23.9	258.1 ± 23.3	262.4 ± 20.8	267.8 ± 20.5

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

Mean body weight　　ﾋﾟﾛｸﾄﾝ ｵﾗﾙ　　(g:mean.sd)

Sex	Dose	Weeks 0	11	12	13	14	15
Male	Control	143.0 ± 6.5	463.2 ± 40.1	474.6 ± 43.6	480.4 ± 44.9	490.6 ± 46.1	498.9 ± 47.4
	PG	143.6 ± 6.0	489.5 ± 32.3	499.6 ± 33.9	508.4 ± 34.9	516.7 ± 34.8	524.7 ± 35.4
	0.5%PO	143.1 ± 6.7	484.1 ± 46.5	492.9 ± 49.2	502.0 ± 48.4	510.9 ± 48.2	519.5 ± 50.4
	1.0%PO	143.3 ± 7.2	486.0 ± 39.9	496.6 ± 40.1	507.5 ± 44.2	515.9 ± 46.1	527.4 ± 48.1
Female	Control	108.9 ± 4.1	277.5 ± 20.2	283.0 ± 21.8	288.4 ± 24.8	295.4 ± 26.7	296.6 ± 23.4
	PG	108.8 ± 4.2	273.7 ± 18.5	278.8 ± 19.3	281.4 ± 19.7	286.0 ± 20.3	292.1 ± 22.5
	0.5%PO	109.1 ± 5.4	280.4 ± 22.9	285.0 ± 24.4	291.9 ± 27.2	296.1 ± 28.9	298.5 ± 30.5
	1.0%PO	108.9 ± 5.5	273.1 ± 20.3	278.5 ± 22.6	282.2 ± 20.3	285.4 ± 22.9	288.8 ± 24.6

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

Mean body weight ﾋﾞｰﾛｳﾄﾝ ｵﾓﾐ (g:mean.sd)

Sex	Dose	Weeks 0	16	17	18	19	20
Male	Control	143.0 ± 6.5	507.1 ± 49.8	512.9 ± 49.7	521.7 ± 49.4	528.1 ± 52.1	534.0 ± 52.1
	PG	143.6 ± 6.0	533.9 ± 35.1	538.3 ± 40.8	547.9 ± 39.8	556.7 ± 39.3	562.6 ± 39.3
	0.5%PO	143.1 ± 6.7	527.6 ± 51.5	533.4 ± 52.4	540.6 ± 52.2	549.1 ± 52.6	555.9 ± 53.5
	1.0%PO	143.3 ± 7.2	533.7 ± 48.7	541.6 ± 51.3	549.1 ± 51.9	556.3 ± 52.9	559.2 ± 52.9
Female	Control	108.9 ± 4.1	299.9 ± 23.9	303.1 ± 25.2	305.2 ± 24.4	310.7 ± 27.0	312.3 ± 29.5
	PG	108.8 ± 4.2	295.8 ± 22.5	297.3 ± 23.1	302.1 ± 23.4	303.6 ± 22.9	305.9 ± 23.3
	0.5%PO	109.1 ± 5.4	300.3 ± 29.5	304.5 ± 31.3	308.8 ± 32.6	310.5 ± 32.5	313.4 ± 34.4
	1.0%PO	108.9 ± 5.5	292.9 ± 23.7	295.9 ± 21.9	302.4 ± 22.9	302.9 ± 24.8	305.7 ± 24.9

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight ﾋﾞｮｳﾀｲ ｵﾓｻﾐﾂ (g:mean.sd)

Sex	Dose	Weeks 0	21	22	23	24	25
Male	Control	143.0 ± 6.5	535.9 ± 53.6	542.6 ± 52.5	548.9 ± 52.1	551.1 ± 54.7	555.9 ± 56.5
	PG	143.6 ± 6.0	567.0 ± 39.7	572.4 ± 40.0	576.4 ± 42.6	577.1 ± 30.6	588.1 ± 41.9
	0.5%PO	143.1 ± 6.7	560.0 ± 56.7	566.2 ± 55.5	572.4 ± 54.0	577.0 ± 55.6	578.9 ± 57.7
	1.0%PO	143.3 ± 7.2	562.2 ± 52.5	569.8 ± 52.7	572.5 ± 51.3	575.6 ± 51.9	582.9 ± 53.4
Female	Control	108.9 ± 4.1	318.1 ± 31.1	320.6 ± 33.2	318.4 ± 34.6	326.1 ± 33.6	328.7 ± 35.0
	PG	108.8 ± 4.2	308.9 ± 25.2	310.0 ± 26.1	314.4 ± 27.9	318.8 ± 28.8	324.6 ± 31.9
	0.5%PO	109.1 ± 5.4	319.4 ± 34.5	318.0 ± 29.3	319.0 ± 30.3	324.9 ± 30.1	326.6 ± 27.4
	1.0%PO	108.9 ± 5.5	309.6 ± 23.3	310.4 ± 23.0	313.2 ± 24.6	316.3 ± 23.4	318.4 ± 23.6

*:Significantry different from control (p<0.05)
**:Significantry different from control (p<0.01)

Mean body weight E°07K2 #552 (g:mean.sd)

Sex	Dose	Weeks 0	26	27	28	29	30
Male	Control	143.0 ± 6.5	555.2 ± 57.4	562.4 ± 52.7	561.5 ± 53.4	566.4 ± 54.5	562.9 ± 59.1
	PG	143.6 ± 6.0	586.9 ± 47.9	592.7 ± 45.3	595.6 ± 46.1	601.7 ± 48.0	603.4 ± 47.4
	0.5%PO	143.1 ± 6.7	582.8 ± 55.3	587.8 ± 55.3	586.6 ± 55.1	592.6 ± 56.5	593.0 ± 56.1
	1.0%PO	143.3 ± 7.2	584.4 ± 54.4	588.2 ± 53.5	588.9 ± 54.4	595.7 ± 54.3	595.3 ± 52.3
Female	Control	108.9 ± 4.1	328.9 ± 35.8	335.1 ± 39.2	336.1 ± 41.0	338.0 ± 41.4	341.4 ± 43.6
	PG	108.8 ± 4.2	325.4 ± 34.8	332.2 ± 37.0	334.4 ± 39.8	337.9 ± 42.0	336.8 ± 44.4
	0.5%PO	109.1 ± 5.4	328.4 ± 28.9	334.0 ± 28.8	336.0 ± 31.2	338.5 ± 28.3	332.9 ± 27.9
	1.0%PO	108.9 ± 5.5	322.9 ± 23.3	325.8 ± 23.4	330.8 ± 27.7	335.1 ± 29.8	332.4 ± 28.1

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight　　ﾋﾞｰｸﾞﾙ ｵｽｽﾒ　　(g:mean.sd)

Sex	Dose	Weeks 0	31	32	33	34	35
Male	Control	143.0 ± 6.5	576.1 ± 58.8	582.5 ± 62.3	586.1 ± 64.1	587.6 ± 64.8	594.7 ± 64.0
	PG	143.6 ± 6.0	608.4 ± 46.8	615.8 ± 48.7	616.1 ± 51.9	617.4 ± 54.6	619.5 ± 61.0
	0.5%PO	143.1 ± 6.7	599.4 ± 57.4	603.9 ± 59.4	609.0 ± 57.8	614.1 ± 56.7	619.9 ± 60.1
	1.0%PO	143.3 ± 7.2	602.3 ± 51.8	603.9 ± 48.2	609.1 ± 52.5	612.7 ± 52.0	614.9 ± 48.6
Female	Control	108.9 ± 4.1	344.1 ± 45.0	346.7 ± 43.8	349.8 ± 44.9	357.4 ± 48.4	360.9 ± 49.1
	PG	108.8 ± 4.2	337.9 ± 45.5	341.2 ± 43.4	343.6 ± 47.3	350.0 ± 47.5	352.9 ± 44.1
	0.5%PO	109.1 ± 5.4	337.6 ± 26.4	341.9 ± 30.1	343.9 ± 30.1	349.9 ± 31.2	352.0 ± 29.3
	1.0%PO	108.9 ± 5.5	331.4 ± 26.1	335.6 ± 26.4	334.6 ± 25.8	341.7 ± 28.7	344.6 ± 32.1

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

Mean body weight ﾋﾟﾛｸﾛﾝ ｵｽﾗﾝ (g:mean.sd)

Sex	Dose	Weeks 0	36	37	38	39	40
Male	Control	143.0 ± 6.5	597.4 ± 64.5	602.6 ± 67.1	606.6 ± 68.7	608.3 ± 68.8	611.4 ± 67.5
	PG	143.6 ± 6.0	607.6 ± 93.7	631.3 ± 54.7	636.1 ± 55.3	637.5 ± 57.1	640.7 ± 59.9
	0.5%PO	143.1 ± 6.7	619.3 ± 60.4	625.0 ± 62.2	631.4 ± 62.5	634.4 ± 63.3	639.6 ± 62.8
	1.0%PO	143.3 ± 7.2	615.0 ± 49.8	620.5 ± 53.4	627.1 ± 53.2	627.6 ± 53.8	631.8 ± 54.4
Female	Control	108.9 ± 4.1	360.9 ± 50.2	362.6 ± 50.3	363.1 ± 50.7	365.9 ± 49.6	372.7 ± 50.3
	PG	108.8 ± 4.2	353.1 ± 50.5	354.0 ± 49.8	356.6 ± 53.6	360.1 ± 50.6	366.3 ± 52.2
	0.5%PO	109.1 ± 5.4	352.9 ± 32.9	353.1 ± 33.7	353.5 ± 33.0	360.8 ± 35.3	364.1 ± 32.3
	1.0%PO	108.9 ± 5.5	341.9 ± 30.5	343.3 ± 28.6	341.4 ± 25.2	346.6 ± 27.6	353.6 ± 28.9

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight　　ﾋﾟﾛｸﾄﾝ ｵﾗﾙﾝ　　(g:mean.sd)

Sex	Dose	Weeks 0	41	42	43	44	45
Male	Control	143.0 ± 6.5	615.8 ± 67.6	616.3 ± 71.3	621.0 ± 69.8	622.5 ± 70.4	626.4 ± 70.6
	PG	143.6 ± 6.0	646.6 ± 60.7	649.3 ± 59.6	650.7 ± 61.2	658.7 ± 59.3	660.7 ± 59.5
	0.5%PO	143.1 ± 6.7	643.8 ± 64.0	645.3 ± 65.5	649.6 ± 68.0	656.5 ± 70.2	661.1 ± 70.0
	1.0%PO	143.3 ± 7.2	625.6 ± 60.1	619.6 ± 83.8	637.0 ± 58.9	640.9 ± 53.9	643.6 ± 54.0
Female	Control	108.9 ± 4.1	368.4 ± 52.0	373.8 ± 51.9	375.7 ± 51.1	381.6 ± 52.8	381.3 ± 50.7
	PG	108.8 ± 4.2	364.2 ± 55.7	370.0 ± 56.2	373.3 ± 58.9	374.5 ± 57.6	378.5 ± 59.8
	0.5%PO	109.1 ± 5.4	364.3 ± 33.6	367.0 ± 31.2	367.4 ± 32.4	374.8 ± 34.0	375.2 ± 33.6
	1.0%PO	108.9 ± 5.5	351.7 ± 34.0	355.4 ± 31.2	356.5 ± 30.8	360.6 ± 31.8	360.2 ± 29.9

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

Mean body weight　　ﾋﾞｰｸﾞﾙ ｵｽ　　(g:mean.sd)

Sex	Dose	Weeks 0	46	47	48	49	50
Male	Control	143.0 ± 6.5	628.4 ± 72.7	631.5 ± 72.8	636.1 ± 73.2	637.2 ± 77.1	642.4 ± 78.5
	PG	143.6 ± 6.0	658.4 ± 63.2	661.0 ± 67.6	666.5 ± 66.9	664.7 ± 67.2	670.8 ± 70.2
	0.5%PO	143.1 ± 6.7	661.2 ± 67.0	663.5 ± 68.4	669.2 ± 69.7	670.1 ± 68.4	672.4 ± 69.3
	1.0%PO	143.3 ± 7.2	644.7 ± 57.2	650.8 ± 57.9	653.7 ± 58.4	652.0 ± 60.5	654.2 ± 58.3
Female	Control	108.9 ± 4.1	386.3 ± 53.2	386.9 ± 55.3	390.3 ± 56.7	389.4 ± 54.1	391.2 ± 57.3
	PG	108.8 ± 4.2	381.6 ± 60.9	383.1 ± 59.9	387.7 ± 62.5	385.1 ± 62.0	388.6 ± 65.5
	0.5%PO	109.1 ± 5.4	376.1 ± 30.7	379.9 ± 34.5	380.7 ± 36.0	381.5 ± 39.1	385.9 ± 40.2
	1.0%PO	108.9 ± 5.5	365.6 ± 31.6	368.9 ± 34.1	370.4 ± 33.1	369.4 ± 31.3	371.1 ± 33.8

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

Mean body weight ﾋﾞﾛｳﾄﾝ ｵﾓﾐﾝ (g:mean.sd)

Sex	Dose	Weeks 0	51	52	53	54	55
Male	Control	143.0 ± 6.5	644.6 ± 79.2	644.1 ± 77.4	636.8 ± 47.5	638.0 ± 47.0	642.8 ± 51.4
	PG	143.6 ± 6.0	675.0 ± 69.0	672.9 ± 70.8	715.3 ± 113.7	717.0 ± 115.3	721.3 ± 114.7
	0.5%PO	143.1 ± 6.7	675.1 ± 69.7	672.8 ± 68.2	643.3 ± 11.0	645.7 ± 11.9	650.3 ± 3.2
	1.0%PO	143.3 ± 7.2	655.6 ± 63.5	653.0 ± 61.3	685.3 ± 47.3	687.0 ± 48.9	692.0 ± 48.8
Female	Control	108.9 ± 4.1	392.4 ± 59.1	393.6 ± 57.0	411.3 ± 57.6	415.5 ± 56.9	418.3 ± 56.5
	PG	108.8 ± 4.2	391.3 ± 64.4	394.6 ± 64.8	449.8 ± 113.0	454.0 ± 110.6	463.3 ± 119.8
	0.5%PO	109.1 ± 5.4	383.9 ± 38.4	386.9 ± 39.3	391.5 ± 47.1	399.3 ± 41.7	397.5 ± 47.8
	1.0%PO	108.9 ± 5.5	367.4 ± 31.7	373.6 ± 30.8	368.5 ± 23.7	369.5 ± 25.8	372.5 ± 25.1

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight ﾋﾞﾛｳﾄﾝｲﾝｵﾝ ｵﾓﾐ (g:mean.sd)

Sex	Dose	Weeks 0	56	57	58	59
Male	Control	143.0 ± 6.5	649.8 ± 53.0	648.0 ± 49.4	647.3 ± 48.7	647.5 ± 50.5
	PG	143.6 ± 6.0	726.8 ± 116.1	730.5 ± 116.8	730.3 ± 118.1	738.5 ± 121.5
	0.5%PO	143.1 ± 6.7	659.7 ± 2.9	640.7 ± 39.8	611.3 ± 103.5	663.0 ± 9.9
	1.0%PO	143.3 ± 7.2	692.3 ± 50.2	692.0 ± 52.4	696.5 ± 52.3	693.8 ± 52.3
Female	Control	108.9 ± 4.1	422.5 ± 56.6	427.8 ± 62.8	426.8 ± 57.7	429.3 ± 61.9
	PG	108.8 ± 4.2	468.8 ± 108.4	468.3 ± 117.6	479.5 ± 119.4	478.0 ± 119.0
	0.5%PO	109.1 ± 5.4	405.8 ± 45.6	410.0 ± 49.8	412.8 ± 51.5	418.0 ± 50.4
	1.0%PO	108.9 ± 5.5	380.0 ± 23.3	382.0 ± 19.9	388.5 ± 23.4	389.5 ± 21.1

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight gain

(Table 2)

Table - 2

Mean body weight gain

Piroctone Olamine

ﾋﾟﾛｸﾄﾝ ｵﾗﾐﾝ

(g:mean.sd)

Sex	Dose	Weeks 1	2	3	4	5
Male	Control	58.4 ± 5.6	112.5 ± 9.0	159.4 ± 14.9	195.5 ± 19.3	223.6 ± 24.8
	PG	61.0 ± 6.9	121.4* ± 11.1	171.4 ± 16.3	209.6 ± 18.2	242.2* ± 20.2
	0.5%PO	58.6 ± 9.4	115.9 ± 15.7	166.2 ± 21.7	203.9 ± 25.9	233.9 ± 30.1
	1.0%PO	62.7 ± 7.4	118.5 ± 17.6	167.6 ± 21.0	208.1 ± 19.3	235.9 ± 22.6
Female	Control	38.2 ± 6.7	62.5 ± 11.7	90.2 ± 12.4	109.3 ± 15.6	122.6 ± 15.6
	PG	35.1 ± 5.7	56.8 ± 7.6	86.4 ± 6.6	102.8 ± 9.7	118.0 ± 14.3
	0.5%PO	38.0 ± 4.8	61.9 ± 9.3	88.1 ± 11.9	106.4 ± 14.6	122.0 ± 17.0
	1.0%PO	36.0 ± 6.9	59.2 ± 10.3	85.8 ± 13.7	105.0 ± 19.9	121.1 ± 18.9

*:Significantry different from control ($p<0.05$)

**:Significantry different from control ($p<0.01$)

Mean body weight gain　　ﾋﾞﾛｸﾄﾝ ｵｽﾗﾝ　　(g:mean.sd)

Sex	Dose	Weeks 6	7	8	9	10
Male	Control	249.8 ± 29.4	266.4 ± 32.2	283.1 ± 32.9	296.6 ± 34.7	308.7 ± 36.9
	PG	265.6 ± 20.6	287.6 ± 22.7	304.1 ± 26.6	321.1 ± 30.1	334.1 ± 31.7
	0.5%PO	257.6 ± 35.7	279.1 ± 35.6	301.4 ± 38.4	314.6 ± 43.2	327.1 ± 45.2
	1.0%PO	261.3 ± 26.8	283.0 ± 26.9	301.1 ± 28.4	311.6 ± 34.1	328.4 ± 35.2
Female	Control	139.6 ± 19.3	148.4 ± 21.3	151.4 ± 24.3	159.6 ± 20.0	166.4 ± 18.5
	PG	132.2 ± 13.5	143.1 ± 14.4	146.7 ± 16.8	153.7 ± 17.7	160.3 ± 17.8
	0.5%PO	135.3 ± 19.8	147.6 ± 22.8	153.2 ± 19.7	160.8 ± 21.8	166.4 ± 21.1
	1.0%PO	134.1 ± 20.3	143.6 ± 20.8	149.3 ± 20.5	153.6 ± 17.5	158.9 ± 17.7

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight gain　　ﾋﾟﾛｸﾛﾝ ｵﾗﾙ　　(g:mean.sd)

Sex	Dose	Weeks 11	12	13	14	15
Male	Control	320.2 ± 38.1	331.6 ± 41.8	337.4 ± 42.9	347.6 ± 43.8	355.9 ± 45.2
	PG	345.9 ± 33.2	356.0 ± 34.8	364.8 ± 35.3	373.1 ± 35.2	381.1 ± 35.8
	0.5%PO	340.9 ± 46.9	349.8 ± 49.6	358.9 ± 48.7	367.8 ± 48.5	376.4 ± 50.7
	1.0%PO	342.7 ± 35.4	353.4 ± 35.3	364.2 ± 39.1	372.6 ± 41.1	384.1 ± 43.2
Female	Control	168.6 ± 18.8	174.1 ± 20.7	179.5 ± 23.4	186.5 ± 25.7	187.7 ± 22.3
	PG	164.9 ± 18.2	170.0 ± 19.5	172.6 ± 19.6	177.2 ± 20.8	183.4 ± 22.5
	0.5%PO	171.3 ± 20.2	175.9 ± 22.1	182.8 ± 25.0	187.1 ± 26.2	189.4 ± 27.8
	1.0%PO	164.2 ± 17.1	169.6 ± 19.9	173.4 ± 17.5	176.6 ± 20.3	179.9 ± 21.8

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

Mean body weight gain　　ﾋﾞﾛｳﾄﾝ ｵﾓﾘﾝ　　(g:mean.sd)

Sex	Dose	Weeks 16	17	18	19	20
Male	Control	364.1 ± 47.4	369.9 ± 47.5	378.7 ± 47.4	385.1 ± 50.4	391.0 ± 50.6
	PG	390.3 ± 35.0	394.7 ± 40.3	404.3 ± 39.5	413.1 ± 39.3	419.1 ± 38.8
	0.5%PO	384.4 ± 51.8	390.2 ± 52.7	397.4 ± 52.4	406.0 ± 52.9	412.8 ± 53.6
	1.0%PO	390.4 ± 43.8	398.4 ± 46.1	405.8 ± 46.8	413.0 ± 47.8	415.9 ± 47.8
Female	Control	191.0 ± 23.0	194.1 ± 24.1	196.3 ± 23.4	201.8 ± 25.9	203.4 ± 28.3
	PG	187.0 ± 22.6	188.5 ± 23.1	193.3 ± 23.7	194.9 ± 23.5	197.1 ± 23.8
	0.5%PO	191.2 ± 26.9	195.4 ± 28.6	199.7 ± 29.8	201.4 ± 29.8	204.4 ± 31.8
	1.0%PO	184.0 ± 20.8	187.1 ± 19.2	193.6 ± 20.0	194.0 ± 22.5	196.9 ± 22.1

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

Mean body weight gain ﾋﾞﾛｳﾀｲｼﾞｭｳ ｿｳｶﾘｮｳ (g:mean.sd)

Sex	Dose	Weeks 21	22	23	24	25
Male	Control	392.9 ± 51.9	399.6 ± 51.1	405.9 ± 50.9	408.1 ± 53.4	412.9 ± 55.3
	PG	423.4 ± 38.8	428.8 ± 39.0	432.9 ± 42.1	433.5 ± 32.1	444.6 ± 41.0
	0.5%PO	416.9 ± 56.8	423.1 ± 55.8	429.3 ± 54.4	433.9 ± 55.6	435.7 ± 58.1
	1.0%PO	418.9 ± 47.3	426.5 ± 47.8	429.2 ± 46.5	432.4 ± 47.2	439.6 ± 48.6
Female	Control	209.2 ± 29.8	211.7 ± 32.1	209.4 ± 33.6	217.2 ± 32.1	219.8 ± 33.7
	PG	200.1 ± 25.6	201.2 ± 26.6	205.6 ± 28.4	210.0 ± 29.3	215.9 ± 32.3
	0.5%PO	210.3 ± 32.3	208.9 ± 26.9	209.9 ± 28.6	215.8 ± 28.3	217.5 ± 25.5
	1.0%PO	200.7 ± 20.5	201.6 ± 20.4	204.4 ± 21.9	207.4 ± 19.8	209.6 ± 20.2

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight gain ﾋﾞｰｶﾞﾝ ｵﾓﾃｷﾝ (g:mean.sd)

Sex	Dose	Weeks 26	27	28	29	30
Male	Control	412.2 ± 56.2	419.4 ± 51.8	418.5 ± 52.3	423.4 ± 53.6	419.9 ± 57.4
	PG	443.4 ± 47.5	449.1 ± 44.3	452.0 ± 44.9	458.1 ± 47.0	459.8 ± 46.4
	0.5%PO	439.6 ± 55.4	444.6 ± 55.4	443.5 ± 55.1	449.5 ± 56.3	449.9 ± 56.0
	1.0%PO	441.1 ± 49.6	444.9 ± 48.7	445.6 ± 49.6	452.4 ± 49.7	452.0 ± 47.6
Female	Control	220.0 ± 34.6	226.1 ± 37.8	227.2 ± 39.6	229.1 ± 40.0	232.4 ± 42.4
	PG	216.6 ± 35.1	223.4 ± 37.4	225.6 ± 40.1	229.1 ± 42.5	228.0 ± 44.7
	0.5%PO	219.4 ± 27.3	224.9 ± 27.5	226.9 ± 30.0	229.4 ± 27.2	223.9 ± 27.0
	1.0%PO	214.0 ± 20.1	216.9 ± 20.6	221.9 ± 25.0	226.3 ± 27.2	223.6 ± 25.3

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight gain ﾋﾟﾛｸﾄﾝ ｵﾄｽﾞﾝ (g:mean.sd)

Sex	Dose	Weeks 31	32	33	34	35
Male	Control	433.1 ± 57.5	439.5 ± 61.3	443.1 ± 62.9	444.6 ± 63.6	451.7 ± 62.6
	PG	464.8 ± 45.9	472.2 ± 47.9	472.5 ± 50.9	473.9 ± 53.5	475.9 ± 60.3
	0.5%PO	456.3 ± 57.2	460.8 ± 59.5	465.9 ± 58.2	471.0 ± 56.9	476.7 ± 60.1
	1.0%PO	459.0 ± 47.1	460.6 ± 44.4	465.9 ± 48.3	469.4 ± 47.8	471.6 ± 44.3
Female	Control	235.1 ± 43.9	237.8 ± 42.5	240.9 ± 43.6	248.5 ± 47.1	252.0 ± 47.7
	PG	229.1 ± 46.1	232.4 ± 43.9	234.9 ± 47.8	241.2 ± 48.1	244.1 ± 44.5
	0.5%PO	228.5 ± 25.3	232.9 ± 29.3	234.9 ± 29.5	240.8 ± 30.1	242.9 ± 28.3
	1.0%PO	222.5 ± 22.9	226.7 ± 23.3	225.8 ± 22.6	232.9 ± 25.9	235.8 ± 29.4

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight gain　　ﾋﾞｰｸﾞﾙ ｵｽｽﾐ　　(g:mean.sd)

Sex	Dose	Weeks 36	37	38	39	40
Male	Control	454.4 ± 63.5	459.6 ± 66.0	463.6 ± 67.8	465.3 ± 67.8	468.4 ± 66.2
	PG	464.1 ± 93.4	487.8 ± 53.3	492.6 ± 54.3	494.1 ± 55.5	497.2 ± 58.4
	0.5%PO	476.1 ± 60.6	481.9 ± 62.4	488.3 ± 63.1	491.3 ± 63.5	496.5 ± 62.9
	1.0%PO	471.7 ± 45.8	477.2 ± 49.2	483.9 ± 49.4	484.4 ± 50.1	488.5 ± 50.5
Female	Control	251.9 ± 49.0	253.7 ± 49.3	254.1 ± 49.8	257.0 ± 48.7	263.8 ± 49.3
	PG	244.4 ± 51.1	245.2 ± 50.3	247.8 ± 54.1	251.4 ± 51.0	257.5 ± 52.8
	0.5%PO	243.8 ± 31.7	244.1 ± 32.8	244.4 ± 32.7	251.7 ± 34.9	255.1 ± 31.9
	1.0%PO	233.1 ± 27.6	234.4 ± 25.7	232.6 ± 23.0	237.8 ± 25.6	244.8 ± 26.5

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

Mean body weight gain ﾋﾞｮｳﾀｲ ｾｲｼﾞｮｳ (g:mean.sd)

Sex	Dose	Weeks 41	42	43	44	45
Male	Control	472.8 ± 66.8	473.3 ± 70.5	478.0 ± 68.9	479.5 ± 69.6	483.4 ± 69.7
	PG	503.2 ± 59.3	505.8 ± 58.2	507.2 ± 59.6	515.2 ± 57.7	517.2 ± 58.2
	0.5%PO	500.6 ± 64.4	502.1 ± 65.9	506.7 ± 68.2	513.6 ± 70.4	518.2 ± 70.5
	1.0%PO	482.4 ± 55.9	476.4 ± 79.6	493.0 ± 55.2	496.9 ± 50.2	499.6 ± 50.7
Female	Control	259.4 ± 51.0	264.9 ± 50.9	266.8 ± 50.1	272.6 ± 51.9	272.4 ± 49.5
	PG	255.4 ± 56.1	261.2 ± 56.7	264.5 ± 59.3	265.7 ± 58.0	269.7 ± 60.3
	0.5%PO	255.2 ± 33.4	257.9 ± 31.5	258.3 ± 32.4	265.7 ± 34.0	266.1 ± 33.2
	1.0%PO	242.9 ± 31.6	246.5 ± 28.8	247.6 ± 28.1	251.7 ± 28.9	251.4 ± 26.8

*:Significantry different from control ($p<0.05$)
**:Significantry different from control ($p<0.01$)

Mean body weight gain　　ﾋﾞｰｸﾞﾙ ｵｽｽ　　(g:mean.sd)

Sex	Dose	Weeks 46	47	48	49	50
Male	Control	485.4 ± 71.9	488.5 ± 72.0	493.1 ± 72.6	494.2 ± 76.6	499.4 ± 77.9
	PG	514.9 ± 61.6	517.5 ± 65.9	523.1 ± 65.3	521.2 ± 65.7	527.3 ± 68.7
	0.5%PO	518.2 ± 67.2	520.6 ± 68.8	526.3 ± 69.9	527.2 ± 68.9	529.5 ± 69.5
	1.0%PO	500.7 ± 53.8	506.8 ± 54.2	509.7 ± 55.5	508.0 ± 57.6	510.2 ± 55.2
Female	Control	277.4 ± 52.4	277.9 ± 54.3	281.4 ± 55.7	280.5 ± 53.3	282.3 ± 56.7
	PG	272.9 ± 61.2	274.4 ± 60.7	278.9 ± 63.2	276.4 ± 62.8	279.8 ± 66.4
	0.5%PO	267.0 ± 30.1	270.8 ± 34.7	271.6 ± 36.2	272.4 ± 39.0	276.8 ± 40.6
	1.0%PO	256.7 ± 28.8	260.1 ± 31.6	261.5 ± 30.4	260.5 ± 28.9	262.3 ± 31.6

*:Significantry different from control (p<0.05)
**:Significantry different from control (p<0.01)

Mean body weight gain　　ﾋﾟﾛｸﾄﾝ ｵﾗﾐﾝ　　(g:mean.sd)

Sex	Dose	Weeks 51	52	53	54	55
Male	Control	501.6 ± 78.9	501.1 ± 77.1	489.0 ± 51.1	490.3 ± 50.1	495.0 ± 54.7
	PG	531.5 ± 67.4	529.5 ± 69.0	565.5 ± 112.6	567.3 ± 114.0	571.5 ± 113.4
	0.5%PO	532.2 ± 69.8	529.9 ± 68.4	493.3 ± 8.4	495.7 ± 9.6	500.3 ± 1.2
	1.0%PO	511.6 ± 60.7	509.0 ± 58.3	536.3 ± 46.9	538.0 ± 49.0	543.0 ± 49.1
Female	Control	283.4 ± 58.5	284.6 ± 56.4	305.8 ± 55.3	310.0 ± 54.8	312.8 ± 54.1
	PG	282.5 ± 65.2	285.8 ± 65.5	344.3 ± 112.6	348.5 ± 110.3	357.8 ± 119.4
	0.5%PO	274.8 ± 38.5	277.8 ± 39.6	285.0 ± 44.4	292.8 ± 39.6	291.0 ± 45.3
	1.0%PO	258.6 ± 30.3	264.8 ± 29.6	263.8 ± 20.8	264.8 ± 23.6	267.8 ± 22.9

*:Significantry different from control　($p<0.05$)
**:Significantry different from control　($p<0.01$)

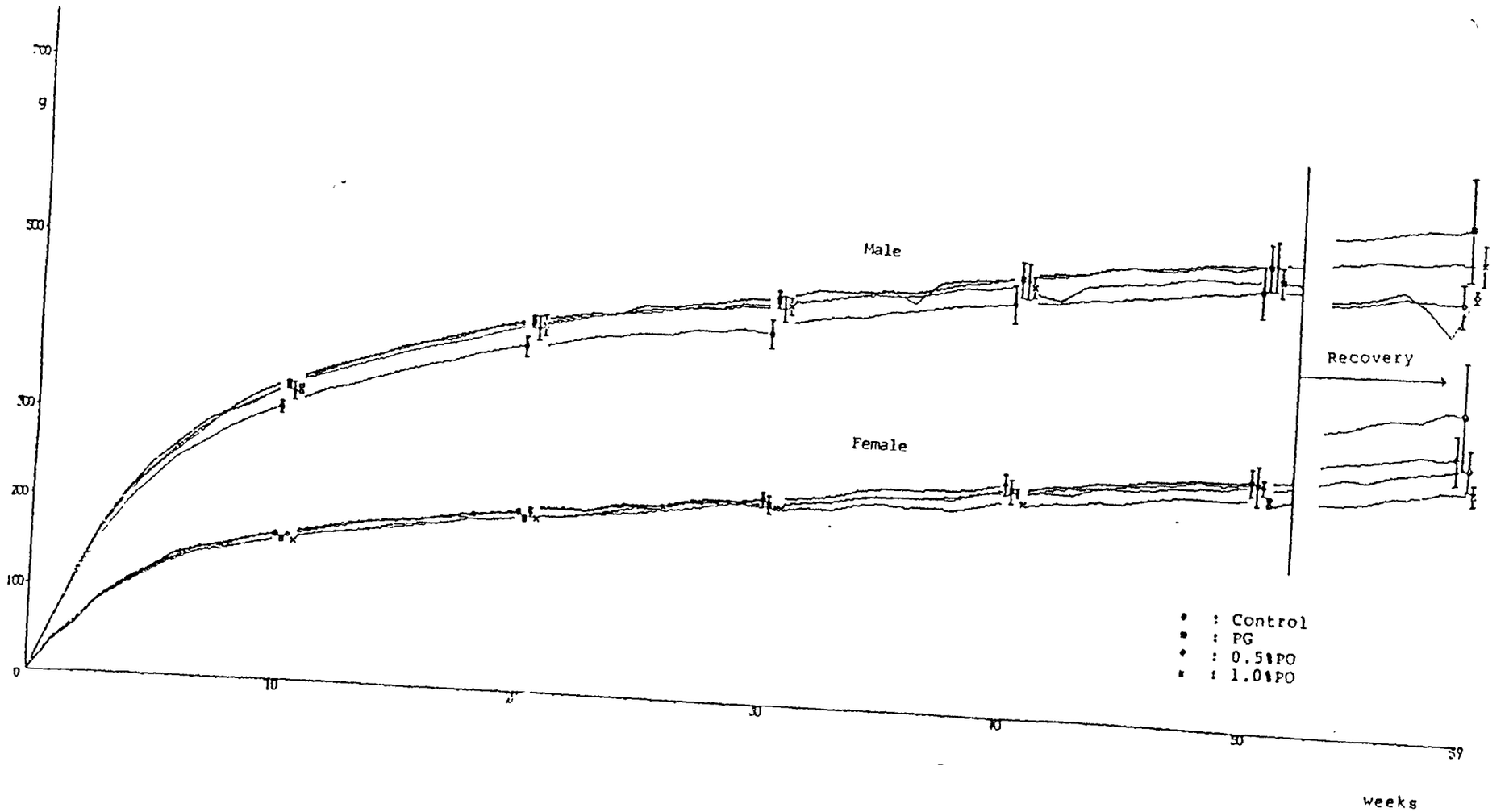
Mean body weight gain　　ﾋﾞｰｸﾞﾙﾝｶﾞｲﾄﾞ　　(g:mean.sd)

Sex	Dose	Weeks 56	57	58	59
Male	Control	502.0 ± 56.9	500.3 ± 53.8	499.5 ± 53.2	499.8 ± 54.8
	PG	577.0 ± 114.5	580.8 ± 115.4	580.5 ± 116.9	588.8 ± 120.1
	0.5%PO	509.7 ± 0.6	490.7 ± 37.9	461.3 ± 101.7	512.0 ± 7.1
	1.0%PO	543.3 ± 50.4	543.0 ± 52.6	547.5 ± 52.6	544.8 ± 52.2
Female	Control	317.0 ± 54.2	322.3 ± 60.6	321.3 ± 55.5	323.8 ± 59.7
	PG	363.3 ± 108.1	362.8 ± 117.4	374.0 ± 119.2	372.5 ± 118.8
	0.5%PO	299.3 ± 43.4	303.5 ± 47.7	306.3 ± 49.7	311.5 ± 48.7
	1.0%PO	275.3 ± 22.2	277.3 ± 18.0	283.8 ± 21.7	284.8 ± 20.0

*:Significantry different from control (p<0.05)
**:Significantry different from control (p<0.01)

Figure - 1

Average body weight gain



Food efficiency
(Table 3)

Table - 3

Food efficiency

ﾋﾟﾛｸﾄﾝ ｵﾗﾐﾝ

Piroctone Olamine

Sex	Dose	Weeks 1	2	3	4	5
Male						
Control	Body weight	58	113	159	196	224
	T.food weight	174	358	553	748	941
	Food efficiency	33	31	29	26	24
PG	Body weight	61	121	171	210	242
	T.food weight	182	377	588	795	1001
	Food efficiency	33	32	29	26	24
0.5%PO	Body weight	59	116	166	204	234
	T.food weight	173	362	568	771	972
	Food efficiency	34	32	29	26	24
1.0%PO	Body weight	63	119	168	208	236
	T.food weight	182	377	582	788	979
	Food efficiency	34	31	29	26	24
Female						
Control	Body weight	38	63	90	109	123
	T.food weight	143	277	422	568	722
	Food efficiency	27	23	21	19	17
PG	Body weight	35	57	86	103	118
	T.food weight	138	268	406	547	693
	Food efficiency	25	21	21	19	17
0.5%PO	Body weight	38	62	88	106	122
	T.food weight	138	269	410	551	703
	Food efficiency	27	23	21	19	17
1.0%PO	Body weight	36	59	86	105	121
	T.food weight	135	264	402	544	693
	Food efficiency	27	22	21	19	17

Food efficiency
ﾋﾟﾛｸﾄﾝ ｵﾗﾙ

Sex	Dose	Weeks 6	7	8	9	10
Male						
Control	Body weight	250	266	283	297	309
	T.food weight	1127	1312	1502	1686	1874
	Food efficiency	22	20	19	18	16
PG	Body weight	266	288	304	321	334
	T.food weight	1198	1395	1597	1796	1995
	Food efficiency	22	21	19	18	17
0.5%PO	Body weight	258	279	301	315	327
	T.food weight	1165	1356	1551	1741	1938
	Food efficiency	22	21	19	18	17
1.0%PO	Body weight	261	283	301	312	328
	T.food weight	1176	1375	1573	1760	1961
	Food efficiency	22	21	19	18	17
Female						
Control	Body weight	140	148	151	160	166
	T.food weight	869	1014	1157	1305	1451
	Food efficiency	16	15	13	12	11
PG	Body weight	132	143	147	154	160
	T.food weight	834	975	1112	1255	1395
	Food efficiency	16	15	13	12	11
0.5%PO	Body weight	135	148	153	161	166
	T.food weight	847	992	1135	1281	1426
	Food efficiency	16	15	13	13	12
1.0%PO	Body weight	134	144	149	154	159
	T.food weight	834	974	1116	1256	1398
	Food efficiency	16	15	13	12	11

Food efficiency
ﾋﾟﾛｸﾄﾝ ｵﾗﾐﾝ

Sex	Dose	Weeks 11	12	13	14	15
Male						
Control	Body weight	320	332	337	348	356
	T.food weight	2058	2238	2417	2592	2768
	Food efficiency	16	15	14	13	13
PG	Body weight	346	356	365	373	381
	T.food weight	2189	2378	2567	2754	2944
	Food efficiency	16	15	14	14	13
0.5%PO	Body weight	341	350	359	368	376
	T.food weight	2129	2313	2500	2684	2869
	Food efficiency	16	15	14	14	13
1.0%PO	Body weight	343	353	364	373	384
	T.food weight	2160	2350	2543	2732	2924
	Food efficiency	16	15	14	14	13
Female						
Control	Body weight	169	174	180	187	188
	T.food weight	1596	1736	1874	2018	2161
	Food efficiency	11	10	10	9	9
PG	Body weight	165	170	173	177	183
	T.food weight	1535	1675	1811	1950	2089
	Food efficiency	11	10	10	9	9
0.5%PO	Body weight	171	176	183	187	189
	T.food weight	1571	1714	1858	1999	2139
	Food efficiency	11	10	10	9	9
1.0%PO	Body weight	164	170	173	177	180
	T.food weight	1539	1677	1815	1952	2090
	Food efficiency	11	10	10	9	9

Food efficiency
ﾋﾟﾛｸﾄﾝ ｵﾗﾐﾝ

Sex	Dose	Weeks 16	17	18	19	20
Male						
Control	Body weight	364	370	379	385	391
	T.food weight	2946	3126	3303	3484	3663
	Food efficiency	12	12	11	11	11
PG	Body weight	390	395	404	413	419
	T.food weight	3135	3323	3510	3701	3890
	Food efficiency	12	12	12	11	11
0.5%PO	Body weight	384	390	397	406	413
	T.food weight	3051	3231	3408	3595	3778
	Food efficiency	13	12	12	11	11
1.0%PO	Body weight	390	398	406	413	416
	T.food weight	3114	3306	3495	3690	3876
	Food efficiency	13	12	12	11	11
Female						
Control	Body weight	191	194	196	202	203
	T.food weight	2305	2448	2588	2737	2882
	Food efficiency	8	8	8	7	7
PG	Body weight	187	189	193	195	197
	T.food weight	2227	2366	2505	2644	2784
	Food efficiency	8	8	8	7	7
0.5%PO	Body weight	191	195	200	201	204
	T.food weight	2282	2425	2570	2715	2860
	Food efficiency	8	8	8	7	7
1.0%PO	Body weight	184	187	194	194	197
	T.food weight	2228	2369	2511	2652	2796
	Food efficiency	8	8	8	7	7

Food efficiency
ﾋﾞﾛｸﾄﾝ ｵﾗﾙ

Sex	Dose	Weeks 21	22	23	24	25
Male						
Control	Body weight	393	400	406	408	413
	T.food weight	3840	4021	4204	4387	4572
	Food efficiency	10	10	10	9	9
PG	Body weight	423	429	433	434	445
	T.food weight	4077	4272	4465	4662	4862
	Food efficiency	10	10	10	9	9
0.5%PO	Body weight	417	423	429	434	436
	T.food weight	3963	4151	4343	4536	4727
	Food efficiency	11	10	10	10	9
1.0%PO	Body weight	419	427	429	432	440
	T.food weight	4061	4254	4445	4641	4837
	Food efficiency	10	10	10	9	9
Female						
Control	Body weight	209	212	209	217	220
	T.food weight	3032	3178	3324	3475	3624
	Food efficiency	7	7	6	6	6
PG	Body weight	200	201	206	210	216
	T.food weight	2925	3066	3214	3362	3512
	Food efficiency	7	7	6	6	6
0.5%PO	Body weight	210	209	210	216	218
	T.food weight	3009	3152	3298	3451	3599
	Food efficiency	7	7	6	6	6
1.0%PO	Body weight	201	202	204	207	210
	T.food weight	2940	3084	3230	3379	3529
	Food efficiency	7	7	6	6	6

Food efficiency
ﾋﾟﾛｸﾄﾝ ｵﾗﾙ

Sex	Dose	Weeks 26	27	28	29	30
Male						
Control	Body weight	412	419	419	423	420
	T.food weight	4757	4948	5132	5326	5518
	Food efficiency	9	8	8	8	8
PG	Body weight	443	449	452	458	460
	T.food weight	5060	5264	5465	5676	5882
	Food efficiency	9	9	8	8	8
0.5%PO	Body weight	440	445	444	450	450
	T.food weight	4921	5120	5314	5509	5705
	Food efficiency	9	9	8	8	8
1.0%PO	Body weight	441	445	446	452	452
	T.food weight	5038	5238	5441	5645	5845
	Food efficiency	9	8	8	8	8
Female						
Control	Body weight	220	226	227	229	232
	T.food weight	3772	3923	4073	4217	4370
	Food efficiency	6	6	6	5	5
PG	Body weight	217	223	226	229	228
	T.food weight	3665	3817	3968	4123	4271
	Food efficiency	6	6	6	6	5
0.5%PO	Body weight	219	225	227	229	224
	T.food weight	3754	3905	4060	4215	4365
	Food efficiency	6	6	6	5	5
1.0%PO	Body weight	214	217	222	226	224
	T.food weight	3679	3831	3985	4143	4298
	Food efficiency	6	6	6	5	5

Food efficiency
ﾋﾟﾛｸﾄﾝ ｵﾗﾙ

Sex	Dose	Weeks 31	32	33	34	35
Male						
Control	Body weight	433	440	443	445	452
	T.food weight	5716	5917	6116	6314	6517
	Food efficiency	8	7	7	7	7
PG	Body weight	465	472	473	474	476
	T.food weight	6093	6305	6514	6719	6926
	Food efficiency	8	7	7	7	7
0.5%PO	Body weight	456	461	466	471	477
	T.food weight	5906	6110	6314	6520	6732
	Food efficiency	8	8	7	7	7
1.0%PO	Body weight	459	461	466	469	472
	T.food weight	6054	6260	6474	6686	6904
	Food efficiency	8	7	7	7	7
Female						
Control	Body weight	235	238	241	249	252
	T.food weight	4524	4679	4838	4998	5154
	Food efficiency	5	5	5	5	5
PG	Body weight	229	232	235	241	244
	T.food weight	4421	4577	4742	4902	5064
	Food efficiency	5	5	5	5	5
0.5%PO	Body weight	229	233	235	241	243
	T.food weight	4522	4685	4853	5017	5182
	Food efficiency	5	5	5	5	5
1.0%PO	Body weight	223	227	226	233	236
	T.food weight	4454	4611	4778	4947	5111
	Food efficiency	5	5	5	5	5

Food efficiency
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Sex	Dose	Weeks 36	37	38	39	40
Male						
Control	Body weight	454	460	464	465	468
	T.food weight	6719	6921	7120	7321	7520
	Food efficiency	7	7	7	6	6
PG	Body weight	464	488	493	494	497
	T.food weight	7121	7335	7548	7765	7976
	Food efficiency	7	7	7	6	6
0.5%PO	Body weight	476	482	488	491	497
	T.food weight	6941	7150	7357	7567	7773
	Food efficiency	7	7	7	6	6
1.0%PO	Body weight	472	477	484	484	489
	T.food weight	7116	7334	7547	7761	7970
	Food efficiency	7	7	6	6	6
Female						
Control	Body weight	252	254	254	257	264
	T.food weight	5311	5470	5627	5783	5941
	Food efficiency	5	5	5	4	4
PG	Body weight	244	245	248	251	258
	T.food weight	5225	5390	5555	5719	5886
	Food efficiency	5	5	4	4	4
0.5%PO	Body weight	244	244	244	252	255
	T.food weight	5347	5511	5676	5844	6012
	Food efficiency	5	4	4	4	4
1.0%PO	Body weight	233	234	233	238	245
	T.food weight	5274	5440	5606	5775	5942
	Food efficiency	4	4	4	4	4

Food efficiency
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Sex	Dose	Weeks 41	42	43	44	45
Male						
Control	Body weight	473	473	478	480	483
	T.food weight	7715	7911	8103	8298	8498
	Food efficiency	6	6	6	6	6
PG	Body weight	503	506	507	515	517
	T.food weight	8186	8396	8608	8822	9036
	Food efficiency	6	6	6	6	6
0.5%PO	Body weight	501	502	507	514	518
	T.food weight	7975	8180	8380	8587	8790
	Food efficiency	6	6	6	6	6
1.0%PO	Body weight	482	476	493	497	500
	T.food weight	8170	8371	8576	8785	8993
	Food efficiency	6	6	6	6	6
Female						
Control	Body weight	259	265	267	273	272
	T.food weight	6100	6259	6419	6579	6738
	Food efficiency	4	4	4	4	4
PG	Body weight	255	261	265	266	270
	T.food weight	6050	6211	6375	6537	6705
	Food efficiency	4	4	4	4	4
0.5%PO	Body weight	255	258	258	266	266
	T.food weight	6178	6342	6505	6674	6839
	Food efficiency	4	4	4	4	4
1.0%PO	Body weight	243	247	248	252	251
	T.food weight	6110	6272	6433	6596	6761
	Food efficiency	4	4	4	4	4

Food efficiency

Sex	Dose	Weeks 46	47	48	49	50
Male						
Control	Body weight	485	489	493	494	499
	T.food weight	8699	8898	9098	9290	9484
	Food efficiency	6	5	5	5	5
PG	Body weight	515	518	523	521	527
	T.food weight	9250	9460	9671	9876	10082
	Food efficiency	6	5	5	5	5
0.5%PO	Body weight	518	521	526	527	529
	T.food weight	8995	9198	9403	9604	9799
	Food efficiency	6	6	6	5	5
1.0%PO	Body weight	501	507	510	508	510
	T.food weight	9206	9416	9627	9834	10037
	Food efficiency	5	5	5	5	5
Female						
Control	Body weight	277	278	281	281	282
	T.food weight	6899	7058	7222	7381	7538
	Food efficiency	4	4	4	4	4
PG	Body weight	273	274	279	276	280
	T.food weight	6863	7023	7187	7341	7495
	Food efficiency	4	4	4	4	4
0.5%PO	Body weight	267	271	272	272	277
	T.food weight	7002	7165	7326	7486	7647
	Food efficiency	4	4	4	4	4
1.0%PO	Body weight	257	260	262	261	262
	T.food weight	6930	7097	7258	7419	7580
	Food efficiency	4	4	4	4	3

Food efficiency
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Sex	Dose	Weeks 51	52	53	54	55
Male						
Control	Body weight	502	501	489	490	495
	T.food weight	9678	9871	10066	10253	10447
	Food efficiency	5	5	5	5	5
PG	Body weight	532	529	566	567	572
	T.food weight	10287	10491	10705	10920	11136
	Food efficiency	5	5	5	5	5
0.5%PO	Body weight	532	530	493	496	500
	T.food weight	9997	10196	10395	10592	10793
	Food efficiency	5	5	5	5	5
1.0%PO	Body weight	512	509	536	538	543
	T.food weight	10244	10443	10657	10866	11074
	Food efficiency	5	5	5	5	5
Female						
Control	Body weight	283	285	306	310	313
	T.food weight	7699	7858	8019	8179	8335
	Food efficiency	4	4	4	4	4
PG	Body weight	283	286	344	349	358
	T.food weight	7656	7816	7987	8151	8326
	Food efficiency	4	4	4	4	4
0.5%PO	Body weight	275	278	285	293	291
	T.food weight	7810	7972	8124	8281	8428
	Food efficiency	4	3	4	4	3
1.0%PO	Body weight	259	265	264	265	268
	T.food weight	7744	7906	8049	8204	8355
	Food efficiency	3	3	3	3	3

Food efficiency
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Sex	Dose	Weeks 56	57	58	59
Male					
Control	Body weight	502	500	500	500
	T.food weight	10641	10834	11019	11205
	Food efficiency	5	5	5	4
PG	Body weight	577	581	581	589
	T.food weight	11353	11565	11777	11990
	Food efficiency	5	5	5	5
0.5%PO	Body weight	510	491	461	512
	T.food weight	10991	11162	11301	11484
	Food efficiency	5	4	4	4
1.0%PO	Body weight	543	543	548	545
	T.food weight	11286	11495	11701	11909
	Food efficiency	5	5	5	5
Female					
Control	Body weight	317	322	321	324
	T.food weight	8501	8659	8823	8984
	Food efficiency	4	4	4	4
PG	Body weight	363	363	374	373
	T.food weight	8500	8665	8839	9005
	Food efficiency	4	4	4	4
0.5%PO	Body weight	299	304	306	312
	T.food weight	8581	8747	8900	9061
	Food efficiency	3	3	3	3
1.0%PO	Body weight	275	277	284	285
	T.food weight	8504	8657	8816	8969
	Food efficiency	3	3	3	3

Table - 10 - 1

Histopathological findings of rats

臓器	所見	♂ Control 10				♂ PG 9				♂ 0.5%PO 10				♂ 1.0%PO 9				♀ Control 10				♀ PG 10				♀ 0.5%PO 10				♀ 1.0%PO 10			
		±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++
Liver	Activation of the Kupffer cells					1																											
	Cell infiltration in the lobule													1																			
	Fatty change					1												2									1						
	Fatty degeneration														1													1					
	Focal necrosis																					1											
Kidney	Interstitial inflammation	5 3	1			5 4	1			1 1	1			1 1	3			1				1				1	1						
	Hyaline cast	5 2	1 2			3 2	2 1			1 1	1			1 1	4			2 2				2 1				1 1	1			1 1	1 1		
	Degeneration of the tubular epithelical cells					1									1																		
	Dilation with flattened epithelium of the tubular lumen																									1				1			
	Calcification	1													1							1				1 1							
	Congestion																					1											
	Yellowish pigment in the epithelium	1																															
	Cyst														1												1						
	Chronic nephritis	1												1												1							

Kidney : Right / Left

± : very slight
+ : slight
++ : medium
+++ : serious

Table - 10 - 2

Histopathological findings of rats

臓器	所見	♂ Control 10				♂ PG 9				♂ 0.5%PO 10				♂ 1.0%PO 9				♀ Control 10				♀ PG 10				♀ 0.5%PO 10				♀ 1.0%PO 10			
		±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++	±	+	++	+++
Spleen	Atrophy of the white pulp					1																											
	Hypertrophy						1																										
Adrenal	Congestion																	3				1				1					1		
	Cyst																						1			1	1			2 3			
	Degeneration																	1															
Heart	Degeneration of the muscle	1																								1							
Lung	Foamy cell	1																1															
Lymphonodi	Axillary lymphonodi Congestion													1																			
	Mesenteric lymphonodi Congestion													1																			
Skin	Thickening of the epidermis									4				4	4											4	1				3	3	
	Necrosis of the epidermis													2																4			
	Proliferation of the deep tissue													1												1				4			

Adrenal : Right / Left

± : very slight
+ : slight
++ : medium
+++ : serious

Table - 4

Urinary findings of rats

Sex	Sample	Number of animals	pH				Protein					Glucose		Ketone body		Occult blood			Bilirubin	Urobilinogen	
			6.0	6.5	7.0	7.5	T	+	++	+++	++++	-	T	-	+	-	+	++	-	±	+
Male	Control	10	2	4	2	2	0	0	4	4	2	9	1	10	0	9	1	0	10	9	1
	PG	9	3	5	1	0	0	0	3	4	2	9	0	9	0	9	0	0	9	8	1
	0.5%PO	10	5	4	1	0	0	0	2	5	3	10	0	10	0	8	2	0	10	10	0
	1.0%PO	9	5	4	0	0	0	0	3	3	3	9	0	9	0	9	0	0	9	7	2
Female	Control	10	8	1	1	0	2	2	3	2	1	10	0	10	0	10	0	0	10	9	1
	PG	10	3	3	3	1	2	6	0	1	1	10	0	10	0	10	0	0	10	8	2
	0.5%PO	10	4	3	2	1	2	2	3	2	1	10	0	10	0	9	0	1	10	10	0
	1.0%PO	10	5	4	0	1	2	2	2	3	1	10	0	9	1	9	0	1	10	7	3

T : Trace

Table - 5

Urinary sediment of rats

Sex	Sample	Number of animals	RBC				WBC				Epithelial cells		Casts	Crystals				Others
			-	±	+	++	-	±	+	++	-	±	-	-	±	+	++	
Male	Control	5	2	2	1	0	3	1	0	1	0	5	5	0	3	1	1	Sp(2)
	PG	5	4	0	0	1	4	1	0	0	0	5	5	2	3	0	0	
	0.5%PO	5	3	1	1	0	3	2	0	0	0	5	5	2	2	1	0	
	1.0%PO	5	2	3	0	0	3	2	0	0	1	4	5	3	2	0	0	Sp(1)
Female	Control	5	5	0	0	0	5	0	0	0	0	5	5	2	3	0	0	
	PG	5	5	0	0	0	4	1	0	0	0	5	5	4	1	0	0	
	0.5%PO	5	5	0	0	0	5	0	0	0	4	1	5	5	0	0	0	
	1.0%PO	5	5	0	0	0	5	0	0	0	2	3	5	3	2	0	0	

RBC , Epithelial cells , Crystals

- : 0 / 100 fields
± : 1-99 / 100 fields
+ : 100-999 / 100 fields
++ : 1000-4999 / 100 fields

WBC , Casts

- : 0 / 100 fields
± : 1-9 / 100 fields
+ : 10-99 / 100 fields
++ : 100-999 / 100 fields

Sp : Spermatozoa

Table - 6

Average hematological findings of rats

Sex	Sample	Number of animals	RBC ($10^4/mm^3$)	Hb (g/dl)	Ht (%)	MCV (μ^3)	MCHC (%)	Platelet ($10^4/mm^3$)	WBC ($10^2/mm^3$)	Differential blood count (%)					
										Baso	Eosino	N-st	N-seg	Lymph	Mono
Male	Control	10	589.5 ±139.6	11.32 ±2.91	37.5 ±6.1	65.6 ±9.9	29.7 ±4.7	66.9 ±11.5	33.8 ±20.4	0.0 ±0.0	0.9 ±1.1	2.0 ±2.4	21.8 ±13.6	73.7 ±15.7	1.6 ±1.2
	PG	9	544.3 ±140.1	11.19 ±3.23	36.6 ±7.5	68.7 ±8.0	30.1 ±3.3	71.4 ±8.7	30.6 ±17.6	0.0 ±0.0	1.1 ±0.9	5.1 ±4.2	27.7 ±12.6	64.3 ±16.2	1.8 ±2.1
	0.5%PO	10	581.3 ±110.3	12.08 ±3.10	37.6 ±6.9	64.8 ±4.0	31.5 ±3.5	80.9 ±19.0	24.4 ±17.1	0.0 ±0.0	1.5 ±1.0	4.0 ±6.2	25.7 ±16.3	67.5 ±20.3	1.3 ±1.3
	1.0%PO	9	608.1 ±132.7	12.21 ±2.90	38.6 ±7.0	64.2 ±4.3	31.4 ±3.0	79.7 ±20.8	31.0 ±17.9	0.0 ±0.0	1.7 ±1.7	3.6 ±4.7	25.6 ±8.4	66.0 ±11.2	3.2 ±4.3
Female	Control	10	596.4 ±99.8	13.64 ±1.69	41.4 ±4.5	70.3 ±7.2	32.9 ±1.1	63.7 ±11.4	20.9 ±6.9	0.0 ±0.0	2.5 ±1.4	2.9 ±2.0	21.8 ±16.3	71.4 ±17.8	1.4 ±1.0
	PG	10	600.9 ±40.7	13.58 ±0.88	40.4 ±1.5	67.4 ±4.6	33.7 ±1.7	55.0* ±6.2	10.7** ±5.9	0.0 ±0.0	2.6 ±1.4	0.9* ±1.5	17.9 ±5.0	77.8 ±7.3	0.7 ±0.8
	0.5%PO	10	492.6* ±122.4	11.69 ±2.56	35.3* ±6.1	73.4 ±10.1	32.9 ±2.5	53.6* ±8.2	20.2 ±11.1	0.0 ±0.0	2.5 ±2.7	1.4* ±0.8	21.7 ±13.3	73.6 ±12.6	0.6 ±0.8
	1.0%PO	10	570.3 ±85.0	12.94 ±1.66	38.6 ±4.6	68.0 ±3.6	33.6 ±1.8	56.4 ±13.8	17.8 ±8.1	0.0 ±0.0	2.3 ±1.5	1.2* ±1.0	18.3 ±6.0	78.0 ±6.9	0.2** ±0.4

(Mean ± S.D.)

* : Significantly different from control ($p<0.05$)

** : Significantly different from control ($p<0.01$)

Table - 7

Average biochemical findings of rats

Sex	Sample	Number of animals	s-GOT (mu/ml)	s-GPT (mu/ml)	Al-phos. (mu/ml)	Biliru-bin (mg/dl)	T. choles-terol (mg/dl)	Glu-cose (mg/dl)	BUN (mg/dl)	Crea-tinine (mg/dl)	T. pro-teine (g/dl)	Al-bumin (g/dl)	A/G (ratio)	Na^+ (mEq/l)	K^+ (mEq/l)	Cl^- (mEq/l)	P (mg/dl)
Male	Control	10	201.8 ±42.8	71.0 ±23.7	106.5 ±24.5	0.23 ±0.05	79.4 ±11.9	250.5 ±27.0	17.9 ±2.2	0.69 ±0.07	5.99 ±0.36	3.23 ±0.21	1.17 ±0.08	153.8 ±6.9	5.18 ±0.33	108.1 ±1.3	6.00 ±0.66
	PG	9	171.1 ±55.4	71.3 ±26.7	98.2 ±7.5	0.28 ±0.07	77.8 ±16.3	246.2 ±27.8	18.1 ±1.6	0.73 ±0.09	5.78 ±0.26	3.00* ±0.19	1.08* ±0.07	155.0 ±5.6	5.11 ±0.18	109.0 ±1.8	5.67 ±0.46
	0.5%PO	10	182.9 ±126.2	73.8 ±38.0	104.5 ±28.1	0.28 ±0.08	87.0 ±21.1	253.6 ±33.3	16.9 ±2.0	0.70 ±0.05	5.97 ±0.26	3.15 ±0.20	1.12 ±0.09	154.9 ±4.5	5.16 ±0.61	109.1 ±2.2	5.56 ±0.40
	1.0%PO	9	190.9 ±92.6	96.3 ±55.0	125.3 ±50.4	0.27 ±0.07	87.1 ±31.8	244.6 ±37.2	17.7 ±1.7	0.72 ±0.08	5.71 ±0.51	2.99 ±0.36	1.11 ±0.16	155.3 ±5.5	5.01 ±0.49	107.9 ±7.6	5.71 ±0.54
Female	Control	10	311.5 ±215.9	151.1 ±133.1	74.2 ±20.8	0.24 ±0.07	92.4 ±16.3	228.3 ±37.5	18.4 ±1.9	0.69 ±0.11	6.71 ±0.46	3.57 ±0.27	1.16 ±0.20	154.2 ±8.0	4.44 ±0.31	107.2 ±1.3	5.65 ±0.50
	PG	10	183.7 ±42.8	89.4 ±36.3	52.6* ±11.9	0.28 ±0.06	109.8* ±18.1	232.7 ±18.1	15.7** ±0.9	0.71 ±0.11	6.78 ±0.39	3.73 ±0.25	1.23 ±0.11	158.0 ±9.1	4.26 ±0.54	108.0 ±2.2	5.12* ±0.39
	0.5%PO	10	187.4 ±67.9	86.1 ±34.7	61.0 ±24.9	0.21 ±0.06	85.5 ±25.9	248.0 ±44.6	17.9 ±2.9	0.71 ±0.09	6.49 ±0.57	3.46 ±0.46	1.15 ±0.18	153.0 ±8.0	4.33 ±0.39	109.4 ±2.9	5.69 ±0.66
	1.0%PO	10	200.2 ±55.6	94.1 ±23.9	60.1 ±17.8	0.28 ±0.06	93.1 ±19.7	210.2 ±31.0	17.9 ±2.4	0.78 ±0.11	6.72 ±0.43	3.74 ±0.28	1.26 ±0.09	154.9 ±5.1	4.32 ±0.35	109.2** ±1.6	5.57 ±0.90

(Mean ± S.D)

* : Significantly different from control ($p<0.05$)

** : Significantly different from control ($p<0.01$)

Table - 8

Average absolute wet organ weight of rats

Sex	Sample	Number of animals	Final B.W.	Liver	Kidney R	Kidney L	Spleen	Adrenal gland R	Adrenal gland L	Heart	Lung	Brain	Pituitary ‖	Thymus ‖	Testis or Ovary ‖ R	Testis or Ovary ‖ L
Male	Control	10	648.7 ±91.7	19.282 ±2.208	1.959 ±0.147	1.905 ±0.129	0.988 ±0.411	27.3 ±4.5	27.6 ±5.3	1.640 ±0.194	1.631 ±0.107	2.091 ±0.087	13.8 ±2.5	0.094 ±0.021	1.679 ±0.127	1.675 ±0.141
	PG	9	660.3 ±44.4	19.030 ±2.133	2.003 ±0.223	1.959 ±0.195	1.150 ±0.625	27.0 ±4.0	28.6 ±4.3	1.794 ±0.190	1.804** ±0.138	2.109 ±0.097	12.4 ±2.1	0.073 ±0.021	1.717 ±0.120	1.716 ±0.120
	0.5%PO	10	686.1 ±75.0	19.688 ±2.355	1.924 ±0.130	1.913 ±0.123	1.056 ±0.398	28.0 ±4.1	28.6 ±4.9	1.755 ±0.250	1.706 ±0.126	2.139 ±0.058	13.4 ±3.7	0.109 ±0.031	1.732 ±0.119	1.719 ±0.103
	1.0%PO	9	644.6 ±64.2	19.462 ±0.304	2.023 ±0.364	1.991 ±0.356	1.142 ±0.439	30.1 ±8.7	33.9 ±8.4	1.782 ±0.203	1.783 ±0.219	2.127 ±0.069	16.4 ±10.2	0.090 ±0.021	1.863* ±0.180	1.844* ±0.183
Female	Control	10	397.1 ±66.7	12.316 ±1.878	1.214 ±0.152	1.146 ±0.133	0.613 ±0.144	36.6 ±6.7	43.3 ±8.3	1.169 ±0.165	1.277 ±0.121	1.941 ±0.096	26.0 ±11.7	0.104 ±0.044	30.2 ±10.2	31.4 ±7.1
	PG	10	379.3 ±26.2	11.913 ±0.743	1.196 ±0.070	1.189 ±0.077	0.572 ±0.075	42.1 ±6.4	45.7 ±6.3	1.176 ±0.053	1.259 ±0.059	1.922 ±0.074	24.7 ±3.9	0.104 ±0.028	30.2 ±12.4	38.4 ±15.1
	0.5%PO	10	387.8 ±37.7	12.010 ±1.462	1.313 ±0.303	1.290 ±0.303	0.908 ±0.591	46.7* ±12.1	47.8 ±14.7	1.236 ±0.155	1.330 ±0.231	1.961 ±0.075	29.3 ±9.6	0.111 ±0.049	28.5 ±7.0	34.5 ±10.0
	1.0%PO	10	379.9 ±36.8	11.988 ±1.280	1.258 ±0.101	1.218 ±0.099	0.625 ±0.117	48.1 ±22.8	49.6 ±18.2	1.238 ±0.098	1.300 ±0.092	1.945 ±0.071	32.7 ±18.4	0.114 ±0.033	37.3 ±18.3	36.3 ±18.2

(g , ‖: mg , Mean ± S.D.)

* : Significantly different from control ($p<0.05$)

** : Significantly different from control ($p<0.01$)

Table - 9

Average relative wet organ weight of rats

Sex	Sample	Number of animals	Final B.W.	Liver	Kidney R	Kidney L	Spleen	Adrenal gland R	Adrenal gland L	Heart	Lung	Brain	Pituitary	Thymus	Testis or Ovary R	Testis or Ovary L
Male	Control	10	648.7 ±91.7	2.992 ±0.298	0.306 ±0.036	0.297 ±0.029	0.156 ±0.070	4.25 ±0.72	4.28 ±0.75	0.257 ±0.038	0.256 ±0.039	0.327 ±0.039	2.15 ±0.39	0.015 ±0.005	0.263 ±0.038	0.263 ±0.039
	PG	9	660.3 ±44.4	2.882 ±0.250	0.304 ±0.028	0.296 ±0.025	0.176 ±0.106	4.14 ±0.81	4.37 ±0.76	0.272 ±0.034	0.274 ±0.025	0.321 ±0.033	1.89 ±0.37	0.010** ±0.000	0.260 ±0.014	0.261 ±0.013
	0.5%PO	10	686.1 ±75.0	2.881 ±0.291	0.282 ±0.029	0.281 ±0.028	0.154 ±0.059	4.11 ±0.62	4.20 ±0.80	0.257 ±0.033	0.250 ±0.024	0.315 ±0.037	1.94 ±0.46	0.014 ±0.005	0.253 ±0.030	0.254 ±0.025
	1.0%PO	9	644.6 ±64.2	3.013 ±0.299	0.316 ±0.045	0.309 ±0.041	0.177 ±0.064	4.77 ±1.18	5.24* ±1.00	0.279 ±0.025	0.277 ±0.034	0.333 ±0.032	2.48 ±1.24	0.013 ±0.005	0.291 ±0.030	0.288 ±0.031
Female	Control	10	397.1 ±66.7	3.114 ±0.045	0.311 ±0.039	0.293 ±0.037	0.154 ±0.031	9.41 ±2.20	11.20 ±2.99	0.296 ±0.024	0.326 ±0.431	0.499 ±0.061	6.65 ±3.01	0.025 ±0.007	7.56 ±1.81	7.96 ±1.36
	PG	10	379.3 ±26.2	3.147 ±0.156	0.317 ±0.026	0.314 ±0.027	0.150 ±0.018	11.18 ±2.11	12.08 ±1.67	0.312 ±0.024	0.333 ±0.017	0.507 ±0.028	5.97 ±2.49	0.027 ±0.007	7.91 ±2.93	10.17 ±4.04
	0.5%PO	10	387.8 ±37.7	3.110 ±0.383	0.341 ±0.087	0.335 ±0.085	0.233 ±0.154	12.21* ±3.41	12.52 ±4.13	0.322 ±0.053	0.344 ±0.067	0.511 ±0.043	7.63 ±2.67	0.028 ±0.010	7.32 ±1.46	8.93 ±2.65
	1.0%PO	10	379.9 ±36.8	3.170 ±0.341	0.335 ±0.044	0.323 ±0.039	0.166 ±0.036	12.74 ±6.16	13.20 ±5.12	0.329* ±0.035	0.346 ±0.034	0.516 ±0.048	8.70 ±4.99	0.029 ±0.007	9.79 ±4.54	9.54 ±4.47

(%, ‰: 10^{-3}, Mean ± S.D.)

* : Significantly different from control ($p<0.05$)

** : Significantly different from control ($p<0.01$)

Table - 11

Urinary findings of rats (after the end of the recovery period)

Sex	Sample	Number of animals	pH				Protein					Glucose	Ketone body		Occult blood		Bilirubin	Urobilinogen
			6.0	6.5	7.0	7.5	T	+	++	+++	++++	-	-	+	-	+	-	±
Male	Control	4	2	1	0	1	0	1	0	2	1	4	4	0	3	1	4	4
	PG	4	1	2	1	0	0	0	0	2	2	4	4	0	4	0	4	4
	0.5%PO	2	1	0	1	0	0	0	0	0	2	2	1	1	1	1	4	4
	1.0%PO	4	0	2	0	2	0	1	0	3	0	4	4	0	3	1	4	4
Female	Control	4	1	2	1	0	1	0	0	3	0	4	4	0	4	0	4	4
	PG	4	2	2	0	0	1	2	0	1	0	4	4	0	4	0	4	4
	0.5%PO	4	3	0	1	0	0	3	0	0	1	4	4	0	3	1	4	4
	1.0%PO	4	3	0	1	0	0	2	1	1	0	4	4	0	4	0	4	4

T : Trace

Table - 12

Average hematological findings of rats (after the end of the recovery period)

Sex	Sample	Number of animals	RBC ($10^4/mm^3$)	Hb (g/dl)	Ht (%)	MCV (μ^3)	MCHC (%)	Platelet ($10^4/mm^3$)	WBC ($10^2/mm^3$)	Differential blood count (%)					
										Baso	Eosino	N-st	N-seg	Lymph	Mono
Male	Control	4	498.0 ±125.5	11.43 ±3.86	34.8 ±8.2	70.3 ±10.1	32.3 ±3.5	57.3 ±7.8	21.8 ±13.6	0.3 ±0.5	3.0 ±2.9	2.3 ±1.7	29.3 ±14.9	63.5 ±16.0	1.8 ±1.3
	PG	4	573.3 ±108.9	12.88 ±2.22	39.5 ±6.0	69.3 ±4.3	32.5 ±0.6	84.0* ±17.0	23.3 ±11.9	0.0 ±0.0	2.5 ±1.7	2.0 ±1.4	22.0 ±5.0	72.3 ±5.9	1.3 ±1.3
	0.5%PO	2	619.5 ±81.3	13.35 ±2.05	41.0 ±5.7	66.0 ±0.0	32.5 ±0.7	74.0 ±14.1	14.0 ±4.2	0.0 ±0.0	2.0 ±1.4	3.0 ±1.4	23.0 ±1.4	71.0 ±2.8	1.0 ±1.4
	1.0%PO	4	458.3 ±115.0	9.68 ±2.92	32.8 ±6.7	72.3 ±6.7	29.3 ±3.4	60.8 ±18.2	47.3 ±38.3	0.0 ±0.0	0.8 ±0.5	2.8 ±1.0	31.8 ±8.1	62.3 ±9.1	2.5 ±1.7
Female	Control	4	461.8 ±138.5	11.90 ±2.31	35.5 ±5.8	79.5 ±13.5	33.5 ±1.7	64.3 ±5.6	16.5 ±12.0	0.0 ±0.0	1.5 ±1.3	1.3 ±1.0	29.0 ±15.9	67.0 ±15.4	1.3 ±1.5
	PG	4	606.8 ±17.1	14.33 ±0.66	41.8 ±0.5	68.8 ±1.7	34.3 ±1.7	68.0 ±7.7	19.8 ±7.0	0.0 ±0.0	0.5 ±0.6	1.0 ±1.4	18.0 ±8.8	80.3 ±10.0	0.3 ±0.5
	0.5%PO	4	480.0 ±162.7	12.08 ±3.65	38.3 ±6.9	84.8 ±20.4	31.3 ±4.6	59.8 ±19.0	13.3 ±8.6	0.0 ±0.0	1.5 ±1.7	1.0 ±0.8	25.3 ±8.7	72.0 ±7.4	0.3 ±0.5
	1.0%PO	4	565.3 ±72.6	12.65 ±0.90	37.8 ±1.7	67.5 ±7.4	33.5 ±1.3	74.0 ±14.0	14.8 ±14.4	0.0 ±0.0	1.3 ±0.5	1.0 ±1.4	25.3 ±6.7	71.3 ±9.1	1.3 ±1.3

(Mean ± S.D.)

* : Significantly different from control ($p<0.05$)

** : Significantly different from control ($p<0.01$)

Table - 13

Average biochemical findings of rats (after the end of the recovery period)

Sex	Sample	Number of animals	s-GOT (mu/ml)	s-GPT (mu/ml)	Al-phos. (mu/ml)	Bilirubin (mg/dl)	T. cholesterol (mg/dl)	Glucose (mg/dl)	BUN (mg/dl)	Creatinine (mg/dl)	T. proteine (g/dl)	Albumin (g/dl)	A/G (ratio)	Na^+ (mEq/l)	K^+ (mEq/l)	Cl^- (mEq/l)	P (mg/dl)
Male	Control	4	205.3 ±35.3	64.0 ±16.5	128.0 ±69.1	0.25 ±0.06	82.8 ±12.6	230.8 ±27.3	15.0 ±1.8	0.65 ±0.06	6.08 ±0.05	2.95 ±0.17	0.95 ±0.10	149.8 ±5.6	5.05 ±0.31	108.5 ±1.0	6.25 ±0.52
	PG	4	241.5 ±63.8	106.3 ±51.5	131.5 ±64.4	0.25 ±0.06	93.5 ±20.1	278.0 ±78.7	15.8 ±1.3	0.70 ±0.00	5.93 ±0.26	2.98 ±0.05	1.01 ±0.09	149.0 ±3.3	5.08 ±0.19	106.5 ±1.7	6.48 ±0.10
	0.5%PO	2	233.5 ±128.0	129.5 ±81.3	102.0 ±29.7	0.20 ±0.00	103.5 ±31.8	256.0 ± 4.2	16.5 ±0.7	0.65 ±0.07	6.30* ±0.14	3.15 ±0.21	1.00 ±0.09	156.5 ±4.9	4.80 ±0.00	108.0 ±0.0	6.05 ±0.49
	1.0%PO	4	200.5 ±44.7	67.8 ±12.4	119.8 ±18.6	0.25 ±0.06	98.3 ±29.1	213.0 ±12.7	15.5 ±2.1	0.73 ±0.10	5.98 ±0.13	2.90 ±0.08	0.94 ±0.05	149.0 ±2.8	5.55 ±0.51	108.0 ±0.8	6.45 ±0.41
Female	Control	4	174.8 ±70.2	108.5 ±41.6	75.3 ±9.7	0.15 ±0.06	94.8 ±23.8	233.0 ±25.5	16.8 ±1.0	0.68 ±0.05	6.53 ±0.30	3.40 ±0.16	1.09 ±0.11	148.5 ±4.1	4.30 ±0.42	106.5 ±2.6	5.90 ±0.41
	PG	4	175.5 ±65.9	106.5 ±52.9	67.5 ±32.0	0.05* ±0.06	93.8 ±16.8	262.5 ±47.3	15.3 ±3.2	0.68 ±0.05	6.50 ±0.20	3.60 ±0.08	1.25 ±0.11	147.0 ±4.3	4.18 ±0.46	107.5 ±1.3	5.33 ±0.30
	0.5%PO	4	177.3 ±34.3	114.0 ±19.7	45.8** ±11.0	0.08 ±0.05	95.0 ±14.0	231.5 ±39.8	14.3* ±1.0	0.73 ±0.05	6.60 ±0.37	3.78 ±0.41	1.34 ±0.20	148.8 ±5.6	4.60 ±0.49	109.3 ±1.5	5.73 ±0.46
	1.0%PO	4	110.0 ±35.9	64.0 ±28.6	45.5** ±11.9	0.23 ±0.05	98.5 ±16.9	232.0 ±25.4	14.5* ±1.0	0.65 ±0.10	6.60 ±0.41	3.50 ±0.45	1.16 ±0.27	149.5 ±4.7	4.53 ±0.45	108.8 ±1.5	5.93 ±0.83

(Mean ± S.D.)

* : Significantly different from control ($p<0.05$)

** : Significantly different from control ($p<0.01$)

Table - 14

Average absoluto wet organ weight of rats (after the end of the recovery period)

Sex	Sample	Number of animals	Final B.W.	Liver	Kidney R	Kidney L	Spleen	Adrenal gland R	Adrenal gland L	Heart	Lung	Brain	Pituitary ‖	Thymus ‖	Testis or Ovary R	Testis or Ovary L
Male	Control	4	647.5 ±50.5	17.970 ±1.543	1.903 ±0.156	1.843 ±0.185	1.043 ±0.191	25.5 ±0.6	26.5 ±3.9	1.708 ±0.138	1.690 ±0.209	2.108 ±0.063	11.8 ±1.9	0.080 ±0.022	1.748 ±0.053	1.758 ±0.117
	PG	4	738.5 ±121.5	21.670 ±6.978	2.078 ±0.398	1.993 ±0.392	1.233 ±0.405	26.5 ±4.7	27.8 ±5.0	1.808 ±0.138	1.635 ±0.108	2.083 ±0.057	14.5 ±2.1	0.105 ±0.053	1.678 ±0.116	1.633 ±0.079
	0.5%PO	2	663.0 ±9.9	18.405 ±1.096	1.905 ±0.290	1.820 ±0.325	0.995 ±0.007	34.5* ±3.5	29.5 ±4.9	1.615 ±0.021	1.675 ±0.035	2.050 ±0.028	13.0 ±4.2	0.100 ±0.042	1.605 ±0.035	1.605 ±0.007
	1.0%PO	4	693.8 ±52.3	19.473 ±2.217	2.075 ±0.127	2.055 ±0.158	1.505 ±0.380	28.5 ±4.4	29.3 ±4.2	1.938 ±0.249	1.875 ±0.185	2.150 ±0.083	14.0 ±2.4	0.098 ±0.021	1.705 ±0.076	1.723 ±0.114
Female	Control	4	429.3 ±61.9	13.780 ±1.587	1.330 ±0.101	1.265 ±0.130	0.765 ±0.037	47.0 ±9.8	49.5 ±18.2	1.320 ±0.028	1.350 ±0.148	1.923 ±0.058	19.3 ±7.9	0.142 ±0.017	37.5 ±18.1	39.3 ±9.4
	PG	4	478.0 ±119.0	13.723 ±2.310	1.353 ±0.123	1.328 ±0.080	0.613 ±0.102	41.8 ±11.2	46.0 ±10.6	1.275 ±0.173	1.230 ±0.049	1.898 ±0.046	18.0 ±4.5	0.120 ±0.012	29.3 ±11.2	29.8 ±17.4
	0.5%PO	4	418.0 ±50.4	12.193 ±1.518	1.158 ±0.066	1.168 ±0.061	0.735 ±0.312	35.5 ±8.7	41.5 ±10.1	1.283 ±0.091	1.293 ±0.139	1.895 ±0.041	23.0 ±2.8	0.125 ±0.019	31.0 ±7.9	32.3 ±9.6
	1.0%PO	4	389.5 ±21.1	12.383 ±1.441	1.210 ±0.106	1.228 ±0.118	0.705 ±0.249	43.8 ±14.4	45.8 ±14.0	1.175 ±0.103	1.233 ±0.100	1.890 ±0.063	61.3 ±58.8	0.100* ±0.000	34.8 ±11.4	41.3 ±23.8

(g , ‖: mg , Mean ± S.D.)

* : Significantly different from control ($p<0.05$)

** : Significantly different from control ($p<0.01$)

Table - 15

Average relative wet organ weight of rats (after the end of the recovery period)

Sex	Sample	Number of animals	Final B.W.	Liver	Kidney R	Kidney L	Spleen	Adrenal gland R	Adrenal gland L	Heart	Lung	Brain	Pituitary	Thymus	Testis or Ovary R	Testis or Ovary L
Male	Control	4	647.5 ±50.5	2.783 ±0.242	0.295 ±0.019	0.285 ±0.017	0.160 ±0.024	3.95 ±0.39	4.13 ±0.82	0.265 ±0.024	0.263 ±0.039	0.328 ±0.030	1.83 ±0.41	0.013 ±0.005	0.273 ±0.026	0.270 ±0.034
	PG	4	738.5 ±121.5	2.895 ±0.488	0.283 ±0.028	0.270 ±0.022	0.165 ±0.048	3.63 ±0.80	3.80 ±0.89	0.248 ±0.035	0.223 ±0.028	0.288 ±0.043	2.00 ±0.37	0.015 ±0.006	0.230 ±0.022	0.225 ±0.026
	0.5%PO	2	663.0 ±9.9	2.775 ±0.120	0.285 ±0.035	0.275 ±0.050	0.150 ±0.000	5.20* ±0.42	4.45 ±0.78	0.245 ±0.007	0.250 ±0.000	0.310 ±0.014	1.95 ±0.64	0.015 ±0.007	0.245 ±0.007	0.245 ±0.007
	1.0%PO	4	693.8 ±52.3	2.803 ±0.110	0.300 ±0.026	0.300 ±0.029	0.220 ±0.054	4.15 ±0.91	4.25 ±0.82	0.283 ±0.043	0.273 ±0.038	0.310 ±0.024	2.03 ±0.30	0.015 ±0.006	0.245 ±0.021	0.248 ±0.017
Female	Control	4	429.3 ±61.9	3.243 ±0.429	0.315 ±0.041	0.298 ±0.051	0.178 ±0.050	11.38 ±4.03	12.18 ±5.89	0.308 ±0.041	0.318 ±0.015	0.455 ±0.065	4.60 ±2.06	0.033 ±0.005	8.60 ±3.21	9.13 ±1.54
	PG	4	478.0 ±119.0	2.915 ±0.328	0.295 ±0.065	0.290 ±0.059	0.133 ±0.033	9.35 ±4.28	10.25 ±4.22	0.273 ±0.046	0.268 ±0.050	0.415 ±0.097	3.83 ±1.03	0.025 ±0.006	6.45 ±2.89	6.48 ±4.10
	0.5%PO	4	418.0 ±50.4	2.925 ±0.251	0.280 ±0.023	0.283 ±0.026	0.178 ±0.083	8.53 ±2.07	9.93 ±1.93	0.308 ±0.041	0.310 ±0.044	0.458 ±0.051	5.58 ±1.08	0.030 ±0.008	7.33 ±1.19	7.63 ±1.93
	1.0%PO	4	389.5 ±21.1	3.190 ±0.473	0.313 ±0.029	0.315 ±0.030	0.185 ±0.068	11.33 ±4.08	11.80 ±3.77	0.303 ±0.029	0.315 ±0.037	0.485 ±0.017	15.58 ±14.89	0.020** ±0.000	9.00 ±3.07	10.40 ±5.64

(%, ‰: 10^{-3}, Mean ± S.D.)

* : Significantly different from control ($p<0.05$)

** : Significantly different from control ($p<0.01$)