

Fig. 6. Sequential food intakes of rats treated with methyltestosterone for 28 days

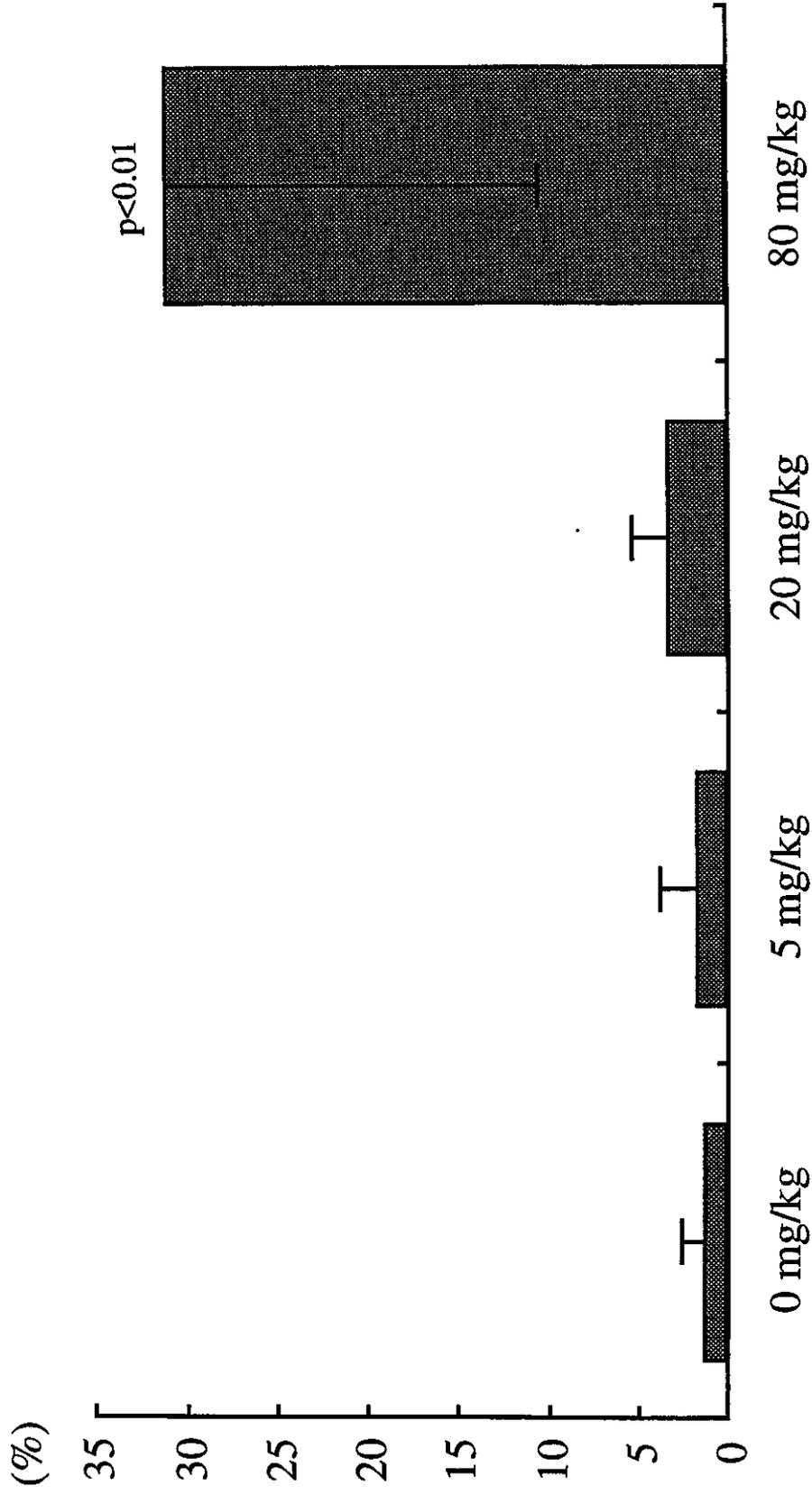


Fig. 7. Percentage of stage VII and VIII tubules with degenerated pachytene spermocytes of male rats treated with methyltestosterone for 28 days

Table 1. Cyclic changes on the vaginal smear of female rats treated with flutamide for 28-31 days

Dose level (mg/kg)	Animal no.	Experimental days											
		20	21	22	23	24	25	26	27	28	29	30	31
4	41	MD	D	P	E	M	D	P	E	MD	D*		
	42	E	MD	D	P	E	D	D	P	E	EM	D*	
	43	P	E	MD	D	P	E	D	D	P	E	M	D*
	44	MD	D	P	E	MD	D	P	E	M	D*		
	45	E	M	D	P	E	E	MD	D	P	E	M	D*
	46	E	M	D	D	E	E	D	D	P	E	M	D*
	47	D	P	E	M	D	P	E	MD	D*			
	48	E	MD	D	P	E	E	D	D	P	E	M	D*
	49	MD	D	E	E	MD	D	P	E	E	EM	D*	
	50	P	E	M	D	P	E	M	D	P	E	M	D*
1	51	E	D	D	P	E	D	D	P	E	D	D*	
	52	E	MD	D	P	E	M	D	P	E	MD	D*	
	53	E	D	D	P	E	D	D	P	E	D	D*	
	54	D	P	E	MD	D	P	E	MD	D*			
	55	M	D	P	E	MD	D	P	E	M	D*		
	56	D	D	P	E	M	D	P	E	M	D*		
	57	P	E	MD	D	P	E	D	D	P	E	M	D*
	58	D	D	P	E	MD	D	P	E	MD	D*		
	59	P	E	MD	D	P	E	M	D	P	E	M	D*
	60	D	P	E	D	D	P	E	D	D*			
0.25	61	D	D	PE	E	M	D	PE	E	MD	D*		
	62	D	P	E	M	D	P	E	E	MD	D*		
	63	MD	D	P	E	D	D	P	E	M	D*		
	64	E	D	D	P	E	E	D	D	D*			
	65	E	M	D	P	E	D	D	P	E	M	D*	
	66	D	P	E	D	D	P	E	MD	D*			
	67	D	E	M	D	P	E	M	D	P	E	D	D*
	68	E	D	D	P	E	D	D	P	E	M	D*	
	69	D	P	E	E	D	D	P	E	E	MD	D*	
	70	P	E	M	D	P	E	MD	D	P	E	M	D*
0 (Control)	71	E	M	D	P	E	D	D	P	E	MD	D*	
	72	E	MD	D	P	E	D	D	P	E	MD	D*	
	73	E	M	D	P	E	M	D	P	E	MD	D*	
	74	D	P	E	M	D	P	E	MD	D*			
	75	D	P	E	M	D	P	E	MD	D*			
	76	P	E	M	D	PE	E	M	D	DP	E	M	D*
	77	D	D	P	E	MD	D	P	E	M	D*		
	78	D	P	E	D	D	P	E	MD	D*			
	79	E	M	D	P	E	M	D	P	E	MD	D*	
	80	E	M	D	P	E	M	D	P	E	MD	D*	

P: proestrus, E: estrus, M: metestrus, D: diestrus, \*: the day sacrificed

Table 2. Cyclic changes on the vaginal smear of female rats treated with methyltestosterone for 28-31 days

Dose level (mg/kg)	Animal no.	Experimental days											
		20	21	22	23	24	25	26	27	28	29	30	31
80	41									*			
	42									*			
	43									*			
	44									*			
	45	Abnormal without cyclic changes									*		
	46									*			
	47									*			
	48									*			
	49									*			
	50									*			
20	51												
	52	E	D	D	D	P	E	MD	D	D*			
	53	D	D	D	D	D	P	E	MD	D*			
	54	D	D	D	D	D	P	E	M	D*			
	55	M	D	D	D	D	D	D	D	P	E	EM	D*
	56	D	D	D	E	MD	D	D	D	D	E	E	MD*
	57	D	D	D	P	E	M	D	D	D*			
	58	M	D	D	D	D	D	DP	E	E	D	D*	
	59	D	D	D	D	D	D	D	D	P	E	MD	D*
60	D	D	E	MD	D	D	D	D	D*				
5	61	D	P	E	EM	D	D	DP	E	EM	D*		
	62	P	E	E	D	D	E	E	MD	D*			
	63	E	E	MD	D	D	E	D	D	D*			
	64	M	D	E	E	EM	D	D	DP	E	E	D*	
	65	D	D	P	E	D	D	D	P	E	EM	D*	
	66	D	D	P	E	EM	D	D	P	E	EM	D*	
	67	D	P	E	E	M	D	P	E	MD	D*		
	68	P	E	E	E	M	D	D	P	E	E	E	EM*
	69	E	E	EM	D	DP	E	M	D	D*			
	70	E	E	M	D	D	P	E	EM	D*			
0 (Control)	71	D	P	E	MD	D	P	E	MD	D*			
	72	E	EM	D	P	E	M	D	P	E	M	D*	
	73	D	P	E	MD	D	P	E	D	D*			
	74	D	DP	E	M	D	P	E	D	D*			
	75	E	M	D	P	E	M	D	P	E	M	D*	
	76	D	P	E	D	D	P	E	M	D*			
	77	P	E	EM	D	P	E	EM	D	D	P	E	M*
	78	E	M	D	P	E	M	D	P	E	E	EM	D*
	79	D	P	E	MD	D	P	E	MD	D*			
	80	E	M	D	P	E	EM	D	P	E	M	D*	

P: proestrus, E: estrus, M: metestrus, D: diestrus, \*: the day sacrificed

Table 3. Hematological data of male and female rats treated with flutamide for 28-31 days

Dose level	0 mg/kg	0.25 mg/kg	1 mg/kg	4 mg/kg
[ Male ]	(10) <sup>a</sup>	(10)	(10)	(10)
WBC (x10 <sup>2</sup> /μl)	92.1 ± 14.6	88.7 ± 19.3	89.1 ± 30.2	84.3 ± 11.8
RBC (x10 <sup>4</sup> /μl)	785.8 ± 39.9	781.3 ± 47.6	778.1 ± 46.5	756.5 ± 48.3
HGB (g/dl)	14.84 ± 0.56	14.47 ± 0.62	14.66 ± 0.69	14.31 ± 0.75
HCT (%)	43.26 ± 1.54	42.51 ± 1.94	42.97 ± 2.07	41.81 ± 2.49
MCV (fl)	55.11 ± 1.53	54.49 ± 2.12	55.30 ± 1.90	55.28 ± 1.32
MCH (pg)	18.91 ± 0.41	18.55 ± 0.76	18.85 ± 0.71	18.93 ± 0.51
MCHC (g/dl)	34.30 ± 0.33	34.04 ± 0.41	34.12 ± 0.36	34.25 ± 0.57
PLT (x10 <sup>4</sup> /μl)	111.6 ± 13.8	104.9 ± 8.4	112.4 ± 12.0	113.3 ± 10.7
[ Female ]	(10) <sup>a</sup>	(10)	(10)	(10)
WBC (x10 <sup>2</sup> /μl)	71.5 ± 9.8	61.3 ± 9.6	67.1 ± 14.7	57.3 ± 16.2
RBC (x10 <sup>4</sup> /μl)	725.6 ± 32.1	711.9 ± 40.6	725.9 ± 27.0	702.9 ± 32.6
HGB (g/dl)	13.72 ± 0.58	13.52 ± 0.57	13.91 ± 0.52	13.47 ± 0.56
HCT (%)	39.16 ± 1.78	38.70 ± 1.91	39.43 ± 1.35	38.73 ± 1.89
MCV (fl)	53.97 ± 1.18	54.40 ± 1.34	54.34 ± 1.51	55.13 ± 1.64
MCH (pg)	18.91 ± 0.30	19.01 ± 0.54	19.16 ± 0.49	19.16 ± 0.54
MCHC (g/dl)	35.03 ± 0.40	34.96 ± 0.49	35.28 ± 0.47	34.79 ± 0.36
PLT (x10 <sup>4</sup> /μl)	108.0 ± 9.9	106.1 ± 11.3	113.0 ± 12.3	109.7 ± 9.7

a : numbers in parentheses represent the numbers of rats examined.  
Data represent mean values ± S.D.

Table 4. Hematological data of male and female rats treated with methyltestosterone for 28-31 days

Dose level	0 mg/kg	5 mg/kg	20 mg/kg	80 mg/kg
[Male]	(10) <sup>a</sup>	(9)	(10)	(10)
WBC (x10 <sup>2</sup> /μl)	77.9±17.4	84.9±16.9	86.5±17.4	69.1±10.7
RBC (x10 <sup>4</sup> /μl)	781±39	781±41	773±29	776±42.1
HGB (g/dl)	14.7±0.5	14.6±0.4	14.5±0.4	14.4±0.6
HCT (%)	42.5±1.9	43.1±0.9	42.2±1.3	42.2±2.5
MCV (fl)	54.5±1.1	55.4±2.6	54.6±1.5	54.3±1.4
MCH (pg)	18.8±0.5	18.7±0.8	18.8±0.5	18.6±0.7
MCHC (g/dl)	34.5±0.4	33.8±0.4	34.5±0.6	34.1±0.9
PLT (x10 <sup>4</sup> /μl)	109±15	105±14	106±12	110±10
[Female]	(10)	(10)	(9)	(9)
WBC (x10 <sup>2</sup> /μl)	66.5±22.9	74.3±21.4	122±158	72.9±17.0
RBC (x10 <sup>4</sup> /μl)	715±44	748±37	737±27	724±26
HGB (g/dl)	13.8±0.7	14.2±0.7	14.3±0.4	13.9±0.5
HCT (%)	39.5±1.8	41.0±2.2	42.0±2.0	40.6±1.9
MCV (fl)	55.3±1.9	54.8±1.9	57.0±2.4	56.0±1.1
MCH (pg)	19.4±0.7	19.0±0.5	19.4±0.8	19.2±0.5
MCHC (g/dl)	35.0±0.5	34.8±0.5	34.0±1.2	34.4±0.6
PLT (x10 <sup>4</sup> /μl)	117±14	99±25	100±13	103±13

<sup>a</sup>: Numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

Table 5. Differential leukocyte counts of male and female rats treated with flutamide for 28-31 days

Dose level	0 mg/kg	0.25 mg/kg	1 mg/kg	4 mg/kg
[ Male ]	(10) <sup>a</sup>	(10)	(10)	(10)
Band form-N (%)	1.4 ± 1.3	1.4 ± 1.1	1.2 ± 0.8	0.8 ± 0.5
Segmented-N (%)	12.2 ± 4.3	10.1 ± 4.5	9.4 ± 3.7	9.8 ± 2.5
Eosinophils (%)	1.2 ± 1.0	1.3 ± 1.0	1.1 ± 0.9	1.4 ± 1.2
Basophils (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Lymphocytes (%)	84.9 ± 4.3	87.0 ± 5.4	88.0 ± 4.0	87.7 ± 3.1
Monocytes (%)	0.2 ± 0.3	0.1 ± 0.2	0.1 ± 0.3	0.2 ± 0.4
[ Female ]	(10) <sup>a</sup>	(10)	(10)	(10)
Band form-N (%)	1.8 ± 1.2	1.6 ± 0.8	1.3 ± 1.3	0.8 ± 1.1
Segmented-N (%)	9.8 ± 4.3	10.1 ± 3.7	8.0 ± 3.8	9.3 ± 5.5
Eosinophils (%)	1.1 ± 1.1	1.1 ± 0.7	1.1 ± 1.3	1.1 ± 0.7
Basophils (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Lymphocytes (%)	87.2 ± 5.7	87.3 ± 4.4	89.5 ± 4.6	88.6 ± 6.0
Monocytes (%)	0.1 ± 0.2	0.1 ± 0.2	0.1 ± 0.2	0.1 ± 0.3

Band form-N : band form neutrophils, Segmented-N : segmented neutrophils.

a : numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

Table 6. Differential leukocyte counts of male and female rats treated with methyltestosterone for 28-31 days

Dose level	0 mg/kg	5 mg/kg	20 mg/kg	80 mg/kg
[ Male ]	(10) <sup>a</sup>	(9)	(10)	(10)
Band form-N (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Segmented-N (%)	13.5 ± 5.7	10.2 ± 2.3	12.7 ± 3.5	10.7 ± 1.1
Eosinophils (%)	0.7 ± 0.7	0.2 ± 0.4	0.8 ± 0.7	0.6 ± 0.6
Basophils (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Lymphocytes (%)	85.8 ± 5.5	89.6 ± 2.4	86.5 ± 3.5	88.5 ± 1.5
Monocytes (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.3 ± 0.4 *
[ Female ]	(10) <sup>a</sup>	(10)	(9)	(10)
Band form-N (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Segmented-N (%)	11.1 ± 5.0	10.7 ± 4.0	7.1 ± 3.1	8.7 ± 3.0
Eosinophils (%)	0.7 ± 0.6	0.5 ± 0.7	0.6 ± 0.6	0.5 ± 0.4
Basophils (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Lymphocytes (%)	88.2 ± 4.9	88.9 ± 4.3	92.3 ± 3.3	90.8 ± 3.2
Monocytes (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0

Band form-N : band form neutrophils, Segmented-N : segmented neutrophils.

<sup>a</sup> : Numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

\* Significantly different from the 0 mg/kg group at p<0.05.

Table 7. Serum biochemical data of male rats treated with flutamide for 28 days

Dose level	0 mg/kg (10) <sup>a</sup>	0.25 mg/kg (10)	1 mg/kg (10)	4 mg/kg (10)
Total protein (g/dl)	6.19 ± 0.33	6.07 ± 0.24	6.18 ± 0.23	6.19 ± 0.31
Albumin/globulin ratio	2.55 ± 0.37	2.56 ± 0.28	2.51 ± 0.26	2.49 ± 0.38
Albumin (g/dl)	4.42 ± 0.19	4.35 ± 0.05	4.40 ± 0.19	4.39 ± 0.22
Total cholesterol (mg/dl)	70.7 ± 6.5	70.5 ± 9.7	63.7 ± 9.5	75.1 ± 12.5
BUN (mg/dl)	15.81 ± 1.66	15.83 ± 1.54	15.48 ± 2.24	15.67 ± 1.01
Creatinine (mg/dl)	0.21 ± 0.03	0.23 ± 0.05	0.24 ± 0.05	0.25 ± 0.05
Ca (mg/dl)	10.32 ± 0.38	10.29 ± 0.24	10.14 ± 0.26	9.62 ± 2.29
P (mg/dl)	8.35 ± 0.87	7.76 ± 0.84	7.39 ± 0.49	8.19 ± 1.14
Na (mEq/l)	148.5 ± 2.0	148.3 ± 1.4	147.1 ± 1.2	147.1 ± 2.8
Cl (mEq/l)	108.9 ± 1.8	108.4 ± 2.1	107.0 ± 1.3	107.7 ± 1.6
K (mEq/l)	5.29 ± 0.28	5.18 ± 0.35	5.11 ± 0.47	5.66 ± 1.60
GOT (IU/l/37°C)	103.3 ± 29.3	114.3 ± 27.5	115.8 ± 23.9	115.5 ± 22.0
GPT (IU/l/37°C)	41.0 ± 5.3	40.4 ± 6.0	39.6 ± 6.3	40.1 ± 5.1
ALP (IU/l/37°C)	657.5 ± 187.8	727.3 ± 205.5	732.9 ± 232.7	645.3 ± 126.8
γ-GTP (IU/l/37°C)	< 2	< 2	< 2	< 2

a : numbers in parentheses represent the numbers of rats examined.  
Data represent mean values ± S.D.

Table 8. Serum biochemical data of female rats treated with flutamide for 28-31 days

Dose level	0 mg/kg (10) <sup>a</sup>	0.25 mg/kg (10)	1 mg/kg (10)	4 mg/kg (10)
Total protein (g/dl)	6.31 ± 0.31	6.33 ± 0.38	6.26 ± 0.25	6.55 ± 0.31
Albumin/globulin ratio	3.44 ± 0.32	3.37 ± 0.55	3.47 ± 0.59	3.24 ± 0.40
Albumin (g/dl)	4.88 ± 0.22	4.86 ± 0.29	4.83 ± 0.15	4.99 ± 0.27
Total cholesterol (mg/dl)	78.3 ± 12.1	70.3 ± 9.2	77.3 ± 8.1	72.9 ± 12.5
BUN (mg/dl)	16.94 ± 4.41	16.73 ± 3.50	16.59 ± 3.35	18.25 ± 3.90
Creatinine (mg/dl)	0.29 ± 0.03	0.29 ± 0.06	0.29 ± 0.06	0.30 ± 0.00
Ca (mg/dl)	10.39 ± 0.22	10.47 ± 0.29	10.35 ± 0.18	10.45 ± 0.32
P (mg/dl)	7.40 ± 1.08	7.70 ± 0.77	7.62 ± 0.72	7.66 ± 0.94
Na (mEQ/l)	147.8 ± 1.6	147.4 ± 1.6	147.9 ± 1.3	148.6 ± 1.6
Cl (mEQ/l)	109.3 ± 1.8	108.9 ± 2.0	109.8 ± 1.7	109.4 ± 1.3
K (mEQ/l)	4.31 ± 0.27	4.50 ± 0.16	4.55 ± 0.21	4.55 ± 0.33
GOT (IU/l/37°C)	86.8 ± 18.9	88.6 ± 12.9	91.2 ± 12.8	88.8 ± 17.4
GPT (IU/l/37°C)	37.3 ± 6.2	36.1 ± 4.5	40.2 ± 6.5	37.5 ± 5.2
ALP (IU/l/37°C)	387.0 ± 89.4	396.4 ± 149.4	401.4 ± 59.5	452.9 ± 130.1
γ-GTP (IU/l/37°C)	< 2	< 2	< 2	< 2

a : numbers in parentheses represent the numbers of rats examined.  
Data represent mean values ± S.D.

Table 9. Serum biochemical data of male rats treated with methyltestosterone for 28 days

Dose level	0 mg/kg (10) <sup>a</sup>	5 mg/kg (9)	20 mg/kg (10)	80 mg/kg (10)
Total protein (g/dl)	5.97 ± 0.32	6.01 ± 0.23	6.02 ± 0.36	6.17 ± 0.50
Albumin/globulin ratio	2.61 ± 0.46	2.53 ± 0.57	2.40 ± 0.29	2.28 ± 0.40
Albumin (g/dl)	4.27 ± 0.14	4.26 ± 0.15	4.23 ± 0.18	4.25 ± 0.20
Total cholesterol (mg/dl)	71.4 ± 8.6	69.2 ± 10.0	57.5 ± 10.9	46.9 ± 9.4
BUN (mg/dl)	13.8 ± 1.8	15.6 ± 0.7	14.3 ± 1.5	15.4 ± 3.9
Creatinine (mg/dl)	0.22 ± 0.04	0.23 ± 0.05	0.25 ± 0.05	0.22 ± 0.04
Ca (mg/dl)	10.3 ± 0.2	10.4 ± 0.3	10.1 ± 0.2	10.1 ± 0.3
P (mg/dl)	8.79 ± 0.91	8.77 ± 1.03	8.45 ± 1.20	8.43 ± 0.97
Na (mEq/l)	148 ± 2	147 ± 1	147 ± 1	147 ± 1
Cl (mEq/l)	108 ± 1	107 ± 1	108 ± 1	107 ± 2
K (mEq/l)	5.09 ± 0.28	4.99 ± 0.16	4.98 ± 0.26	4.93 ± 0.36
GOT (IU/l/37°C)	103.6 ± 20.9	91.4 ± 16.0	97.0 ± 15.0	108.4 ± 25.4
GPT (IU/l/37°C)	43.8 ± 4	41.0 ± 4.3	41.4 ± 5.1	49.3 ± 6.9
ALP (IU/l/37°C)	795 ± 314	743 ± 122	720 ± 161	974 ± 156
γ-GTP (IU/l/37°C)	< 2	< 2	< 2	< 2

<sup>a</sup>: Numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

Table 10. Serum biochemical data of female rats treated with methyltestosterone for 28-31 days

Dose level	0 mg/kg (10) <sup>a</sup>	5 mg/kg (10)	20 mg/kg (9)	80 mg/kg (10)
Total protein (g/dl)	6.23 ± 0.33	5.89 ± 0.39	5.86 ± 0.23	5.92 ± 0.48
Albumin/globulin ratio	3.41 ± 0.54	2.81 ± 0.49	2.78 ± 0.37	2.45 ± 0.51
Albumin (g/dl)	4.80 ± 0.28	4.32 ± 0.31	4.29 ± 0.13	4.15 ± 0.18
Total cholesterol (mg/dl)	74.9 ± 10.2	72.1 ± 11.9	54.3 ± 10.1	46.5 ± 4.90
BUN (mg/dl)	14.7 ± 2.5	15.3 ± 2.11	13.2 ± 2.0	16.2 ± 3.8
Creatinine (mg/dl)	0.29 ± 0.06	0.27 ± 0.05	0.28 ± 0.04	0.25 ± 0.05
Ca (mg/dl)	10.3 ± 0.2	10.2 ± 0.5	10.2 ± 0.3	10.3 ± 0.4
P (mg/dl)	8.51 ± 0.67	8.04 ± 0.82	7.34 ± 2.80	8.14 ± 1.31
Na (mEQ/l)	146 ± 1	147 ± 2	147 ± 1	146 ± 1
Cl (mEQ/l)	106 ± 1	107 ± 7	106 ± 2	106 ± 2
K (mEQ/l)	4.50 ± 0.16	4.80 ± 0.29	4.64 ± 0.42	4.70 ± 0.33
GOT (IU/l/37°C)	96.0 ± 25.7	92.2 ± 23.6	91.6 ± 19.7	90.8 ± 28.1
GPT (IU/l/37°C)	36.9 ± 8.1	40.1 ± 6.2	40.9 ± 6.2	39.5 ± 6.3
ALP (IU/l/37°C)	480 ± 181	607 ± 165	604 ± 113	774 ± 227
γ-GTP (IU/l/37°C)	< 2	< 2	< 2	< 2

<sup>a</sup>: Numbers in parentheses represent the numbers of rats examined.  
Data represent mean values ± S.D.

Table 11. Serum hormonal data of male and female rats treated with flutamide for 28-31 days

Dose level	0 mg/kg	0.25 mg/kg	1 mg/kg	4 mg/kg
[ Male ]	(10) <sup>a</sup>	(10)	(10)	(10)
Testosterone (ng/ml)	2.2±1.1	2.3±1.4	3.0±1.6	3.9±0.7*
Estradiol (pg/ml)	4.7±0.8	4.8±0.7	5.2±0.6	5.7±0.7*
FSH (ng/ml)	17.5±4.2	15.9±2.3	17.7±3.8	19.1±2.4
LH (ng/ml)	3.0±0.4	2.9±0.3	3.1±0.4	3.3±0.6
Prolactin (ng/ml)	22.9±24.5	17.7±13.3	28.3±13.7	28.9±14.6
[ Female ]	(10) <sup>a</sup>	(10)	(10)	(10)
Testosterone (ng/ml)	<0.1	<0.1	<0.1	<0.1
Estradiol (pg/ml)	10.3±1.3	8.9±2.5	12.1±2.7	9.7±2.2
FSH (ng/ml)	11.1±1.7	10.6±1.1	10.3±2.1	12.6±1.3
LH (ng/ml)	2.8±0.2	2.7±0.3	2.8±0.2	2.9±0.1
Prolactin (ng/ml)	14.1±13.6	19.6±22.7	21.6±17.6	16.0±13.9

a : numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

\* : significantly different from the 0 mg/kg-group at  $p < 0.05$ .

Table 12. Serum hormonal data of male and female rats treated with methyltestosterone for 28-31 days

Dose level	0 mg/kg (10) <sup>a</sup>	5 mg/kg (9)	20 mg/kg (10)	80 mg/kg (10)
[ Male ]				
Testosterone (ng/ml)	1.6±0.7	3.2±1.6	2.6±1.7	1.1±1.5
E2 (pg/ml)	4.4±0.7	5.2±0.7	4.9±0.9	4.3±0.8
LH (ng/ml)	2.6±0.4	2.7±0.3	2.6±0.3	2.4±0.2
FSH (ng/ml)	14.3±1.4	15.4±1.5	16.1±2.0	13.6±1.6
Prolactin (ng/ml)	14.6±8.4	11.7±6.9	13.0±4.9	15.0±10.5
[ Female ]				
Testosterone (ng/ml)	<0.1	<0.1	<0.1	<0.1
E2 (pg/ml)	11.4±5.0	11.5±7.1	8.3±1.5	8.7±2.4
LH (ng/ml)	2.6±0.3	2.7±0.3	2.6±0.2	2.5±0.2
FSH (ng/ml)	9.8±0.9	10.2±1.7	10.0±1.6	11.7±1.6*
Prolactin (ng/ml)	12.1±7.7	99.1±249	12.2±11.3	24.8±22.5

<sup>a</sup>. Numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

\* Significantly different from the 0 mg/kg group at p<0.05.

Table 13. Absolute and relative organ weights of male rats treated with flutamide for 28 days

Dose level	0 mg/kg	0.25 mg/kg	1 mg/kg	4 mg/kg
	(10) <sup>a</sup>	(10)	(10)	(10)
	Absolute organ weights (g)			
Body weight	389.9 ± 29.0	372.8 ± 16.7	374.1 ± 19.1	373.5 ± 17.2
Liver	15.4 ± 1.9	13.7 ± 1.5	14.1 ± 1.1	14.5 ± 1.1
Adrenal	0.050 ± 0.005	0.045 ± 0.007	0.048 ± 0.006	0.051 ± 0.007
Kidney	2.69 ± 0.30	2.50 ± 0.21	2.56 ± 0.17	2.43 ± 0.28
Pituitary	0.012 ± 0.002	0.011 ± 0.001	0.013 ± 0.002	0.013 ± 0.001
Thyroid	0.023 ± 0.005	0.021 ± 0.004	0.021 ± 0.004	0.020 ± 0.003
Testis	3.16 ± 0.30	3.08 ± 0.15	3.01 ± 0.22	3.02 ± 0.12
Epididymis	0.914 ± 0.056	0.864 ± 0.042	0.816 ± 0.059**	0.777 ± 0.061**
Ventral prostate	0.52 ± 0.07	0.47 ± 0.10	0.50 ± 0.09	0.43 ± 0.10
Seminal vesicle/ Coagulating gland/ Dorsolateral prostate	1.80 ± 0.23	1.74 ± 0.17	1.77 ± 0.27	1.47 ± 0.26**
	Relative organ weights (%)			
Liver	3.954 ± 0.382	3.659 ± 0.257*	3.771 ± 0.136	3.869 ± 0.210
Adrenal	0.0128 ± 0.0018	0.0122 ± 0.0019	0.0121 ± 0.0026	0.0136 ± 0.0017
Kidney	0.690 ± 0.069	0.670 ± 0.046	0.648 ± 0.142	0.650 ± 0.064
Pituitary	0.0031 ± 0.0003	0.0029 ± 0.0003	0.0034 ± 0.0005	0.0035 ± 0.0003
Thyroid	0.0059 ± 0.0012	0.0057 ± 0.0012	0.0057 ± 0.0010	0.0054 ± 0.0010
Testis	0.815 ± 0.089	0.829 ± 0.058	0.755 ± 0.150	0.812 ± 0.058
Epididymis	0.236 ± 0.025	0.232 ± 0.018	0.204 ± 0.038*	0.209 ± 0.021
Ventral prostate	0.135 ± 0.021	0.127 ± 0.027	0.135 ± 0.023	0.117 ± 0.029
Seminal vesicle/ Coagulating gland/ Dorsolateral prostate	0.461 ± 0.055	0.467 ± 0.054	0.472 ± 0.062	0.394 ± 0.070*

a : numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

\*\*, \* : significantly different from the 0 mg/kg-group at  $p < 0.01$  and  $p < 0.05$ , respectively.

Table 14. Absolute and relative organ weights of female rats treated with flutamide for 28-31 days

Dose level	0 mg/kg	0.25 mg/kg	1 mg/kg	4 mg/kg
	(10) <sup>a</sup>	(10)	(10)	(10)
	Absolute organ weights (g)			
Body weight	251.5 ± 16.3	250.9 ± 15.1	249.7 ± 13.0	256.2 ± 17.9
Liver	8.97 ± 0.84	9.23 ± 0.82	8.92 ± 0.55	9.56 ± 0.90
Adrenal	0.062 ± 0.008	0.060 ± 0.008	0.064 ± 0.008	0.058 ± 0.006
Kidney	1.70 ± 0.17	1.76 ± 0.12	1.76 ± 0.11	1.69 ± 0.11
Pituitary	0.015 ± 0.001	0.015 ± 0.002	0.015 ± 0.002	0.016 ± 0.002
Thyroid	0.017 ± 0.003	0.018 ± 0.002	0.017 ± 0.002	0.018 ± 0.003
Ovary	0.091 ± 0.016	0.102 ± 0.019	0.102 ± 0.025	0.102 ± 0.021
Uterus	0.505 ± 0.049	0.520 ± 0.049	0.553 ± 0.046	0.532 ± 0.067
	Relative organ weights (%)			
Liver	3.568 ± 0.230	3.675 ± 0.192	3.574 ± 0.174	3.727 ± 0.179
Adrenal	0.0248 ± 0.0035	0.0240 ± 0.0026	0.0256 ± 0.0030	0.0227 ± 0.0025
Kidney	0.679 ± 0.075	0.704 ± 0.058	0.704 ± 0.035	0.662 ± 0.031
Pituitary	0.0059 ± 0.0004	0.0060 ± 0.0007	0.0060 ± 0.0007	0.0063 ± 0.0005
Thyroid	0.0069 ± 0.0015	0.0071 ± 0.0009	0.0067 ± 0.0010	0.0069 ± 0.0007
Ovary	0.0364 ± 0.0074	0.0404 ± 0.0069	0.0409 ± 0.0090	0.0398 ± 0.0072
Uterus	0.201 ± 0.021	0.208 ± 0.021	0.221 ± 0.015	0.209 ± 0.033

a : numbers in parentheses represent the numbers of rats examined.  
Data represent mean values ± S.D.

Table 15. Absolute and relative organ weights of male rats treated with methyltestosterone for 28 days

Dose level	0 mg/kg (10) <sup>a</sup>	5 mg/kg (9)	20 mg/kg (10)	80 mg/kg (10)
Organs	Absolute organ weights (g)			
Body weight	376.1 ± 32.1	385.1 ± 26.9	382.7 ± 14.0	364.8 ± 22.6
Liver	13.3 ± 1.5	14.6 ± 1.8	14.2 ± 1.3	14.6 ± 1.3
Adrenal	0.051 ± 0.006	0.050 ± 0.007	0.049 ± 0.009	0.050 ± 0.009
Kidney	2.51 ± 0.25	2.57 ± 0.32	2.51 ± 0.16	2.62 ± 0.24
Pituitary	0.012 ± 0.001	0.012 ± 0.002	0.012 ± 0.002	0.011 ± 0.002
Thyroid	0.018 ± 0.002	0.021 ± 0.004	0.019 ± 0.006	0.023 ± 0.007
Testis	3.25 ± 0.26	3.29 ± 0.28	3.13 ± 0.17	2.37 ± 0.66**
Epididymis	0.97 ± 0.08	0.96 ± 0.05	0.94 ± 0.08	0.82 ± 0.13**
Prostate (ventral)	0.53 ± 0.06	0.57 ± 0.12	0.54 ± 0.08	0.50 ± 0.14
Seminal vesicle + Prostate	1.75 ± 0.19	1.84 ± 0.18	1.72 ± 0.17	1.57 ± 0.41
Relative organ weights (%)				
Liver	3.54 ± 0.15	3.78 ± 0.23	3.72 ± 0.28	4.00 ± 0.18**
Adrenal	0.014 ± 0.002	0.013 ± 0.002	0.013 ± 0.002	0.014 ± 0.003
Kidney	0.67 ± 0.03	0.67 ± 0.05	0.66 ± 0.04	0.72 ± 0.07*
Pituitary	0.003 ± 0.000	0.003 ± 0.001	0.003 ± 0.000	0.003 ± 0.001
Thyroid	0.005 ± 0.001	0.005 ± 0.001	0.005 ± 0.002	0.006 ± 0.002
Testis	0.87 ± 0.09	0.86 ± 0.05	0.82 ± 0.05	0.64 ± 0.15**
Epididymis	0.26 ± 0.03	0.25 ± 0.02	0.25 ± 0.03	0.23 ± 0.03*
Prostate (ventral)	0.14 ± 0.01	0.15 ± 0.03	0.14 ± 0.02	0.14 ± 0.04
Seminal vesicle + Prostate	0.47 ± 0.06	0.48 ± 0.07	0.45 ± 0.04	0.43 ± 0.12

<sup>a</sup>: Numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

\*,\*\* Significantly different from the 0 mg/kg group at p<0.05 and p<0.01, respectively.

Table 16. Absolute and relative organ weights of female rats treated with methyltestosterone for 28-31 days

Dose level	0 mg/kg	5 mg/kg	20 mg/kg	80 mg/kg
	(10) a	(10)	(9)	(10)
Organs	Absolute organ weights (g)			
Body weight	259.2±13.3	272.2±16.4	284.3±10.1**	285.4±16.4**
Liver	9.7±1.3	9.7±0.9	10.4±1.1	11.5±1.3**
Adrenal	0.067±0.008	0.050±0.006**	0.052±0.009**	0.040±0.010**
Kidney	1.75±0.18	1.89±0.09	1.91±0.13	2.21±0.26**
Pituitary	0.017±0.003	0.014±0.002	0.013±0.002	0.012±0.002
Thyroid	0.016±0.003	0.022±0.003	0.021±0.004	0.018±0.004
Ovary	0.091±0.009	0.070±0.018**	0.068±0.013**	0.050±0.006**
Uterus	0.50±0.07	0.44±0.11	0.39±0.08*	0.50±0.07
Relative organ weights (%)				
Liver	3.73±0.44	3.57±0.24	3.67±0.28	4.05±0.40
Adrenal	0.026±0.003	0.019±0.003**	0.018±0.003**	0.014±0.003**
Kidney	0.68±0.05	0.70±0.05	0.67±0.04	0.78±0.11**
Pituitary	0.006±0.001	0.005±0.001*	0.005±0.001**	0.004±0.001**
Thyroid	0.006±0.001	0.008±0.001**	0.007±0.001	0.006±0.001
Ovary	0.035±0.003	0.026±0.006**	0.024±0.005**	0.017±0.002**
Uterus	0.19±0.03	0.16±0.05	0.14±0.03*	0.18±0.03

<sup>a</sup>: Numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D.

\*,\*\* Significantly different from the 0 mg/kg group at p<0.05 and p<0.01, respectively.

Table 17. Histopathological findings in the mammary gland of male rats treated with flutamide for 28 days

Dose level	Number of rats with lesions			
	0 mg/kg (10) a	0.25 mg/kg (10)	1 mg/kg (10)	4 mg/kg (10)
Atrophy of lobules :				
Slight degree	0	0	3	4
Moderate degree	0	0	0	3
Total	0	0	3	7**

a : numbers in parentheses represent the numbers of rats examined.

\*\* : Significantly different from the 0 mg/kg-group at  $p < 0.01$ .

Table 18. Fluctuations of germ cells in the seminiferous epithelia of male rats treated with flutamide for 28 days

Dose level		0 mg/kg	4 mg/kg
Groups	Cell types	(5) <sup>a</sup>	(5)
1 (Stage I-VI)	Spermatogonia	0.83 ± 0.07	0.93 ± 0.14
	Pachytene spermatocyte	1.95 ± 0.19	2.08 ± 0.09
	Round spermatid	6.18 ± 0.09	6.53 ± 0.35
2 (Stage VII-VIII)	Spermatogonia	0.15 ± 0.08	0.10 ± 0.03
	Preleptotene spermatocyte	1.79 ± 0.26	1.96 ± 0.19
	Pachytene spermatocyte	2.65 ± 0.32	2.61 ± 0.23
	Round spermatid	7.06 ± 0.74	7.06 ± 0.68
3 (Stage IX-XI)	Spermatogonia	0.17 ± 0.03	0.23 ± 0.06
	Leptotene spermatocyte	1.79 ± 0.20	2.02 ± 0.10*
	Pachytene spermatocyte	2.45 ± 0.16	2.61 ± 0.25
4 (Stage XII-XIV)	Spermatogonia	0.18 ± 0.04	0.20 ± 0.07
	Zygotene/pachytene spermatocyte	1.88 ± 0.26	1.97 ± 0.24
	Pachytene/diprotene spermatocyte	2.51 ± 0.18	2.47 ± 0.15

a : numbers in parentheses represent the numbers of rats examined.

Data represent mean values ± S.D. in the number of germ cells per Sertoli cell.

\* : significantly different from the 0 mg/kg-group at  $p < 0.05$ .