

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) ^a	(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	5 mg/kg	20 mg/kg	80 mg/kg
	(10) ^a	(9)	(10)	(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

^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 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

^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 and p<0.01, respectively.

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

Number of rats with lesions				
Dose level	0 mg/kg	0.25 mg/kg	1 mg/kg	4 mg/kg
	(10) a	(10)	(10)	(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) ^a	(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 $p < 0.05$.

Table 19. Histopathological findings for male rats treated with methyltestosterone for 28 days

Dose level	0 mg/kg	5 mg/kg	20 mg/kg	80 mg/kg
	(10) ^a	(9)	(10)	(10)
Testis				
Atrophy of seminiferous tubules, diffuse	0	0	0	6*
Atrophy of Leydig cells	0	0	0	8**
Vacuolation of Sertoli cells	3	6	7	7
Multinucleated giant cell formation	1	0	0	1
Epididymis				
Degenerated germ cells in lumen	0	1	3	6*
Spermatic granuloma	0	0	1	1
Prostate				
Interstitial lymphocyte infiltration	3	2	1	2

a. Numbers in parentheses represent the number of rats examined.

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

Table 20. Histopathological findings for 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)
Ovary				
Multiple follicular cysts	0	4*	9**	10**
Follicles cyst	0	0	2	0
Lutein cyst	0	0	1	2
Uterus				
Dilatation of lumen	0	2	1	6*
Vacuolation of endometrial cells	0	0	1	8**
Vagina				
Abnormal estrus cycle	0	0	1	10**
Mammary gland				
Hyperplasia	0	0	3	10**
Adrenal				
Atrophy of zona reticularis	0	0	4*	10**

^a: Numbers in parentheses represent the number of rats examind.
 **, * Significantly different from the 0 mg/kg group at p<0.05 and p<0.01, respectively.

Table 21. Sperm number, motility and morphology in male rats treated with flutamide for 28 days

Dose level	0 mg/kg (5) ^a	0.25 mg/kg (5)	1 mg/kg (5)	4 mg/kg (5)
No. of sperms in the testis (x10 ⁶ /g)	147.9 ± 11.0	150.1 ± 14.5	158.1 ± 19.5	137.7 ± 11.9
No. of sperms in the epididymis (x10 ⁶ /g)	711.4 ± 116.0	626.5 ± 152.6	675.7 ± 208.0	541.6 ± 148.3
Motility of sperms (%)	82.6 ± 3.5	81.2 ± 8.3	76.1 ± 9.4	78.4 ± 7.4
No. of sperms examined	128 ± 37	114 ± 44	91 ± 45	72 ± 22
No. of moveless sperms	22 ± 8	19 ± 5	20 ± 8	15 ± 5
Incidences of abnormal sperms (%)	6.9 ± 0.9	7.4 ± 3.2	6.6 ± 3.0	6.7 ± 3.5
No hook (no./1000 sperms)	1	0	1	1
Excessive hook (no./1000 sperms)	0	0	0	0
Amorphous (no./1000 sperms)	33	32	35	38
No head (no./1000 sperms)	35	42	30	27
Pin head (no./1000 sperms)	0	0	0	1
Two head (no./1000 sperms)	0	0	0	0
Short tail (no./1000 sperms)	0	0	0	0
Two tail (no./1000 sperms)	0	0	0	0

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

Table 22. Sperm number, motility and morphology in male rats treated with methyltestosterone for 28 days

Dose level	0 mg/kg	5 mg/kg	20 mg/kg	80 mg/kg
	(5) ^a	(5)	(5)	(5)
No. of sperms in the testis (x10 ⁶ /g)	153.8±23.7	166.1±15.1	153.8±11.5	170.8±19.7
No. of sperms in the epididymis (x10 ⁶ /g)	936.9±110.1	845.5±123.2	739.8±229.9	768.0±193.2
Motility of sperms (%)	82.7±10.1	82.7±7.9	65.0±29.6	78.7±17.1
No. of sperms examined	112±28	87±13	89±27	94±50
No. of moveless sperms	17±6	14±5	25±13	16±6
Incidences of abnormal sperms (%)	9.8±4.6	14.2±5.0	19.7±13.7	15.3±3.1
No hook (no./1000 sperms)	0	1	0	0
Excessive hook (no./1000 sperms)	0	0	0	0
Amorphous (no./1000 sperms)	60	79	37	76
No head (no./1000 sperms)	38	61	160	77
Pin head (no./1000 sperms)	0	1	0	0
Two head (no./1000 sperms)	0	0	0	0
Short tail (no./1000 sperms)	0	0	0	0
Two tail (no./1000 sperms)	0	0	0	0

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