

Table 8-1

Twenty-eight-day repeat dose oral toxicity study of methoxychlor in rats

Relative organ weights in males											
Group	Body weight (g)	Liver (mg/g)	Kidneys (mg/g)	Adrenal glands (mg/g)	Pituitary gland (mg/g)	Thyroid gland (mg/g)	Prostate (mg/g)	Seminal vesicles (mg/g)	Testes (mg/g)	Epididymides (mg/g)	Accessory reproductive gland (mg)
Control	10	10	10	10	10	10	10	10	10	10	10
	420.0	38.445	6.257	0.129	0.024	0.036	1.117	3.207	7.809	2.223	5.9
25 mg/kg	18.5	2.589	0.636	0.019	0.002	0.007	0.266	0.760	0.357	0.165	1.1
	10	10	10	10	10	10	10	10	10	10	10
401.7	37.891	6.639	0.125	0.027 *	0.042	1.149	3.244	7.692	2.180	5.6	
	22.7	2.891	0.411	0.012	0.002	0.007	0.265	0.523	0.555	0.9	
100 mg/kg	10	10	10	10	10	10	10	10	10	10	10
	312.1 **	39.800	6.739	0.176 **	0.029 **	0.043 *	0.469 **	0.872 **	8.389	2.172	2.0 **
29.2	2.728	0.701	0.025	0.002	0.006	0.272	0.751	1.887	0.671	1.2	
	10	10	10	10	10	10	10	10	10	10	10
400 mg/kg	307.0 **	47.327 **	7.375 **	0.213 **	0.030 **	0.044 *	0.200 **	0.270 **	5.176 *	1.192 **	0.8 **
	20.2	2.271	0.684	0.014	0.003	0.007	0.213	0.065	2.072	0.572	0.4
Parameter, number of animals											
mean											
S.D.											

*, significantly different from control, $p < 0.05$ **, significantly different from control, $p < 0.01$

Table 8-2

Twenty-eight-day repeat dose oral toxicity study of methoxychlor in rats

Relative organ weights in females

Group	Body weight (g)	Liver (mg/g)	Kidneys (mg/g)	Adrenal glands (mg/g)	Pituitary gland (mg/g)	Thyroid gland (mg/g)	Uterus (mg/g)	Ovaries (mg/g)
Control	10 264.4 19.6	10 35.710 2.034	10 6.524 0.380	10 0.238 0.030	10 0.054 0.005	10 0.049 0.007	10 1.436 0.278	10 0.322 0.042
25 mg/kg	10 250.4 15.8	10 37.149 2.199	10 6.542 0.260	10 0.259 0.027	10 0.050 0.005	10 0.053 0.008	10 1.554 0.357	10 0.345 0.043
100 mg/kg	10 227.8 ** 15.4	10 41.521 ** 1.948	10 6.924 0.367	10 0.314 ** 0.044	10 0.053 0.004	10 0.055 0.016	10 2.133 * 0.868	10 0.300 0.036
400 mg/kg	10 228.3 ** 16.0	10 47.535 ** 2.997	10 7.521 * 1.715	10 0.258 0.031	10 0.047 ** 0.005	10 0.052 0.006	10 1.460 0.242	10 0.151 ** 0.029

Parameter, number of animals

*, significantly different from control, $p < 0.05$ **, significantly different from control, $p < 0.01$ mean
S.D.

Table 9
Twenty-eight-day repeat dose oral toxicity study of methoxychlor in rats
Sperm findings

Group	Sperm motility(%)	Caudal epididymal sperm counts (million)	Caudal epididymal sperm counts /caudal weight (million/g)	Testicular sperm head counts (million)	Testicular sperm head counts /testis weight (million/g)
Control	5	5	5	5	5
	87.3 6.9	137.4 20.4	803.0 116.2	175.5 58.4	116.1 34.5
25 mg/kg	5	5	5	5	5
	93.2 1.3	149.9 46.5	897.6 194.4	150.6 12.4	107.3 8.5
100 mg/kg	5	5	5	5	5
	85.0 16.8	75.6 * 27.2	747.2 123.9	133.1 10.5	118.4 9.1
400 mg/kg	5	5	5	5	5
	58.2 36.9	27.7 ** 38.4	300.0 ** 252.8	92.7 71.7	89.2 59.7

Parameter, number of animals
mean
S.D.

*, significantly different from control, p<0.05.
**, significantly different from control, p<0.01.

Table 9 (continued)
Twenty-eight-day repeat dose oral toxicity study of methoxychlor in rats

Sperm findings

Group	Total number of sperm examined	Total number of abnormal sperm	Sperm morphological abnormality(%) mean S.D.	Abnormal sperm; types and frequencies (N)									
				Pin head	Amorphous	Short head	Banana head	Reduced hook	No hook	Bent flagellum	Coiled flagellum	Broken flagellum	Detached flagellum
Control	1000	49	4.9 3.0	0.10 (1)	0.10 (1)	0.30 (3)	0.10 (1)	0.60 (6)	0.20 (2)	0.30 (3)	0.10 (1)	0.60 (6)	2.50 (25)
25 mg/kg	1000	50	5.0 1.7	0.30 (3)	0.30 (3)	0 (0)	0 (0)	0.80 (8)	0.10 (1)	0.10 (1)	0.30 (3)	0.40 (4)	2.70 (27)
100 mg/kg	1000	59	5.9 3.6	0.20 (2)	0.50 (5)	0 (0)	0 (0)	1.60 (16)	0 (0)	0 (0)	0.60 (6)	0.60 (6)	2.40 (24)
400 mg/kg	975	200	21.7 25.4	0.30 (3)	0.10 (1)	0 (0)	0 (0)	1.23 (12)	0.10 (1)	1.01 (10)	0.50 (5)	3.59 (32)	14.82 (136)

*, significantly different from control, $p < 0.05$.

**, significantly different from control, $p < 0.01$.

Table 10-1
Twenty-eight-day repeat dose oral toxicity study of methoxychlor in rat
Summary of macroscopic findings in males

Group Grade	Control	25 mg/kg		100 mg/kg		400mg/kg	
		-	+	-	+	-	+
(Testis)							
Small (Epididymis)	[10] 10	[10] 10	0	[10] 10	[10] 5	0	[10] 2
Small Nodule, cauda, unilateral (Prostate)	[10] 10	[10] 10	0	[10] 10	[10] 9	0	[10] 10
Small (Seminal vesicle)	[10] 10	[10] 10	0	[10] 10	[10] 1	0	[10] 1
Small Area, edematous, unilateral (Lung)	[10] 10	[10] 10	0	[10] 10	[10] 9	0	[10] 10
Spot, dark red (Liver)	[10] 9	[10] 9	1	[10] 10	[10] 10	0	[10] 10
Diaphragmatic nodule (Kidney)	[10] 9	[10] 9	1	[10] 10	[10] 10	0	[10] 10
Dilatation, renal pelvis, unilateral			2			0	
Area, pale, tessellated			0			0	
	8 10	8 10	2 0	10 10	10 10	0 0	10 9
							0 1

- , negative; + , positive
[], Number of animals examined

Table 10-2
Twenty-eight-day repeat dose oral toxicity study of methoxychlor in rat
Summary of macroscopic findings in females

Group Grade (Ovary)	Control		25 mg/kg		100 mg/kg		400 mg/kg	
	-	+	-	+	-	+	-	+
(Uterus)								
	[10]	0	[10]	0	[10]	0	[10]	0
Small								
	[10]	0	[10]	0	[10]	0	[10]	0
Dilatation, lumen								
	[10]	0	[10]	0	[10]	1	[10]	0
Cyst, horn, unilateral								
	[10]	0	[10]	0	[10]	0	[10]	1
Pale								
	[10]	0	[10]	0	[10]	0	[10]	1
(Kidney)								
Enlargement								
	[10]	0	[10]	0	[10]	0	[10]	0
Area, pale, cortex								
	[10]	0	[10]	0	[10]	0	[10]	0
Soft								
	[10]	0	[10]	0	[10]	0	[10]	0
Adhesion, capsule, unilateral								
	[10]	1	[10]	0	[10]	0	[10]	0
(Skin)								
Alopecia								
	[10]	0	[10]	0	[10]	0	[10]	0
Soiled perineal region								
	[10]	0	[10]	0	[10]	1	[10]	2
	[10]	0	[10]	0	[10]	0	[10]	1

- , Negative; +, Positive

[], Number of animals examined

Table 11-1
Twenty-eight-day repeat dose oral toxicity study of methoxychlor in rats
Summary of histopathological findings in males

Group	Control		25 mg/kg		100 mg/kg		400 mg/kg		Pos
	-	+	-	+	-	+	-	+	
(Testis)	10	0	8	2	3	6	0	5	7
Atrophy, seminiferous tubule	[10]	0	[10]	0	[10]	1	0	0	7
Necrosis/degeneration, spermatocyte, in seminiferous tubule	10	0	10	0	0	3	0	0	7
Decrease, spermatid, in seminiferous tubule	10	0	10	0	0	3	0	0	7
Degeneration, spermatid, in seminiferous tubule	10	0	10	0	0	7	2	0	3
Decrease, sperm, in seminiferous tubule	10	0	10	0	0	7	2	1	3
Multinucleated giant cell, in seminiferous tubule	10	0	10	0	0	7	2	1	3
Vacuolization, germ cell layer, in seminiferous tubule	10	0	9	1	0	9	1	0	1
Atrophy, Leydig cell, diffuse	10	0	10	0	0	9	0	1	1
Cellular infiltration, lymphocyte, perivascular, focal (Epididymis)	10	0	10	0	0	0	3	7	10
Decrease, sperm, in lumen	10	0	10	0	0	9	1	0	1
Cell debris, in lumen	10	0	10	0	0	6	1	2	4
Spermatid granuloma, unilateral	10	0	10	0	0	7	2	0	3
(Prostate Ventral & Dorsolateral lobes)	10	0	10	0	0	9	0	0	1
Atrophy, with decreased secretion	10	0	10	0	0	0	3	5	2
Cellular infiltration, lymphocyte, interstitium	7	2	6	1	3	8	1	1	10
Cellular infiltration, lymphocyte and plasma cell, epithelial layer (Seminiferous vesicle)	7	3	8	2	0	10	0	0	2
Atrophy, with decreased secretion (Mammary gland)	10	0	10	0	0	1	2	5	9
Atrophy (Adrenal gland)	6	0	10	0	0	1	0	2	7
Hypertrophy, cortical cell	10	0	10	0	0	4	5	1	0

- Negative, 3. Very slight, 4. Slight, 5. Moderate, 6. Mild, 7. Severe, 8. Very severe, 9. Extreme, 10. Total of positive grade
[] Number of animals examined
* Significant different from control p<0.05 (Two-tailed Mann-Whitney U test)
** Significant different from control p<0.01 (Two-tailed Mann-Whitney U test)
Significant different from control p<0.05 (One-tailed Fisher exact test)
Significant different from control p<0.01 (One-tailed Fisher exact test)

Table 11-1 (Continued)
Twenty-eight-day repeat dose oral toxicity study of methoxychlor in rats
Summary of histopathological findings in males

Group	Control			25 mg/kg			100 mg/kg			400 mg/kg		
	+	±	Pos	+	±	Pos	+	±	Pos	+	±	Pos
(Kidney)												
Esophageal body	9	1	0	9	0	1	9	0	1	9	0	1
Basophilic tubule	4	6	0	7	3	0	8	2	0	8	0	0
Basophilic tubule, medulla	10	0	0	10	0	0	10	0	0	10	0	0
Degeneration, vascular, epithelium proximal tubule	10	0	0	10	0	0	10	0	0	10	0	0
Dilatation, distal tubule, cortex	10	0	0	10	0	0	10	0	0	10	0	0
Dilatation, collecting tubule, medulla/papilla	10	0	0	10	0	0	10	0	0	10	0	0
Cell debris, distal tubule, cortex	10	0	0	10	0	0	10	0	0	10	0	0
Cell debris, collecting tubule, medulla/papilla	10	0	0	10	0	0	10	0	0	10	0	0
Cellular infiltration, neutrophil, lumen, distal/collecting tubule	10	0	0	10	0	0	10	0	0	10	0	0
Cellular infiltration, neutrophil, papilla	10	0	0	10	0	0	10	0	0	10	0	0
Mineralization, papilla	10	0	0	10	0	0	10	0	0	10	0	0
Dilatation, renal pelvis (Liver)	8	1	1	10	0	0	10	0	0	10	0	0
(10)												
Hypertrophy, hepatocyte, centrilobular	10	0	0	10	0	0	10	0	0	10	0	0
Degeneration, fatty, focal	9	1	0	10	0	0	10	0	0	10	0	0
Necrosis, focal	10	0	0	10	0	0	10	0	0	10	0	0
Fibrosis, capsula, focal, on diaphragmatic nodule (Spleen)	9	1	0	10	0	0	10	0	0	10	0	0
(10)												
Hematomas, extramedullary Deposit, pigment, brown (Lung & Bronchus)	0	7	3	1	6	3	0	6	4	0	6	4
(10)												
Accumulation, foam cell Mineralization, artery Hemorrhage, focal Cellular infiltration, neutrophil & lymphocyte, focal	5	4	1	5	5	0	5	4	1	5	4	1
Cellular infiltration, neutrophil & lymphocyte, focal	8	2	0	7	3	0	8	2	0	7	3	0
Cellular infiltration, neutrophil & lymphocyte, focal	9	1	0	10	0	0	9	1	0	10	0	0
Cellular infiltration, eosinophil (Heart)	9	1	0	10	0	0	8	2	0	10	0	0
(10)												
Mucosal degeneration/fibrosis, (Thyroid gland)	10	0	0	10	0	0	10	0	0	10	0	0
(10)												
Ectopic thymic tissue	9	1	0	10	0	0	10	0	0	10	0	0

- Negative, ± Very slight, + Slight, ++ Moderate, +++ Severe, Pos., Total of positive grade
 [] Number of animals examined
 * Significantly different from control p<0.05 (Two-tailed Mann-Whitney U test)
 ** Significantly different from control p<0.01 (Two-tailed Mann-Whitney U test)
 # Significantly different from control p<0.05 (One-tailed Fisher exact test)
 ## Significantly different from control p<0.01 (One-tailed Fisher exact test)

Table 11-2
Twenty-eight day lowest dose oral toxicity study of methoxychlor in rats
Summary of histopathological findings in females

Group	Control			25 mg/kg			100 mg/kg			400 mg/kg			Pgs	
	-	+	++	-	+	++	-	+	++	-	+	++		
(Ovary)	[10]			[10]			[10]			[10]			Pgs	
Decrease, corpus luteum	10	0	0	10	0	0	7	1	1	0	3	3	1	**
Increase, atresia, follicle	9	1	0	9	1	0	6	2	2	0	3	3	4	**
Follicular cyst	8	1	0	10	0	0	9	1	0	0	10	0	0	**
Mineralization														
Dispersed oocyte	10	0	0	10	0	0	10	0	0	0	8	2	0	0
(Uterus, horn & cervix)	[10]			[10]			[10]			[10]				2
Hypertrophy														
Luminal epithelial cell	10	0	0	10	0	0	5	0	3	2	0	0	0	0
Mitosis	1	4	2	3	4	3	1	2	5	2	0	0	0	5
Luminal epithelial cell														7
Vacuolation with cell debris	0	9	0	0	10	0	3	3	4	0	0	0	0	7
Vacuolation with cell debris														10
Distention, lumen, uterus	2	7	1	0	0	0	0	6	4	0	0	0	6	0
Glandular epithelium	9	0	1	9	1	0	1	2	4	3	0	0	0	10
Cyst, gland, serosa	10	0	0	10	0	0	10	0	0	0	0	0	0	9
Cellular infiltration, endometrium	0	0	6	3	1	10	0	1	0	9	0	0	0	0
Cellular infiltration														10
Lymphocyte, endometrium	10	0	0	0	0	0	0	1	0	9	0	0	0	10
Metaplasia, squamous														1
Luminal epithelium	10	0	0	0	9	1	10	0	0	0	0	0	0	0
(Vagina)	[9]			[10]			[9]			[10]				0
Coronation, epithelium	9	0	0	0	0	0	10	0	0	0	0	0	0	0
Mucification, epithelium	9	0	0	0	0	0	8	0	1	0	0	0	0	1
Increase, thickness														3
epithelial layer	8	1	0	0	0	0	4	3	0	2	0	0	0	5
Cellular infiltration														0
metaplasia, epithelium	0	2	3	3	1	9	2	2	5	0	0	0	2	5
(uterine cervix)	[10]			[10]			[10]			[10]				10
Hypertrophy, superficial cell	9	1	0	0	0	0	3	7	0	0	0	0	0	7
														7
														4
														10

-, Negative; +, Very slight; ++, Slight; +++, Moderate; ****, Severe; Pgs, Total of positive grade.
 [] Number of animals examined
 *, Significantly different from control p<0.05 (Two-tailed Mann-Whitney U test)
 **, Significantly different from control p<0.01 (Two-tailed Mann-Whitney U test)
 #, Significantly different from control p<0.05 (One-tailed Fisher exact test)
 ##, Significantly different from control p<0.01 (One-tailed Fisher exact test)

Table 11-2 (continued)
Twenty-eight day repeat dose oral toxicity study of methoxychlor in rats
Summary of histopathological findings in females

Group	Control		25 mg/kg		100 mg/kg		400 mg/kg		Pos
	↓	↑	↓	↑	↓	↑	↓	↑	
(Kidney)									
Basophilic tubule cortex	5	5	8	2	4	6	1	5	3
Basophilic tubule medulla	10	0	10	0	10	0	7	2	0
Degeneration vascular epithelium proximal tubule	10	0	10	0	10	0	1	7	2
Dilatation proximal tubule cortex	10	0	10	0	10	0	9	0	1
Dilatation distal tubule cortex	10	0	10	0	10	0	1	7	1
Dilatation collecting tubule medulla/papilla	10	0	10	0	10	0	7	2	0
Cell debris distal tubule cortex	10	0	10	0	10	0	3	5	1
Cell debris collecting tubule medulla/papilla	10	0	10	0	10	0	6	3	1
Cellular infiltration, neutrophil lumen distal/collecting tubule	10	0	10	0	10	0	8	1	1
Cellular infiltration, neutrophil cortex	10	0	10	0	10	0	9	0	1
Mineralization cortex	10	0	10	0	10	0	9	1	0
Cellular infiltration lymphocyte interstitium (Liver)	10	0	10	0	9	1	10	0	0
Hepatocyte, hepatocyte centrilobular (Spleen)	10	0	10	0	5	5	0	2	5
Hemorrhage, extramedullary (Lung & Bronchus)	0	5	0	2	0	1	0	4	6
Accumulation foam cell	0	0	0	1	0	2	0	1	9
Mineralization artery	8	1	4	6	5	5	6	4	0
Hemorrhage focal cellular infiltration, neutrophil & lymphocyte focal	9	1	9	1	9	1	8	2	0
Metaplasia, oesophagus	9	0	10	0	10	0	10	0	0
Fibrosis, focal, pleura (Thyroid gland)	10	0	8	2	10	0	9	1	0
Ectopic thymic cell	10	0	10	0	10	0	10	0	0

- Negative, ±, Very slight, +, Slight, ++, Moderate, +++, Severe, Pos., Total of positive grade
[] Number of animals examined
* Significantly different from control p<0.05 (Two-tailed Mann-Whitney U test)
** Significantly different from control p<0.01 (Two-tailed Mann-Whitney U test)
Significantly different from control p<0.05 (One-tailed Fisher exact test)
Significantly different from control p<0.01 (One-tailed Fisher exact test)

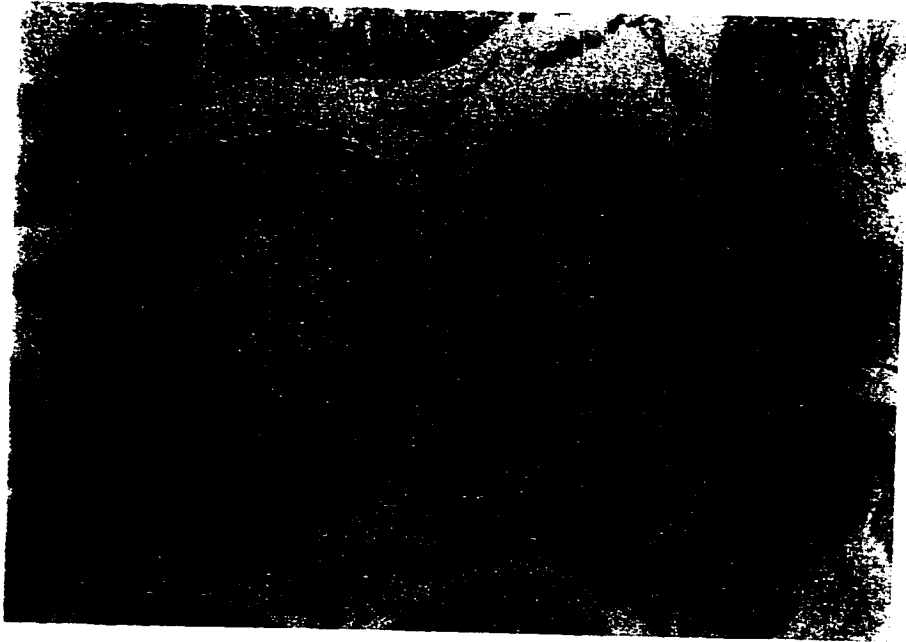


Photo 1 A microphotography of the testis from the male animal of methoxychlor, control group (Animal No. 4) showing no abnormality in seminiferous tubule. x 170, Hematoxylin-eosin stain.

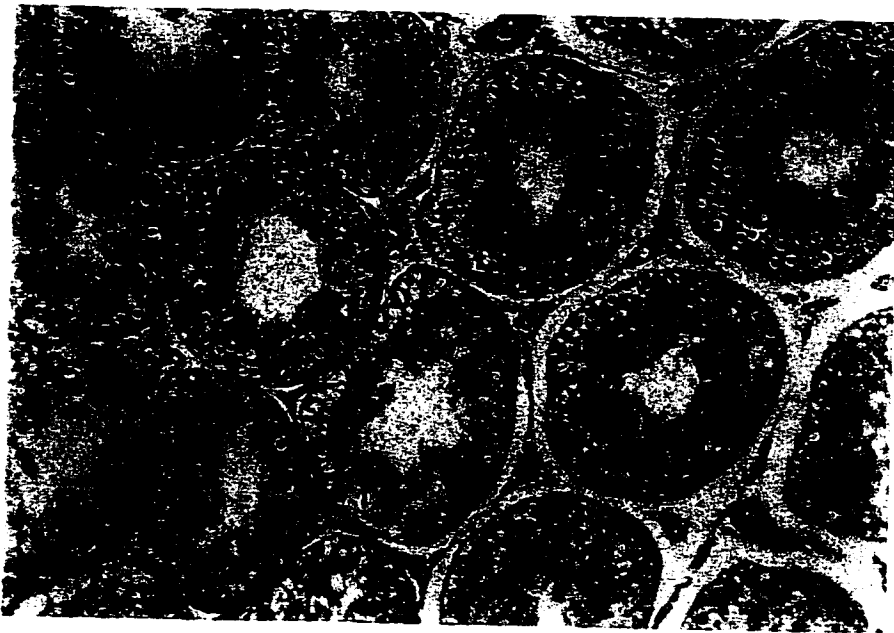


Photo 2 A microphotography of the testis from the male animal of methoxychlor, 400 mg/kg group (Animal No. 38) showing necrosis/degeneration of spermatocyte, degeneration of spermatid, vacuolization of germ cell layer, decrease of spermatid and sperm in atrophic seminiferous tubule, with atrophy of leydig cell. x 170, Hematoxylin-eosin stain.



Photo 3 A microphotography of the ovary from the female animal of methoxychlor, 400 mg/kg control group (Animal No. 80) showing decrease of corpus luteum and increase of follicle with atresia. x 35, Hematoxylin-eosin stain.



Photo 4 A microphotography of the uterus from the female animal of methoxychlor, 400 mg/kg group (Animal No. 80) showing hypertrophy of luminal epithelial cell. x 35, Hematoxylin-eosin stain.