

1,4 - ジクロロ - 2 - ニトロベンゼンのラットを用いた
経口投与による 13 週間毒性試験(混餌試験)報告書

試験番号：0301

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TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS
IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Week on Study	Control			1481ppm			2222ppm			3333ppm			5000ppm			7500ppm		
	Av.Wt.	No. of		Av.Wt.	% of	No. of	Av.Wt.	% of	No. of	Av.Wt.	% of	No. of	Av.Wt.	% of	No. of	Av.Wt.	% of	No. of
	<10>	Surviv.		<10>	cont.	Surviv.	<10>	cont.	Surviv.	<10>	cont.	Surviv.	<10>	cont.	Surviv.	<10>	cont.	Surviv.
0	120	(10)	10/10	120	(10)	100	120	(10)	100	120	(10)	100	120	(10)	100	120	(10)	100
1	148	(10)	10/10	148	(10)	100	145	(10)	98	144	(10)	97	133	(10)	90	115	(10)	78
2	181	(10)	10/10	179	(10)	99	175	(10)	97	172	(10)	95	153	(10)	85	113	(10)	62
3	201	(10)	10/10	198	(10)	99	193	(10)	96	185	(10)	92	164	(10)	82	120	(10)	60
4	221	(10)	10/10	218	(10)	99	210	(10)	95	198	(10)	90	175	(10)	79	126	(10)	57
5	238	(10)	10/10	234	(10)	98	224	(10)	94	210	(10)	88	183	(10)	77	128	(10)	54
6	250	(10)	10/10	244	(10)	98	235	(10)	94	219	(10)	88	189	(10)	76	133	(10)	53
7	262	(10)	10/10	256	(10)	98	242	(10)	92	226	(10)	86	194	(10)	74	140	(10)	53
8	269	(10)	10/10	265	(10)	99	250	(10)	93	234	(10)	87	200	(10)	74	141	(10)	52
9	283	(10)	10/10	276	(10)	98	261	(10)	92	244	(10)	86	207	(10)	73	142	(10)	50
10	290	(10)	10/10	282	(10)	97	269	(10)	93	250	(10)	86	211	(10)	73	144	(10)	50
11	297	(10)	10/10	292	(10)	98	277	(10)	93	257	(10)	87	217	(10)	73	147	(10)	49
12	304	(10)	10/10	298	(10)	98	283	(10)	93	265	(10)	87	225	(10)	74	153	(10)	50
13	308	(10)	10/10	304	(10)	99	289	(10)	94	272	(10)	88	232	(10)	75	156	(10)	51

< > : No.of effective animals, () : No.of measured animals Av.Wt.:g

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS
IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Week on Study	Control			1481ppm			2222ppm			3333ppm			5000ppm			7500ppm		
	Av.Wt.	No. of		Av.Wt.	% of	No. of	Av.Wt.	% of	No. of	Av.Wt.	% of	No. of	Av.Wt.	% of	No. of	Av.Wt.	% of	No. of
	<10>	Surviv.		<10>	cont.	Surviv.	<10>	cont.	Surviv.	<10>	cont.	Surviv.	<10>	cont.	Surviv.	<10>	cont.	Surviv.
0	97 (10)	10/10		97 (10)	100	10/10	97 (10)	100	10/10	97 (10)	100	10/10	97 (10)	100	10/10	97 (10)	100	10/10
1	112 (10)	10/10		112 (10)	100	10/10	109 (10)	97	10/10	106 (10)	95	10/10	104 (10)	93	10/10	93 (10)	83	10/10
2	126 (10)	10/10		126 (10)	100	10/10	123 (10)	98	10/10	118 (10)	94	10/10	115 (10)	91	10/10	96 (10)	76	10/10
3	133 (10)	10/10		131 (10)	98	10/10	128 (10)	96	10/10	122 (10)	92	10/10	118 (10)	89	10/10	99 (10)	74	10/10
4	141 (10)	10/10		139 (10)	99	10/10	135 (10)	96	10/10	126 (10)	89	10/10	123 (10)	87	10/10	103 (10)	73	10/10
5	149 (10)	10/10		145 (10)	97	10/10	140 (10)	94	10/10	132 (10)	89	10/10	129 (10)	87	10/10	108 (10)	72	10/10
6	154 (10)	10/10		148 (10)	96	10/10	141 (10)	92	10/10	133 (10)	86	10/10	131 (10)	85	10/10	110 (10)	71	10/10
7	154 (10)	10/10		149 (10)	97	10/10	141 (10)	92	10/10	135 (10)	88	10/10	132 (10)	86	10/10	112 (10)	73	10/10
8	159 (10)	10/10		152 (10)	96	10/10	141 (10)	89	10/10	137 (10)	86	10/10	132 (10)	83	10/10	113 (10)	71	10/10
9	163 (10)	10/10		156 (10)	96	10/10	145 (10)	89	10/10	138 (10)	85	10/10	135 (10)	83	10/10	118 (10)	72	10/10
10	165 (10)	10/10		155 (10)	94	10/10	146 (10)	88	10/10	139 (10)	84	10/10	135 (10)	82	10/10	118 (10)	72	10/10
11	168 (10)	10/10		160 (10)	95	10/10	147 (10)	88	10/10	141 (10)	84	10/10	137 (10)	82	10/10	121 (10)	72	10/10
12	171 (10)	10/10		161 (10)	94	10/10	149 (10)	87	10/10	144 (10)	84	10/10	139 (10)	81	10/10	123 (10)	72	10/10
13	172 (10)	10/10		163 (10)	95	10/10	150 (10)	87	10/10	144 (10)	84	10/10	140 (10)	81	10/10	123 (10)	72	10/10
< > : No.of effective animals, () : No.of measured animals Av.Wt.:g																		

TABLE 3 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Week on Study	Control			1481ppm			2222ppm			3333ppm			5000ppm			7500ppm							
	Av.FC.	No. of Surviv.		Av.FC.	% of cont.	No. of Surviv.	Av.FC.	% of cont.	No. of Surviv.	Av.FC.	% of cont.	No. of Surviv.	Av.FC.	% of cont.	No. of Surviv.	Av.FC.	% of cont.	No. of Surviv.					
	<10>			<10>			<10>			<10>			<10>			<10>							
1	13.5	(10)	10/10	13.0	(10)	96	10/10	12.4	(10)	92	10/10	12.2	(10)	90	10/10	11.5	(10)	85	10/10	9.6	(10)	71	10/10
2	14.3	(10)	10/10	14.4	(10)	101	10/10	13.7	(10)	96	10/10	13.7	(10)	96	10/10	12.6	(10)	88	10/10	9.5	(8)	66	10/10
3	15.1	(10)	10/10	14.7	(10)	97	10/10	14.1	(10)	93	10/10	13.5	(10)	89	10/10	11.4	(10)	75	10/10	7.4	(7)	49	10/10
4	14.8	(9)	10/10	14.5	(10)	98	10/10	13.6	(10)	92	10/10	12.9	(10)	87	10/10	11.2	(10)	76	10/10	7.8	(7)	53	10/10
5	15.4	(10)	10/10	15.2	(10)	99	10/10	14.1	(10)	92	10/10	13.5	(10)	88	10/10	11.6	(10)	75	10/10	8.3	(7)	54	10/10
6	14.8	(10)	10/10	14.8	(10)	100	10/10	13.7	(10)	93	10/10	13.5	(10)	91	10/10	11.5	(10)	78	10/10	8.3	(7)	56	10/10
7	15.1	(7)	10/10	15.0	(10)	99	10/10	13.8	(10)	91	10/10	13.7	(10)	91	10/10	12.0	(10)	79	10/10	8.6	(7)	57	10/10
8	14.6	(10)	10/10	14.9	(10)	102	10/10	13.6	(10)	93	10/10	13.4	(10)	92	10/10	11.7	(10)	80	10/10	8.9	(6)	61	10/10
9	15.3	(10)	10/10	15.3	(10)	100	10/10	14.0	(10)	92	10/10	13.5	(10)	88	10/10	11.8	(10)	77	10/10	7.8	(7)	51	10/10
10	15.1	(10)	10/10	15.3	(10)	101	10/10	14.0	(10)	93	10/10	13.3	(10)	88	10/10	11.5	(10)	76	10/10	8.5	(7)	56	10/10
11	15.1	(10)	10/10	15.6	(10)	103	10/10	14.3	(10)	95	10/10	13.4	(10)	89	10/10	11.8	(10)	78	10/10	8.2	(5)	54	10/10
12	14.9	(10)	10/10	15.3	(10)	103	10/10	14.1	(10)	95	10/10	13.4	(10)	90	10/10	11.9	(10)	80	10/10	9.0	(7)	60	10/10
13	15.2	(10)	10/10	15.6	(10)	103	10/10	14.6	(10)	96	10/10	13.6	(10)	89	10/10	12.5	(10)	82	10/10	9.3	(7)	61	10/10
< > : No.of effective animals, () : No.of measured animals Av.FC.:g																							

< > : No.of effective animals, () : No.of measured animals Av.FC.:g

TABLE 4 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Week on Study	Control			1481ppm				2222ppm				3333ppm				5000ppm				7500ppm			
	Av.FC.		No. of Surviv.	Av.FC.		% of cont.	No. of Surviv.	Av.FC.		% of cont.	No. of Surviv.	Av.FC.		% of cont.	No. of Surviv.	Av.FC.		% of cont.	No. of Surviv.				
	<10>			<10>				<10>				<10>				<10>				<10>			
1	10.8	(10)	10/10	10.1	(10)	94	10/10	9.8	(10)	91	10/10	9.4	(10)	87	10/10	8.8	(10)	81	10/10	7.5	(10)	69	10/10
2	10.7	(10)	10/10	10.4	(10)	97	10/10	10.2	(10)	95	10/10	9.7	(10)	91	10/10	9.2	(10)	86	10/10	6.8	(10)	64	10/10
3	10.7	(10)	10/10	10.3	(10)	96	10/10	9.8	(10)	92	10/10	9.5	(10)	89	10/10	8.3	(10)	78	10/10	6.1	(10)	57	10/10
4	10.7	(10)	10/10	10.0	(10)	93	10/10	9.9	(10)	93	10/10	9.2	(10)	86	10/10	8.3	(10)	78	10/10	6.4	(10)	60	10/10
5	11.0	(10)	10/10	10.7	(10)	97	10/10	10.7	(10)	97	10/10	9.5	(10)	86	10/10	9.1	(10)	83	10/10	6.6	(10)	60	10/10
6	10.9	(10)	10/10	10.2	(10)	94	10/10	10.0	(9)	92	10/10	9.3	(10)	85	10/10	9.0	(10)	83	10/10	6.4	(10)	59	10/10
7	11.1	(10)	10/10	10.6	(10)	95	10/10	9.8	(9)	88	10/10	9.4	(10)	85	10/10	9.0	(10)	81	10/10	6.5	(9)	59	10/10
8	10.9	(10)	10/10	10.7	(10)	98	10/10	9.6	(9)	88	10/10	9.4	(10)	86	10/10	8.6	(10)	79	10/10	6.8	(10)	62	10/10
9	10.9	(10)	10/10	10.6	(10)	97	10/10	9.9	(10)	91	10/10	9.3	(10)	85	10/10	9.0	(10)	83	10/10	6.8	(10)	62	10/10
10	10.3	(10)	10/10	9.8	(10)	95	10/10	9.8	(10)	95	10/10	9.0	(10)	87	10/10	8.2	(10)	80	10/10	6.5	(10)	63	10/10
11	10.8	(10)	10/10	10.4	(10)	96	10/10	10.4	(10)	96	10/10	9.4	(10)	87	10/10	8.9	(10)	82	10/10	7.0	(10)	65	10/10
12	10.5	(10)	10/10	10.1	(10)	96	10/10	9.9	(10)	94	10/10	9.3	(10)	89	10/10	8.7	(10)	83	10/10	6.8	(10)	65	10/10
13	10.6	(10)	10/10	10.1	(9)	95	10/10	10.0	(10)	94	10/10	9.2	(10)	87	10/10	8.9	(10)	84	10/10	6.7	(10)	63	10/10
< > : No.of effective animals, () : No.of measured animals Av.FC.:g																							

< > : No.of effective animals, () : No.of measured animals Av.FC.:g

TABLE 5 HEMATOLOGY OF MALE RATS IN THE 13-WEEK FEED STUDY
OF 1,4-DICHLORO-2-NITROBENZENE

Group Name	Control	1481 ppm	2222 ppm	3333 ppm	5000 ppm	7500 ppm
No. of examined animals	10	10	10	10	9	9
Red blood cell ($10^6/\mu\text{L}$)	9.76 $\pm$ 0.22	9.82 $\pm$ 0.33	9.34 $\pm$ 0.54	9.17 $\pm$ 0.44 **	9.01 $\pm$ 0.36 **	8.01 $\pm$ 0.39 **
Hemoglobin (g/dL)	16.7 $\pm$ 0.4	16.3 $\pm$ 0.5	15.8 $\pm$ 0.4 **	15.5 $\pm$ 0.4 **	15.6 $\pm$ 0.2 **	15.0 $\pm$ 0.5 **
Hematocrit (%)	48.7 $\pm$ 1.4	47.9 $\pm$ 1.7	46.1 $\pm$ 2.3 *	45.6 $\pm$ 2.5 **	46.3 $\pm$ 1.7	45.1 $\pm$ 2.3 **
MCV (fL)	49.9 $\pm$ 0.7	48.8 $\pm$ 0.4 **	49.4 $\pm$ 0.6	49.7 $\pm$ 0.6	51.4 $\pm$ 0.6 **	56.3 $\pm$ 0.9 **
MCHC (g/dL)	34.3 $\pm$ 0.5	34.0 $\pm$ 0.5	34.4 $\pm$ 1.5	34.1 $\pm$ 1.9	33.7 $\pm$ 1.2	33.3 $\pm$ 1.4 **
Platelet ($10^3/\mu\text{L}$)	667 $\pm$ 33	694 $\pm$ 30	674 $\pm$ 33	641 $\pm$ 49	608 $\pm$ 34 *	484 $\pm$ 56 **
Reticulocyte(%)	25 $\pm$ 6	26 $\pm$ 7	28 $\pm$ 4	33 $\pm$ 8	36 $\pm$ 8 **	57 $\pm$ 8 **
Methnoglobin(%)	0.2 $\pm$ 0.1	0.2 $\pm$ 0.1	0.2 $\pm$ 0.1	0.3 $\pm$ 0.1	0.3 $\pm$ 0.1	0.4 $\pm$ 0.2 **
APTT (sec)	23.8 $\pm$ 2.1	22.7 $\pm$ 3.5	21.6 $\pm$ 1.7	20.1 $\pm$ 2.0 **	21.5 $\pm$ 2.1	18.2 $\pm$ 2.8 **

Mean $\pm$ S.D.

* Significant difference, $p < 0.05$ (Test of Dunnett)

** Significant difference, $p < 0.01$ (Test of Dunnett)

TABLE 6 HEMATOLOGY OF FEMALE RATS IN THE 13-WEEK FEED STUDY
OF 1,4-DICHLORO-2-NITROBENZENE

Group Name	Control	1481 ppm	2222 ppm	3333 ppm	5000 ppm	7500 ppm
No. of examined animals	10	9	10	9	9	9
Red blood cell ($10^6/\mu\text{L}$)	8.98 $\pm$ 0.22	8.70 $\pm$ 0.35	8.63 $\pm$ 0.28	8.10 $\pm$ 0.50 **	8.15 $\pm$ 0.51 **	7.91 $\pm$ 0.27 **
Hemoglobin (g/dL)	16.4 $\pm$ 0.3	15.6 $\pm$ 0.6 **	15.4 $\pm$ 0.4 **	15.0 $\pm$ 0.6 **	14.8 $\pm$ 0.6 **	14.6 $\pm$ 0.4 **
Hematocrit (%)	46.9 $\pm$ 0.9	44.9 $\pm$ 2.1	44.8 $\pm$ 1.2	42.4 $\pm$ 2.5 **	43.3 $\pm$ 3.1 **	44.0 $\pm$ 1.6 **
MCV (fL)	52.3 $\pm$ 0.5	51.6 $\pm$ 0.9	51.9 $\pm$ 0.7	52.3 $\pm$ 0.6	53.1 $\pm$ 0.8	55.6 $\pm$ 1.1 **
MCHC (g/dL)	34.9 $\pm$ 0.3	34.7 $\pm$ 0.5	34.3 $\pm$ 0.4	35.6 $\pm$ 2.5	34.4 $\pm$ 1.9	33.2 $\pm$ 1.2 **
Platelet ($10^3/\mu\text{L}$)	672 $\pm$ 33	662 $\pm$ 50	638 $\pm$ 51	588 $\pm$ 37 *	567 $\pm$ 82 **	485 $\pm$ 99 **
Reticulocyte(%)	24 $\pm$ 5	28 $\pm$ 8	27 $\pm$ 7	32 $\pm$ 6	37 $\pm$ 9 **	50 $\pm$ 10 **
Methnoglobin(%)	0.2 $\pm$ 0.1	0.2 $\pm$ 0.1	0.2 $\pm$ 0.1	0.2 $\pm$ 0.1	0.4 $\pm$ 0.1 **	0.3 $\pm$ 0.1 **
Prothrombin time (sec)	11.6 $\pm$ 0.3	11.3 $\pm$ 0.2	11.6 $\pm$ 0.5	11.7 $\pm$ 0.6	11.9 $\pm$ 0.4	12.9 $\pm$ 0.5 **
WBC ($10^3/\mu\text{L}$)	3.59 $\pm$ 0.92	3.92 $\pm$ 1.48	2.97 $\pm$ 0.80	2.49 $\pm$ 0.91	2.65 $\pm$ 0.66	2.06 $\pm$ 1.25 **

Mean $\pm$ S.D.

* Significant difference, $p < 0.05$ (Test of Dunnett)

** Significant difference, $p < 0.01$ (Test of Dunnett)

TABLE 7 BIOCHEMISTRY OF MALE RATS IN THE 13-WEEK FEED STUDY
OF 1,4-DICHLORO-2-NITROBENZENE

Group Name	Control	1481 ppm	2222 ppm	3333 ppm	5000 ppm	7500 ppm
No. of examined animals	10	10	10	10	9	9
Total protein (g/dL)	6.3 ± 0.1	7.1 ± 0.1 **	7.2 ± 0.2 **	7.2 ± 0.2 **	7.3 ± 0.3 **	6.5 ± 0.2
Albumin (g/dL)	3.9 ± 0.0	4.5 ± 0.1 *	4.6 ± 0.1 **	4.6 ± 0.1 **	4.7 ± 0.1 **	4.2 ± 0.2
A/G ratio	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.8 ± 0.1	1.8 ± 0.1	1.9 ± 0.1 **
T-Bilirubin (mg/dL)	0.14 ± 0.01	0.15 ± 0.01	0.15 ± 0.01	0.16 ± 0.01 *	0.17 ± 0.01 **	0.19 ± 0.02 **
Glucose (mg/dL)	178 ± 10	183 ± 21	185 ± 31	183 ± 17	174 ± 10	149 ± 5 **
T-Cholesterol (mg/dL)	67 ± 10	118 ± 14 **	126 ± 11 **	140 ± 14 **	143 ± 10 **	126 ± 11 **
Triglyceride (mg/dL)	52 ± 11	63 ± 27	67 ± 16	65 ± 14	51 ± 14	25 ± 11 **
Phospholipid (mg/dL)	114 ± 12	186 ± 15 **	206 ± 13 **	231 ± 19 **	246 ± 19 **	220 ± 20 **
GOT (IU/L)	76 ± 12	77 ± 16	71 ± 12	62 ± 7 *	84 ± 58	84 ± 14
GPT (IU/L)	45 ± 6	56 ± 22	42 ± 7	42 ± 5	74 ± 64	78 ± 17 **
γ-GTP(IU/L)	2 ± 1	2 ± 1	2 ± 1	3 ± 1	6 ± 1 **	26 ± 4 **
Urea Nitrogen(mg/L)	19.1 ± 1.8	21.4 ± 1.2 *	22.1 ± 2.3 **	22.3 ± 1.3 **	19.2 ± 1.6	20.8 ± 2.4
Creatinine(mg/dL)	0.5 ± 0.0	0.6 ± 0.1	0.6 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0.0 **
Sodium (mEq/L)	141 ± 1	141 ± 1	140 ± 1	140 ± 1	139 ± 1 **	138 ± 1 **
Chloride (mEq/L)	106 ± 1	104 ± 2 *	105 ± 1	104 ± 1 *	104 ± 1 **	105 ± 2
Calcium(mg/dL)	10.2 ± 0.1	10.6 ± 0.3 *	10.7 ± 0.3 **	10.8 ± 0.1 **	10.7 ± 0.3 **	10.1 ± 0.3
Inorganic phosphorus (mg/dL)	5.6 ± 0.5	5.5 ± 0.4	5.6 ± 0.6	5.7 ± 0.7	5.7 ± 0.4	6.3 ± 0.5 *

Mean ± S.D.

*) Significant difference, p<0.05 (Test of Dunnett)

**) Significant difference, p<0.01 (Test of Dunnett)

TABLE 8 BIOCHEMISTRY OF FEMALE RATS IN THE 13-WEEK FEED STUDY
OF 1,4-DICHLORO-2-NITROBENZENE

Group Name	Control	1481 ppm	2222 ppm	3333 ppm	5000 ppm	7500 ppm
No. of examined animals	10	9	10	9	9	9
Total protein (g/dL)	6.3 ± 0.2	6.8 ± 0.2 **	6.7 ± 0.2 **	6.8 ± 0.2 **	6.9 ± 0.2 **	6.5 ± 0.2
Albumin (g/dL)	3.9 ± 0.1	4.2 ± 0.1 **	4.2 ± 0.2 **	4.3 ± 0.1 **	4.3 ± 0.2 **	4.2 ± 0.2 **
T-Bilirubin (mg/dL)	0.16 ± 0.01	0.17 ± 0.01	0.16 ± 0.01	0.16 ± 0.02	0.18 ± 0.01 *	0.19 ± 0.02 **
Glucose (mg/dL)	139 ± 16	146 ± 10	154 ± 9 *	151 ± 14	156 ± 9 *	156 ± 15 *
T-Cholesterol (mg/dL)	73 ± 5	136 ± 14 **	136 ± 10 **	148 ± 11 **	154 ± 12 **	142 ± 13 **
Phospholipid (mg/dL)	135 ± 10	220 ± 20 **	221 ± 19 **	241 ± 19 **	255 ± 21 **	244 ± 16 **
ALP (IU/L)	195 ± 22	166 ± 17	167 ± 25	161 ± 21 *	168 ± 27	232 ± 34 *
γ-GTP(U/L)	2 ± 1	3 ± 1	4 ± 1	6 ± 2 **	18 ± 7 **	49 ± 6 **
Urea Nitrogen(mg/L)	18.3 ± 1.5	18.7 ± 1.1	20.1 ± 2.2	20.2 ± 2.1	20.7 ± 3.3	22.6 ± 2.8 **
Creatinine(mg/dL)	0.5 ± 0.1	0.5 ± 0.0	0.5 ± 0.0 **	0.5 ± 0.1 **	0.5 ± 0.1 **	0.4 ± 0.0 **
Sodium (mEq/L)	140 ± 1	140 ± 1	140 ± 1	139 ± 1	139 ± 1 *	138 ± 2 **
Potassium (mEq/L)	3.7 ± 0.2	3.8 ± 0.2	3.8 ± 0.3	3.7 ± 0.3	3.9 ± 0.2	4.1 ± 0.3 **
Calcium(mg/dL)	9.9 ± 0.1	10.2 ± 0.2	10.2 ± 0.3 *	10.2 ± 0.2	10.3 ± 0.3 **	10.0 ± 0.2

Mean ± S.D.

*) Significant difference, p<0.05 (Test of Dunnett)

**) Significant difference, p<0.01 (Test of Dunnett)

TABLE 9 URINALYSIS OF MALE RATS IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Group	Control	1481 ppm	2222 ppm	3333 ppm	5000 ppm	7500 ppm
Number of examined animals	10	10	10	10	10	10
Ketone body	Grade					
	—	0	2 *	3 *	6 **	4 *
	±	5	8	7	4	6
	+	5	0	0	0	0
	2+	0	0	0	0	0
	3+	0	0	0	0	0
	4+	0	0	0	0	0

Significant difference * : $p < 0.05$ ** : $p < 0.01$ Chi square test

TABLE 10 ORGAN WEIGHTS OF MALE RATS IN THE 13-WEEK FEED STUDY
OF 1,4-DICHLORO-2-NITROBENZENE

Group Name	Control	1481 ppm	2222 ppm	3333 ppm	5000 ppm	7500 ppm
No. of examined animals	10	10	10	10	10	10
Body weight (g)	282 ± 15	273 ± 11	264 ± 12	247 ± 8	210 ± 13	144 ± 15
			**	**	**	**
Thymus (g)	0.204 ± 0.020	0.182 ± 0.024	0.184 ± 0.030	0.185 ± 0.022	0.161 ± 0.027	0.104 ± 0.022
						**
Thymus (%)	0.072 ± 0.006	0.067 ± 0.009	0.070 ± 0.011	0.075 ± 0.008	0.077 ± 0.013	0.071 ± 0.010
Adrenals (g)	0.061 ± 0.013	0.064 ± 0.011	0.059 ± 0.010	0.063 ± 0.009	0.058 ± 0.007	0.049 ± 0.008
						*
Adrenals (%)	0.022 ± 0.005	0.024 ± 0.004	0.022 ± 0.004	0.025 ± 0.003	0.028 ± 0.003	0.034 ± 0.004
					**	**
Testes (g)	2.988 ± 0.125	3.041 ± 0.079	2.619 ± 0.139	1.621 ± 0.106	1.138 ± 0.082	0.857 ± 0.097
			**	**	**	**
Testes (%)	1.061 ± 0.040	1.113 ± 0.041	0.996 ± 0.070	0.657 ± 0.050	0.542 ± 0.037	0.596 ± 0.037
			*	**	**	**
Heart (g)	0.928 ± 0.050	0.905 ± 0.056	0.871 ± 0.072	0.863 ± 0.059	0.757 ± 0.039	0.525 ± 0.058
					**	**
Heart (%)	0.330 ± 0.017	0.331 ± 0.018	0.330 ± 0.021	0.350 ± 0.023	0.360 ± 0.010	0.365 ± 0.022
					**	**
Lungs (g)	1.013 ± 0.054	1.004 ± 0.035	0.975 ± 0.044	0.964 ± 0.054	0.862 ± 0.052	0.692 ± 0.055
					**	**
Lungs (%)	0.360 ± 0.016	0.368 ± 0.015	0.370 ± 0.012	0.391 ± 0.026	0.410 ± 0.012	0.483 ± 0.029
					**	**
Kidneys (g)	1.809 ± 0.086	2.063 ± 0.128	2.076 ± 0.133	2.070 ± 0.084	1.813 ± 0.100	1.389 ± 0.069
		**	**	**	**	**
Kidneys (%)	0.643 ± 0.026	0.755 ± 0.038	0.787 ± 0.029	0.839 ± 0.035	0.864 ± 0.043	0.971 ± 0.068
				**	**	**
Spleen (g)	0.533 ± 0.021	0.520 ± 0.042	0.542 ± 0.042	0.549 ± 0.120	0.465 ± 0.030	0.377 ± 0.046
					**	**
Spleen (%)	0.190 ± 0.007	0.190 ± 0.011	0.206 ± 0.016	0.223 ± 0.053	0.221 ± 0.008	0.262 ± 0.015
				*	**	**
Liver (g)	7.042 ± 0.323	9.681 ± 0.740	9.946 ± 0.686	9.976 ± 0.490	9.163 ± 0.646	6.352 ± 0.802
		**	**	**	**	**
Liver (%)	2.499 ± 0.039	3.539 ± 0.195	3.772 ± 0.124	4.040 ± 0.144	4.361 ± 0.167	4.412 ± 0.253
				**	**	**
Brain (g)	1.879 ± 0.044	1.865 ± 0.043	1.859 ± 0.048	1.848 ± 0.040	1.793 ± 0.041	1.665 ± 0.040
					**	**
Brain (%)	0.668 ± 0.035	0.683 ± 0.022	0.706 ± 0.027	0.749 ± 0.028	0.856 ± 0.048	1.168 ± 0.110
				*	**	**

Mean ± S.D.

^{*)} Significant difference, p<0.05 (Test of Dunnett)

^{**)} Significant difference, p<0.01 (Test of Dunnett)

TABLE 11 ORGAN WEIGHTS OF FEMALE RATS IN THE 13-WEEK FEED STUDY
OF 1,4-DICHLORO-2-NITROBENZENE

Group Name	Control	1481 ppm	2222 ppm	3833 ppm	5000 ppm	7500 ppm
No. of examined animals	10	10	10	10	10	10
Body weight (g)	159 ± 9	149 ± 12	138 ± 12	133 ± 8	129 ± 7	113 ± 9
Thymus (g)	0.168 ± 0.023	0.166 ± 0.019	0.152 ± 0.025	0.147 ± 0.024	0.140 ± 0.019	0.124 ± 0.026
Thymus (%)	0.106 ± 0.014	0.112 ± 0.010	0.110 ± 0.013	0.110 ± 0.017	0.109 ± 0.016	0.109 ± 0.017
Adrenals (g)	0.062 ± 0.008	0.060 ± 0.004	0.058 ± 0.006	0.055 ± 0.007	0.051 ± 0.005	0.047 ± 0.007
Adrenals (%)	0.039 ± 0.005	0.040 ± 0.005	0.042 ± 0.005	0.042 ± 0.004	0.040 ± 0.004	0.042 ± 0.006
Ovary (g)	0.105 ± 0.010	0.097 ± 0.012	0.101 ± 0.013	0.094 ± 0.009	0.088 ± 0.014	0.063 ± 0.009
Ovary (%)	0.066 ± 0.007	0.065 ± 0.010	0.074 ± 0.010	0.071 ± 0.008	0.068 ± 0.010	0.055 ± 0.007
Heart (g)	0.619 ± 0.029	0.592 ± 0.045	0.557 ± 0.029	0.547 ± 0.067	0.522 ± 0.026	0.435 ± 0.052
Heart (%)	0.391 ± 0.021	0.398 ± 0.018	0.405 ± 0.019	0.410 ± 0.034	0.407 ± 0.019	0.385 ± 0.024
Lungs (g)	0.748 ± 0.049	0.736 ± 0.045	0.701 ± 0.044	0.691 ± 0.022	0.667 ± 0.042	0.587 ± 0.041
Lungs (%)	0.472 ± 0.022	0.495 ± 0.027	0.509 ± 0.018	0.551 ± 0.024	0.518 ± 0.016	0.522 ± 0.031
Kidneys (g)	1.126 ± 0.069	1.215 ± 0.066	1.178 ± 0.102	1.193 ± 0.048	1.181 ± 0.059	1.062 ± 0.047
Kidneys (%)	0.711 ± 0.045	0.818 ± 0.054	0.855 ± 0.050	0.900 ± 0.064	0.919 ± 0.033	0.945 ± 0.045
Spleen (g)	0.376 ± 0.026	0.357 ± 0.030	0.333 ± 0.029	0.332 ± 0.025	0.341 ± 0.027	0.299 ± 0.037
Spleen (%)	0.238 ± 0.021	0.239 ± 0.010	0.241 ± 0.007	0.250 ± 0.012	0.265 ± 0.016	0.264 ± 0.016
Liver (g)	3.828 ± 0.268	4.871 ± 0.387	4.855 ± 0.356	5.149 ± 0.314	5.444 ± 0.346	5.126 ± 0.569
Liver (%)	2.414 ± 0.091	3.270 ± 0.122	3.525 ± 0.119	3.876 ± 0.145	4.233 ± 0.150	4.538 ± 0.229
Brain (g)	1.736 ± 0.027	1.738 ± 0.047	1.721 ± 0.045	1.714 ± 0.032	1.687 ± 0.060	1.625 ± 0.034
Brain (%)	1.098 ± 0.065	1.172 ± 0.096	1.255 ± 0.100	1.294 ± 0.077	1.314 ± 0.061	1.447 ± 0.095

Mean ± S.D.

^{*} Significant difference, $p < 0.05$ (Test of Dunnett)

^{**} Significant difference, $p < 0.01$ (Test of Dunnett)

TABLE 12 INCIDENCES OF SELECTED LESIONS OF MALE RATS IN THE 13-WEEK
FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Group	Control	1481 ppm	2222 ppm	3333 ppm	5000 ppm	7500 ppm
Number of examined animals	10	10	10	10	10	10
Organ	Grade of Nonneoplastic finding					
Findings						
Spleen						
Deposit of hemosiderin	1+	0	1	10 **	10 **	10 **
Increased extramedullary hematopoiesis	1+	0	0	1	4	9 **
Liver						
Swelling:central	1+	0	6 *	10 **	10 **	9 **
Vacuolic change:ventral	1+ 2+	0 0	0 0	0 0	6 * 0	7 ** 3
Kidney						
Basophilic change	1+	0	10 **	10 **	10 **	1
Eosinophilic body	1+ 2+ 3+	0 8 2	0 ** 0 10	0 ** 0 10	0 ** 0 10	0 ** 0 10
Desquamation:tubular epith	1+ 2+	0 0	4 ** 6	3 ** 7	2 ** 8	0 0
Testis						
germ cell necrosis	1+ 2+ 3+	0 0 0	0 0 0	6 * 0 0	0 ** 9 1	0 ** 0 10
Epididymis						
debris of spermatc element	1+	0	0	6 *	10 **	10 **
disappear:sperma	3+	0	0	0	10 **	10 **
Grade	1+: Slight	2+: Moderate	3+: Marked	4+: Severe		
Significant difference	* : p<0.05	** : p<0.01	Chi square test for non-neoplastic lesion			

TABLE 13 INCIDENCES OF SELECTED LESIONS OF FEMALE RATS IN THE 13-WEEK
FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Group Number of examined animals Organ	Grade of Nonneoplastic finding	Control	14814 ppm	2222 ppm	3333 ppm	5000 ppm	7500 ppm
		10	10	10	10	10	10
Bone marrow granulation	1+	3	1	1	0 *	0 *	0 *
	2+	2	1	0	0	0	0
Spleen Deposit of hemosiderin	1+	0	8 **	10 **	10 **	10 **	9 **
	1+	0	0	0	2	8 **	9 **
Liver Swelling:central	1+	0	10 **	10 **	10 **	10 **	10 **
	1+	0	0	0	0	0	8 **
Kidney Fosinophilic droplet: proximal tubule	1+	0	2 **	3 **	0 **	2 **	3
	2+	0	8	7	10	8	1
Grade	1+: Slight	2+: Moderate	3+: Marked	4+: Severe			
Significant difference	* : p<0.05	** : p<0.01	Chi square test for non-neoplastic lesion				