

p-ニトロアニソール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：0369

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TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

13-week study

<Method of Administration>	Mixed feed
<Number of Groups>	Male 6, Female 6
<Size of Groups>	10 males and 10 females of each group
<Animals>	
Strain and Species	F344/DuCrj (Fischer) rat
Animal Source	Charles River Japan, Inc.
Duration Held Before Study	2 wk
Age When Placed on Study	6 wk
Age When Killed	19 wk
<Doses>	
<Male>	0, 1250, 2500, 5000, 8000 or 10000 ppm
<Female>	0, 1250, 2500, 5000, 8000 or 10000 ppm
<Duration of Dosing>	7d/wk for 13wk
<Animal Maintenance>	
Feed	CRF-1 (Oriental Yeast Co., Ltd.) Sterilized by γ -ray Available <i>ad libitum</i>
Water	Filtrated and sterilized by ultraviolet ray Automatic watering system Available <i>ad libitum</i>
Animal per Cage	Single (stainless steel wire)
Animal Room Environment	Barrier system Temperature : 23±2°C Humidity : 55±15% Fluorescent light 12h/d 15~17 room air changes /h
<Type and Frequency of Observation>	
Clinical Sign	Observed 1×wk for 13wk
Body Weight	Weighed 1×wk for 13wk
Food Consumption	Weighed 1×wk for 13wk

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
(Continued) IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

13-week study

<Hematology>

Red blood cell (RBC), Hemoglobin, Hematocrit,
Mean corpuscular volume (MCV),
Mean corpuscular hemoglobin (MCH),
Mean corpuscular hemoglobin concentrate (MCHC),
Platelet, Reticulocyte,
White blood cell (WBC), Differential WBC,
Prothrombin time (PT),
Activated partial thromboplastin time (APTT).

<Biochemistry>

Total protein, Albumin, A/G ratio,
Total bilirubin, Glucose, Total cholesterol, Triglyceride,
Phospholipid, Glutamic oxaloacetic transaminase (GOT),
Glutamic pyruvic transaminase (GPT),
Lactate dehydrogenase (LDH),
Alkaline phosphatase (ALP),
 γ -Glutamyl transpeptidase (G-GTP),
Creatine phosphokinase (CPK),
Urea nitrogen, Creatinine,
Sodium, Potassium, Chloride,
Calcium, Inorganic phosphorus.

<Urinalysis>

pH, Protein, Glucose, Ketone body, bilirubin,
Occult blood, Urobilinogen

<Necropsy>

Necropsy performed on all animals.

<Organ Weight>

Organ weight measurement performed on
schedule sacrificed animals.

The following organs were weighed;
kidney, spleen, liver, and brain.

<Histopathologic Examination>

Histopathologic examination performed on at least
two animals per sex per group.

The following organs were examined;

skin, nasal cavity, nasopharynx, larynx, trachea, lung, bone marrow,
lymph node, thymus, spleen, heart, tongue, salivary gland, esophagus,
stomach, small intestine, large intestine, liver, pancreas,
kidney, urinary bladder, pituitary, thyroid, parathyroid, adrenal, testis,
epididymis, seminal vesicle, prostate, ovary, uterus, vagina,
mammary gland, brain, spinal cord, peripheral nerve,
eye, Harderian gland, muscle, bone, other organs/tissues with gross lesions.

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS
IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

Week-day on Study	Control			1250ppm			2500ppm			5000ppm			8000ppm			10000ppm			
	Av.Wt.	No. of Surviv. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	
0	126	(10)	10/10	126	(10)	100	10/10	126	(10)	100	10/10	126	(10)	100	10/10	126	(10)	100	10/10
1	155	(10)	10/10	155	(10)	100	10/10	153	(10)	99	10/10	148	(10)	95	10/10	137	(10)	88	10/10
2	182	(10)	10/10	180	(10)	99	10/10	178	(10)	98	10/10	173	(10)	95	10/10	161	(10)	88	10/10
3	203	(10)	10/10	202	(10)	100	10/10	198	(10)	98	10/10	194	(10)	96	10/10	180	(10)	89	10/10
4	224	(10)	10/10	219	(10)	98	10/10	216	(10)	96	10/10	212	(10)	95	10/10	197	(10)	88	10/10
5	239	(10)	10/10	236	(10)	99	10/10	230	(10)	96	10/10	226	(10)	95	10/10	211	(10)	88	10/10
6	251	(10)	10/10	248	(10)	99	10/10	246	(10)	98	10/10	240	(10)	96	10/10	222	(10)	88	10/10
7	264	(10)	10/10	260	(10)	98	10/10	260	(10)	98	10/10	249	(10)	94	10/10	234	(10)	89	10/10
8	276	(10)	10/10	273	(10)	99	10/10	269	(10)	97	10/10	258	(10)	93	10/10	242	(10)	88	10/10
9	286	(10)	10/10	281	(10)	98	10/10	280	(10)	98	10/10	269	(10)	94	10/10	250	(10)	87	10/10
10	295	(10)	10/10	290	(10)	98	10/10	289	(10)	98	10/10	279	(10)	95	10/10	256	(10)	87	10/10
11	303	(10)	10/10	298	(10)	98	10/10	298	(10)	98	10/10	288	(10)	95	10/10	268	(10)	87	10/10
12	309	(10)	10/10	306	(10)	99	10/10	306	(10)	99	10/10	294	(10)	95	10/10	269	(10)	87	10/10
13	315	(10)	10/10	312	(10)	99	10/10	314	(10)	100	10/10	301	(10)	96	10/10	276	(10)	88	10/10

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

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS
IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

Week-day on Study	Control			1250ppm			2500ppm			5000ppm			8000ppm			10000ppm			
	Av.Wt.	No. of Surviv. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	Av.Wt.	% of cont. <10>	No. of Surviv.	
0	100	(10)	10/10	100	(10)	100	10/10	100	(10)	100	10/10	100	(10)	100	10/10	100	(10)	100	10/10
1	112	(10)	10/10	111	(10)	99	10/10	107	(10)	96	10/10	104	(10)	93	10/10	96	(10)	86	10/10
2	123	(10)	10/10	118	(10)	96	10/10	115	(10)	93	10/10	111	(10)	90	10/10	105	(10)	85	10/10
3	130	(10)	10/10	125	(10)	96	10/10	119	(10)	92	10/10	115	(10)	88	10/10	112	(10)	86	10/10
4	138	(10)	10/10	130	(10)	94	10/10	125	(10)	91	10/10	120	(10)	87	10/10	118	(10)	86	10/10
5	144	(10)	10/10	136	(10)	94	10/10	130	(10)	90	10/10	124	(10)	86	10/10	122	(10)	85	10/10
6	149	(10)	10/10	140	(10)	94	10/10	134	(10)	90	10/10	129	(10)	87	10/10	126	(10)	85	10/10
7	154	(10)	10/10	142	(10)	92	10/10	138	(10)	90	10/10	131	(10)	85	10/10	130	(10)	84	10/10
8	157	(10)	10/10	143	(10)	91	10/10	139	(10)	89	10/10	133	(10)	85	10/10	133	(10)	85	10/10
9	163	(10)	10/10	146	(10)	90	10/10	142	(10)	87	10/10	135	(10)	83	10/10	133	(10)	82	10/10
10	166	(10)	10/10	152	(10)	92	10/10	145	(10)	87	10/10	138	(10)	83	10/10	137	(10)	83	10/10
11	171	(10)	10/10	152	(10)	89	10/10	149	(10)	87	10/10	140	(10)	82	10/10	139	(10)	81	10/10
12	172	(10)	10/10	157	(10)	91	10/10	152	(10)	88	10/10	142	(10)	83	10/10	144	(10)	84	10/10
13	175	(10)	10/10	159	(10)	91	10/10	154	(10)	88	10/10	144	(10)	82	10/10	146	(10)	83	10/10

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

TABLE 4 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

Week-day on Study	Control			1250ppm			2500ppm			5000ppm			8000ppm			10000ppm							
	Av.FC.	No. of Surviv. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.					
1	12.6	(10)	10/10	12.6	(10)	100	10/10	11.8	(10)	94	10/10	10.1	(10)	80	10/10	8.5	(10)	67	10/10	7.0	(10)	56	10/10
2	13.3	(10)	10/10	13.3	(10)	100	10/10	13.1	(10)	98	10/10	12.9	(10)	97	10/10	11.7	(10)	88	10/10	9.7	(10)	73	10/10
3	13.7	(10)	10/10	14.0	(10)	102	10/10	13.5	(10)	99	10/10	13.3	(10)	97	10/10	12.6	(10)	92	10/10	10.8	(10)	79	10/10
4	14.4	(10)	10/10	14.2	(10)	99	10/10	13.7	(10)	95	10/10	13.7	(10)	95	10/10	13.0	(10)	90	10/10	11.5	(10)	80	10/10
5	14.5	(10)	10/10	14.6	(10)	101	10/10	13.7	(10)	94	10/10	13.8	(10)	95	10/10	13.1	(10)	90	10/10	11.5	(10)	79	10/10
6	14.4	(10)	10/10	14.2	(10)	99	10/10	13.9	(10)	97	10/10	13.8	(10)	96	10/10	13.3	(10)	92	10/10	12.0	(10)	83	10/10
7	14.7	(10)	10/10	14.4	(10)	98	10/10	14.5	(10)	99	10/10	14.0	(10)	95	10/10	14.1	(10)	96	10/10	12.2	(10)	83	10/10
8	14.5	(10)	10/10	14.3	(10)	99	10/10	13.9	(10)	96	10/10	13.6	(10)	94	10/10	13.9	(10)	96	10/10	12.4	(10)	86	10/10
9	14.3	(10)	10/10	14.4	(10)	101	10/10	14.4	(10)	101	10/10	14.2	(10)	99	10/10	13.7	(10)	96	10/10	12.1	(10)	85	10/10
10	14.2	(10)	10/10	14.2	(10)	100	10/10	14.2	(10)	100	10/10	14.3	(10)	101	10/10	13.7	(10)	96	10/10	12.3	(10)	87	10/10
11	14.2	(10)	10/10	14.4	(10)	101	10/10	14.3	(10)	101	10/10	14.3	(10)	101	10/10	13.9	(10)	98	10/10	12.4	(10)	87	10/10
12	14.0	(10)	10/10	14.3	(10)	102	10/10	14.2	(10)	101	10/10	14.4	(10)	103	10/10	14.3	(10)	102	10/10	12.8	(10)	91	10/10
13	14.2	(10)	10/10	14.7	(10)	104	10/10	14.4	(10)	101	10/10	14.3	(10)	101	10/10	14.8	(10)	104	10/10	13.1	(10)	92	10/10

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

TABLE 5 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

Week-day on Study	Control			1250ppm			2500ppm			5000ppm			8000ppm			10000ppm							
	Av.FC.	No. of Surviv. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.	Av.FC.	% of cont. <10>	No. of Surviv.					
1	9.8	(10)	10/10	9.4	(10)	96	10/10	8.6	(10)	88	10/10	8.2	(10)	84	10/10	6.2	(10)	63	10/10	7.1	(10)	72	10/10
2	9.8	(10)	10/10	9.2	(10)	94	10/10	8.5	(10)	87	10/10	8.2	(10)	84	10/10	7.4	(10)	76	10/10	7.4	(10)	76	10/10
3	10.0	(10)	10/10	9.4	(10)	94	10/10	8.8	(10)	88	10/10	8.2	(10)	82	10/10	7.8	(10)	78	10/10	7.8	(10)	78	10/10
4	10.2	(10)	10/10	9.5	(10)	93	10/10	9.1	(10)	89	10/10	8.3	(10)	81	10/10	8.1	(10)	79	10/10	8.2	(10)	80	10/10
5	10.3	(10)	10/10	9.7	(10)	94	10/10	9.0	(10)	87	10/10	8.3	(10)	81	10/10	8.1	(10)	79	10/10	8.0	(10)	78	10/10
6	10.0	(10)	10/10	9.3	(10)	93	10/10	9.3	(10)	93	10/10	8.3	(10)	83	10/10	8.1	(10)	81	10/10	8.3	(10)	83	10/10
7	10.2	(10)	10/10	9.3	(10)	91	10/10	9.5	(10)	93	10/10	8.4	(10)	82	10/10	8.1	(10)	79	10/10	8.6	(10)	84	10/10
8	9.8	(10)	10/10	8.8	(10)	90	10/10	8.8	(10)	90	10/10	8.2	(10)	84	10/10	8.0	(10)	82	10/10	8.7	(10)	89	10/10
9	9.8	(10)	10/10	9.0	(10)	92	10/10	8.8	(10)	90	10/10	8.3	(10)	85	10/10	7.7	(10)	79	10/10	8.6	(10)	88	10/10
10	9.7	(10)	10/10	9.1	(10)	94	10/10	8.8	(10)	91	10/10	8.1	(10)	84	10/10	7.8	(10)	80	10/10	8.7	(10)	90	10/10
11	9.9	(10)	10/10	9.1	(10)	92	10/10	8.8	(10)	89	10/10	7.9	(10)	80	10/10	7.6	(10)	77	10/10	8.8	(10)	89	10/10
12	9.8	(10)	10/10	9.1	(10)	93	10/10	8.8	(10)	90	10/10	7.9	(10)	81	10/10	8.0	(10)	82	10/10	10.2	(10)	104	10/10
13	9.9	(10)	10/10	9.2	(10)	93	10/10	9.1	(10)	92	10/10	8.1	(10)	82	10/10	8.3	(10)	84	10/10	9.7	(10)	98	10/10

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