

Table 8-2 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Organ weight of male rats (Main group)

Dose mg/kg		No.	Spleen	Kidney (R+L)	Adrenal (R+L)	Body weight g	Testis (R+L)	Epididymis (R+L)
			g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	g	g(g/100g BW)	mg(mg/100g BW)
0	No.	5		5	5	12	12	12
	Mean		0.68	3.12	60	478	3.31	1242
	S.D.		0.08	0.38	13	32	0.33	117
Absolute 100	No.	5		5	5	12	12	12
	Mean		0.77	3.22	60	474	3.16	1206
	S.D.		0.08	0.14	4	32	0.44	109
300	No.	5		5	5	12	12	12
	Mean		0.66	3.11	56	469	3.27	1254
	S.D.		0.04	0.13	5	26	0.21	68
1000	No.	5		5	5	12	12	12
	Mean		0.69	2.94	56	417**	3.17	1210
	S.D.		0.04	0.20	6	35D	0.20	79
0	No.	5		5	5	12	12	12
	Mean		0.15	0.66	12	0.69	0.69	260
	S.D.		0.01	0.05	2	0.07	0.07	25
Relative 100	No.	5		5	5	12	12	12
	Mean		0.16	0.66	12	0.67	0.67	256
	S.D.		0.02	0.03	1	0.10	0.10	32
300	No.	5		5	5	12	12	12
	Mean		0.14	0.68	12	0.70	0.70	268
	S.D.		0.01	0.04	1	0.07	0.07	23
1000	No.	5		5	5	12	12	12
	Mean		0.17*	0.75*	14	0.76	0.76	292*
	S.D.		0.02D	0.07D	2	0.05	0.05	24D

*: p<0.05; **: p<0.01 (Significant difference from control group)
D: Dunnett's test

Table 8-3 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Organ weight of female rats (Main group)

Dose mg/kg		No.	Body weight g	Brain	Thyroid (R+L)	Thymus	Heart	Liver
			g	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)
0	No.	5		5	5	5	5	5
	Mean		299	1.90	15.2	213	0.91	9.71
	S.D.		9	0.07	2.3	65	0.04	0.71
Absolute 100	No.	5		5	5	5	5	5
	Mean		290	1.91	16.9	192	0.91	10.11
	S.D.		14	0.10	3.6	48	0.04	0.82
300	No.	5		5	5	5	5	5
	Mean		289*	1.89	14.6	105*	0.86	9.20
	S.D.		27D	0.10	2.7	57D	0.06	1.46
1000	No.	5		5	5	5	5	5
	Mean		238**	1.89	14.5	76**	0.78**	9.88
	S.D.		15D	0.09	2.7	54D	0.05D	0.87
0	No.	5		5	5	5	5	5
	Mean		0.64	5.1	71	0.31	3.25	
	S.D.		0.02	0.8	21	0.02	0.16	
Relative 100	No.	5		5	5	5	5	5
	Mean		0.66	5.8	67	0.31	3.49	
	S.D.		0.02	1.1	18	0.02	0.20	
300	No.	5		5	5	5	5	5
	Mean		0.71	5.4	38*	0.32	3.40	
	S.D.		0.07	0.7	17D	0.02	0.35	
1000	No.	5		5	5	5	5	5
	Mean		0.80**	6.1	31*	0.33	4.15**	
	S.D.		0.06D	0.8	21D	0.02	0.31D	

*: p<0.05; **: p<0.01 (Significant difference from control group)
D: Dunnett's test

Table 8-4 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Organ weight of female rats (Main group)

Dose mg/kg		No.	Spleen	Kidney (R+L)	Adrenal (R+L)
			g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)
Absolute	0	No.	5	5	5
		Mean	0.65	1.84	80
		S.D.	0.07	0.10	8
	100	No.	5	5	5
		Mean	0.63	1.91	80
		S.D.	0.11	0.12	8
	300	No.	5	5	5
		Mean	0.55	1.87	69
		S.D.	0.12	0.21	6
	1000	No.	5	5	5
		Mean	0.58	1.86	62**
		S.D.	0.23	0.18	6D
Relative	0	No.	5	5	5
		Mean	0.22	0.62	27
		S.D.	0.03	0.02	3
	100	No.	5	5	5
		Mean	0.22	0.66	27
		S.D.	0.04	0.03	3
	300	No.	5	5	5
		Mean	0.20	0.70	26
		S.D.	0.03	0.08	2
	1000	No.	5	5	5
		Mean	0.24	0.78**	26
		S.D.	0.09	0.08D	3

** : p<0.01 (Significant difference from control group)
D: Dunnett's test

Table 8-5 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Organ weight of male rats (Recovery group)

Dose mg/kg	No. of animals		Body weight	Brain	Thyroid (R+L)	Thymus	Heart	Liver		
			g	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)		
Absolute	0	5	Mean	479	2.11	21.6	266	1.37	12.46	
			S.D.	42	0.12	2.6	33	0.18	1.21	
	1000	5	Mean	459	2.11	24.6	258	1.42	12.82	
			S.D.	27	0.10	3.7	92	0.12	1.47	
	Relative	0	5	Mean		0.44	4.5	56	0.28	2.60
				S.D.		0.04	0.5	8	0.03	0.10
1000		5	Mean		0.46	5.3	56	0.31	2.79	
			S.D.		0.03	0.7	18	0.01	0.20	

No significant difference between treated group and control group.

Table 8-6 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Organ weight of male rats (Recovery group)

Dose mg/kg	No. of animals		Spleen		Kidney (R+L)		Adrenal (R+L)		Testis (R+L)		Epididymis (R+L)	
			g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)		
Absolute	0	5	Mean	0.76	3.21	61	3.15	1297				
			S.D.	0.16	0.38	7	0.27	131				
1000	5	5	Mean	0.75	3.14	62	3.40	1340				
			S.D.	0.07	0.31	8	0.41	89				
Relative	0	5	Mean	0.16	0.67	13	0.86	272				
			S.D.	0.03	0.05	1	0.06	33				
1000	5	5	Mean	0.16	0.68	14	0.74	292				
			S.D.	0.01	0.04	2	0.05	9				

No significant difference between treated group and control group.

Table 8-7 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Organ weight of female rats (Recovery group)

Dose mg/kg	No. of animals		Body weight		Brain		Thyroid (R+L)		Thymus		Heart		Liver	
			g	g	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)		
Absolute	0	5	Mean	264	1.92	16.7	253	0.83	6.42					
			S.D.	24	0.05	2.6	73	0.08	0.55					
1000	5	5	Mean	256	1.93	19.0	218	0.84	7.29					
			S.D.	23	0.11	2.7	43	0.04	1.09					
Relative	0	5	Mean		0.73	6.4	94	0.32	2.44					
			S.D.		0.06	1.5	19	0.03	0.18					
1000	5	5	Mean		0.76	7.5	86	0.33	2.84*					
			S.D.		0.10	1.3	20	0.02	0.21T					

*: p<0.05 (Significant difference from control group)
T: Student's t-test

Table 8-8 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Organ weight of female rats (Recovery group)

Dose mg/kg	No. of animals		Spleen		Kidney (R+L)	Adrenal (R+L)
			g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	
Absolute	0	5	Mean	0.47	1.75	67
			S.D.	0.03	0.16	8
1000	5	5	Mean	0.56	1.86	74
			S.D.	0.16	0.19	9
Relative	0	5	Mean	0.18	0.66	25
			S.D.	0.01	0.03	3
1000	5	5	Mean	0.22	0.73	29
			S.D.	0.04	0.08	3

No significant difference between treated group and control group.

Table 9-1 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Gross pathological findings (Dead animal)

Organs	Sex:	F
Findings	Dose(mg/kg):	1000
	Number:	1
Spleen		
Small		1
Thymus		
Small		1

Table 9-2 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Organs	Sex: Dose(mg/kg): Number:	M				F			
		0 12	100 12	300 12	1000 12	0 12	100 12	300 12	1000 11
Gross pathological findings (Main group)									
General descriptions									
Undernourishment		0	0	0	0	0	0	0	1
Cerebrum									
Focus, depressed		0	0	0	0	0	1	0	0
Epididymis									
Small		0	1	0	0	-	-	-	-
Focus, yellow		0	0	0	1	-	-	-	-
Liver									
Discoloration, dark		0	0	0	8	0	0	0	0
Adhesion		0	1	0	0	0	0	0	0
Stomach									
Focus, white, glandular stomach		1	0	0	0	0	0	0	0
Focus, depressed, forestomach		0	0	0	0	0	0	1	0
Focus, dark red, glandular stomach		0	0	0	0	0	0	1	1
Focus, dark red, forestomach		0	0	0	0	0	0	1	0
Thickening, limiting ridge		0	0	0	0	0	0	1	0
Testis									
Small		0	1	0	0	-	-	-	-
Thymus									
Small		0	0	0	0	0	0	1	3
Uterus									
Hypoplasia		-	-	-	-	0	1	0	0

- : Not applicable.

Table 9-3 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Organs	Sex: Dose(mg/kg): Number:	M		F	
		0 5	1000 5	0 5	1000 5
Gross pathological findings (Recovery group)					
All tissues					
Not remarkable		5	5	5	5

Table 10-1 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Histopathological findings (Dead animal)

Organs	Sex: Dose(mg/kg): Number:	F 1000 1
Bone+Bone marrow, sternal		
Number examined		1
Degeneration, chondromucinous		1
minimal		1
Liver		
Number examined		1
Vacuolation, hepatocyte, periportal		1
minimal		1
Spleen		
Number examined		1
Atrophy, white pulp		1
minimal		1
Thymus		
Number examined		1
Atrophy		1
moderate		1

Table 10-2 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Histopathological findings (Main group)

Organs	Sex: Dose(mg/kg): Number:	M 0 12	M 100 12	M 300 12	M 1000 12	F 0 12	F 100 12	F 300 12	F 1000 11
Bone+Bone marrow, sternal									
Number examined		5	0	0	5	5	0	0	5
Degeneration, chondromucinous		5	0	0	5	5	0	0	4
minimal		5	0	0	5	5	0	0	4
Cerebrum									
Number examined		5	0	0	5	5	1	0	5
Malformation		0	0	0	0	0	1	0	0
minimal		0	0	0	0	0	1	0	0
Epididymis									
Number examined		5	1	0	5	-	-	-	-
Hypospermia		0	1	0	0	-	-	-	-
severe		0	1	0	0	-	-	-	-
Cell debris, ductal		0	1	0	0	-	-	-	-
minimal		0	1	0	0	-	-	-	-
Heart									
Number examined		5	0	0	5	5	0	0	5
Cardiomyopathy		0	0	0	0	0	0	0	1
minimal		0	0	0	0	0	0	0	1
Intestine, cecum									
Number examined		12	12	12	12	12	12	12	11
Cell infiltration, mucosal		3	1	1	5	1	0	1	3
minimal		2	1	1	5	1	0	1	3
mild		1	0	0	0	0	0	0	0
Cell infiltration, serosal		0	0	0	0	0	0	0	1
minimal		0	0	0	0	0	0	0	1
Necrosis, single cell, mucosal		0	4	3	8	0	2	3	7
minimal		0	4	3	8	0	2	3	7
mild		0	0	1	0	0	0	0	0
Hyperplasia, mucosal, diffuse		0	1	3	7	0	1	4	6
minimal		0	1	3	7	0	1	4	6
Intestine, colon									
Number examined		5	0	0	5	5	0	0	5
Cell infiltration, serosal		0	0	0	0	0	0	0	1
minimal		0	0	0	0	0	0	0	1
Kidney									
Number examined		5	0	0	5	5	0	0	5
Vacuolation, tubular cell		0	0	0	0	0	0	0	1
minimal		0	0	0	0	0	0	0	1
Regeneration, tubular		4	0	0	2	1	0	0	0
minimal		4	0	0	2	1	0	0	0
Mineralization		0	0	0	0	0	0	0	2
minimal		0	0	0	0	0	0	0	2
Hyperplasia, transitional cell		0	0	0	0	0	0	0	1
minimal		0	0	0	0	0	0	0	1
Liver									
Number examined		12	12	12	12	12	12	12	11
Vacuolation, hepatocyte, periportal		11	10	7	0	5	4	1	0
minimal		8	9	7	0	5	4	1	0
mild		3	1	0	0	0	0	0	0
Necrosis, focal		0	0	0	0	0	0	1	0
minimal		0	0	0	0	0	0	1	0
Hematopoiesis, extramedullary		0	0	0	0	1	0	0	1
minimal		0	0	0	0	1	0	0	1
Microgranuloma		10	10	8	8	2	2	2	3
minimal		10	10	8	8	2	2	2	3

- : Not applicable

Table 10-3 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Histopathological findings (Main group)

Organs	Sex: Dose(mg/kg): Number:	M 0	M 100	M 300	M 1000	F 0	F 100	F 300	F 1000
Findings		12	12	12	12	12	12	12	11
Liver (continued)									
Fibrosis, capsular		0	1	0	0	0	0	0	0
minimal		0	1	0	0	0	0	0	0
Altered cell focus, eosinophilic		0	0	0	0	0	1	0	0
minimal		0	0	0	0	0	1	0	0
Lung (bronchus)									
Number examined		5	0	0	5	5	0	0	5
Mineralization, arterial wall		1	0	0	0	2	0	0	0
minimal		1	0	0	0	2	0	0	0
Accumulation, foamy cell		2	0	0	2	0	0	0	1
minimal		1	0	0	2	0	0	0	1
mild		1	0	0	0	0	0	0	0
Inflammatory change, focal		0	0	0	0	1	0	0	0
minimal		0	0	0	0	1	0	0	0
Spleen									
Number examined		5	0	0	5	12	12	12	11
Hematopoiesis, extramedullary		2	0	0	3	12	12	11	8
minimal		2	0	0	3	5	6	3	3
mild		0	0	0	0	7	6	2	5
Stomach									
Number examined		5	0	0	5	5	0	4	5
Inflammation, muscular layer/serosa		0	0	0	0	0	0	0	1
mild		0	0	0	0	0	0	0	1
Erosion, glandular stomach		2	0	0	0	0	0	1	1
minimal		2	0	0	0	0	0	1	1
Ulcer, forestomach		2	0	0	0	0	0	2	1
minimal		0	0	0	0	0	0	1	0
mild		0	0	0	0	0	0	1	0
Testis									
Number examined		5	1	0	5	-	-	-	-
Atrophy, seminiferous tubular		1	1	0	0	-	-	-	-
minimal		1	0	0	0	-	-	-	-
severe		0	1	0	0	-	-	-	-
Thymus									
Number examined		5	0	0	5	12	12	12	11
Atrophy		0	0	0	0	1	1	4	5
minimal		0	0	0	0	0	1	2	1
mild		0	0	0	0	1	0	1	1
moderate		0	0	0	0	0	0	1	2
severe		0	0	0	0	0	0	0	1
Thyroid									
Number examined		5	0	0	5	5	0	0	5
Cyst, ultimobranchial		1	0	0	0	1	0	0	1
minimal		1	0	0	0	1	0	0	1
Urinary bladder									
Number examined		5	0	0	5	5	0	0	5
Cell infiltration, mucosal		1	0	0	0	0	0	0	0
minimal		1	0	0	0	0	0	0	0
Hyperplasia, mucosal, diffuse		0	0	0	0	0	0	0	1
mild		0	0	0	0	0	0	0	1
Uterus									
Number examined		-	-	-	-	5	1	0	5
Hypoplasia		-	-	-	-	0	1	0	0
mild		-	-	-	-	0	1	0	0

- : Not applicable

Table 10-4 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Histopathological findings (Recovery group)

Organs	Sex: Dose(mg/kg): Number:	M 5	M 1000 5	F 0 5	F 1000 5
Intestine, cecum					
Number examined		5	5	5	5
Cell infiltration, mucosal		1	2	0	2
minimal		1	2	0	2
Hyperplasia, mucosal, diffuse		0	1	0	0
minimal		0	1	0	0
Liver					
Number examined		5	5	5	5
Vacuolation, hepatocyte, periportal		1	0	1	0
minimal		1	0	1	0
Microgranuloma		4	4	5	5
minimal		4	4	5	5
Spleen					
Number examined		0	0	5	5
Hematopoiesis, extramedullary		0	0	2	2
minimal		0	0	2	2

Table 11 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Estrous cycle in female rats during the pre-mating period (Main group)

Dose mg/kg	No. of animals	Count of estrus					Mean±S.D.	Mean duration of cycles Mean±S.D.
		0	1	2	3	4		
0	12	0	0	0	5	7	3.6±0.5	4.1±0.3
100	12	0	0	0	7	5	3.4±0.5	4.4±0.5
300	12	0	0	0	6	6	3.5±0.5	4.1±0.2
1000	12	0	0	0	8	4	3.3±0.5	4.4±0.5

No significant difference in any treated groups from control group.

Table 12 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Mating and fertility of animals

Dose mg/kg	No. of males	Male			Female			
		Days until copulation Mean±S.D.	Copulation index (%) a)	Insemination index (%) b)	No. of females	Days until copulation Mean±S.D.	Copulation index (%) a)	Fertility index (%) c)
0	12	2.8±1.1	12/12(100.0)	12/12(100.0)	12	2.8±1.1	12/12(100.0)	12/12(100.0)
100	12	3.0±1.0	12/12(100.0)	12/12(100.0)	12	3.0±1.0	12/12(100.0)	12/12(100.0)
300	12	2.4±1.3	12/12(100.0)	12/12(100.0)	12	2.4±1.3	12/12(100.0)	12/12(100.0)
1000	12	2.7±1.2	12/12(100.0)	11/12(91.7)	12	2.7±1.2	12/12(100.0)	11/12(91.7)

a): (No. of copulated animals / No. of mated animals) X 100
b): (No. of pregnant females / No. of copulated males) X 100
c): (No. of pregnant animals / No. of copulated females) X 100
No significant difference in any treated groups from control group.

Table 13 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Delivery data on dams

Dose mg/kg		No. of pregnant females	No. of females with live pups	Delivery index % a)	Gestation period	No. of corpora lutea	No. of implantation sites	Implantation index % b)	No. of stillborn pups (%)c)	No. of liveborn pups	Live birth index % d)
0	Total	12	12	100.0		193	181		2	166	
	Mean				22.2	16.1	15.1	93.8	(1.0)	13.8	99.0
	S.D.				0.2	1.0	1.7	8.8	(2.4)	2.2	2.4
100	Total	12	12	100.0		195	183		2	173	
	Mean				22.0	16.3	15.3	93.9	(1.1)	14.4	98.9
	S.D.				0.3	1.7	2.3	10.6	(3.8)	2.4	3.8
300	Total	12	12	100.0		209	191		2	175	
	Mean				22.0	17.4	15.9	91.5	(1.4)	14.6	98.7
	S.D.				0.3	1.5	1.6	6.8	(3.2)	1.9	3.2
1000	Total	11	11	100.0		172	162		2	151	
	Mean				22.1	15.6	14.7	94.7	(1.3)	13.7	98.7
	S.D.				0.4	1.9	1.5	6.9	(3.0)	1.4	3.0

a): (No. of females which delivered live pups / No. of pregnant females) × 100
b): (No. of implantation sites / No. of corpora lutea) × 100
c): (No. of stillborn pups / No. of stillborn and liveborn pups) × 100
d): (No. of liveborn pups / No. of stillborn and liveborn pups) × 100
No significant difference in any treated groups from control group.

Table 14 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
External examination of liveborn pups

Dose mg/kg	No. of dams		No. of males	No. of females	Sex ratio a)	Body weight(g)		External b) abnormalities(%)c)
						Male	Female	
0	12	Total	82	84	0.49			0
		Mean	6.8	7.0		6.5	6.3	(0.0)
		S.D.	2.4	2.0		0.5	0.4	(0.0)
100	12	Total	80	93	0.46			0
		Mean	6.7	7.8		6.5	6.1	(0.0)
		S.D.	1.5	1.9		0.5	0.5	(0.0)
300	12	Total	95	80	0.54			0
		Mean	7.9	6.7		6.2	6.1	(0.0)
		S.D.	2.9	1.4		0.4	0.4	(0.0)
1000	11	Total	81	70	0.54			0
		Mean	7.4	6.4		5.5**	5.1**	(0.0)
		S.D.	3.0	2.1		0.6D	0.6D	(0.0)

a): No. of males / (No. of males + No. of females)
b): No. of liveborn pups with external abnormalities
c): (No. of liveborn pups with external abnormalities / No. of liveborn pups) × 100
** : p < 0.01 (Significant difference from control group)
D: Dunnett's test

Table 15 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Viability index of pups

Dose mg/kg	No. of dams	No. of live pups		Viability index on day 4 after birth % a)
		Day 0	Day 4	
0	Total	12	166	166
	Mean		13.8	13.8
	S.D.		2.2	2.2
100	Total	12	173	173
	Mean		14.4	14.4
	S.D.		2.4	2.4
300	Total	12	175	172
	Mean		14.6	14.3
	S.D.		1.9	1.8
1000	Total	10	136	131
	Mean		13.6	13.1
	S.D.		1.4	1.2

a): (No. of live pups on day 4 / No. of liveborn pups on day 0) X 100
No significant difference in any treated groups from control group.

Table 16 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Body weight of pups

Dose mg/kg		Male		Female	
		0	4	0	4a)
0	No.	12	12	12	12
	Mean	6.5	10.1	6.3	9.8
	S.D.	0.5	1.4	0.4	1.3
100	No.	12	12	12	12
	Mean	6.5	10.1	6.1	9.5
	S.D.	0.5	1.1	0.5	1.1
300	No.	12	12	12	12
	Mean	6.2	8.6*	6.1	8.3*
	S.D.	0.4	1.1D	0.4	1.1D
1000	No.	11 ^{b)}	10	11	10
	Mean	5.5**	7.1**	5.1**	6.7**
	S.D.	0.6D	1.7D	0.6D	1.3D

Unit: g

No.: No. of dams

a): Day after birth

b): One dam died on day 0 of lactation.

*: p<0.05; **: p<0.01 (Significant difference from control group)

D: Dunnett's test

Table 17 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Gross pathological findings in pups on day 4 after birth

	Dose (mg/kg)				
	0	100	300	1000	
Male					
No. of pups examined	92	90	93	68	
No. of pups with abnormal findings	0	1	0	9	
Thymic remnant in neck	0	1	0	0	
Diaphragmatic hernia	0	0	0	1	
Undernourishment	0	0	0	8	
Female					
No. of pups examined	84	93	79	63	
No. of pups with abnormal findings	1	0	0	5	
Thymic remnant in neck	1	0	0	1	
Undernourishment	0	0	0	4	

[要 約]

イソシアヌル酸 (ICA) は、CHL/IU 細胞 (チャイニーズ・ハムスター、肺) に染色体異常を誘発しなかった。

ICA は CHL/IU 細胞に対して、連続処理 (新鮮培地中で24時間処理) および短時間処理の S9 mix 存在下および非存在下 (それぞれ S9 反応液および MEM 培地中で 6時間処理後 18時間の回復時間) で、最高処理濃度である 1.3 mg/ml (10 mM) においても 50%を越える増殖抑制は認められなかった。

このことから染色体異常試験において、連続処理 (24時間および 48時間処理) および短時間処理 (S9 mix 存在下および非存在下) とともに 1.3 mg/ml (10 mM) を最高処理濃度とし、公比 2 で各濃度を設定した。染色体分析は、全ての系列で 1.3 mg/ml (10 mM) の濃度含む 3濃度群を観察対象とした。

ICA はいずれの処理条件下においても、染色体の構造異常および倍数性細胞を誘発しなかった。