

Table 2-75

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

Detailed clinical signs in male rats: open field observation (Recovery group, Week 4 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		4± 0	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		4	4
Small amount		1	1

No significant difference between treated group and control group.

Table 2-76

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

Detailed clinical signs in male rats: open field observation (Recovery group, Week 5 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		3± 2	2± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		3	5
Small amount		1	0
Moderate amount		1	0

No significant difference between treated group and control group.

Table 2-77

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

Detailed clinical signs in male rats: open field observation (Recovery group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		5± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		3	3
Small amount		1	2
Moderate amount		1	0

No significant difference between treated group and control group.

Table 2-78

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

Detailed clinical signs in male rats: open field observation (Recovery group, Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		3± 1	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	4
Small amount		0	1

No significant difference between treated group and control group.

Table 2-79

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in male rats: open field observation (Recovery group, Week 2 of recovery)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		4± 2	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		3	3
Small amount		0	1
Moderate amount		2	1

No significant difference between treated group and control group.

Table 2-80

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: open field observation (Recovery group, Week 1 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		6± 3	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-81 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: open field observation (Recovery group, Week 2 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		7± 2	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-82 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: open field observation (Recovery group, Week 3 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		8± 3	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-83

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

Detailed clinical signs in female rats: open field observation (Recovery group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		10± 2	8± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-84

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

Detailed clinical signs in female rats: open field observation (Recovery group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		9± 2	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-85

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

Detailed clinical signs in female rats: open field observation (Recovery group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		8± 2	7± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-86

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

Detailed clinical signs in female rats: open field observation (Recovery group, Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		9± 3	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-87

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

Detailed clinical signs in female rats: open field observation (Recovery group, Week 2 of recovery)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		7± 2	7± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-88

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

Manipulative test of male rats (Main group, Week 6 of administration)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass. both		5	5	5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		83±16	87±13	73±18	76±14

No significant difference in any treated groups from control group.

Table 2-89 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Manipulative test of female rats (Main group, Day 4 of lactation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex (Total score: Mean±S.D.)		0±0	0±0	0±0	0±0
Landing foot splay (mm: Mean±S.D.)		56±11	58±18	66±18	83±11-D

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

Table 2-90 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Manipulative test of male rats (Recovery group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex (Total score: Mean±S.D.)		0±0	0±0
Landing foot splay (mm: Mean±S.D.)		82±20	80±17

No significant difference between treated group and control group.

Table 2-91 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Manipulative test of female rats (Recovery group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response Normal		5	5
Approach response Normal		5	5
Touch response Normal		5	5
Tail pinch response Normal		5	5
Pupillary reflex Pass, both		5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		60±19	72±13

No significant difference between treated group and control group.

Table 2-92 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Manipulative test of male rats (Recovery group, Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response Normal		5	5
Approach response Normal		5	5
Touch response Normal		5	5
Tail pinch response Normal		5	5
Pupillary reflex Pass, both		5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		90±13	83±12

No significant difference between treated group and control group.

Table 2-93 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Manipulative test of female rats (Recovery group, Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass. both		5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		70±14	61± 4

No significant difference between treated group and control group.

Table 2-94 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Grip strength of male rats (Main group, Week 6 of administration)

Dose mg/kg		Fore limb	Hind limb
		g	g
0	No.	5	5
	Mean	1601	894
	S.D.	115	77
100	No.	5	5
	Mean	1579	812
	S.D.	176	50
300	No.	5	5
	Mean	1563	823
	S.D.	172	122
1000	No.	5	5
	Mean	1359	707*
	S.D.	130	96D

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

Table 2-95 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Grip strength of female rats (Main group, Day 4 of lactation)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1288	822
	S.D.	166	108
100	No.	5	5
	Mean	1335	764
	S.D.	193	113
300	No.	5	5
	Mean	1133	682
	S.D.	90	97
1000	No.	5	5
	Mean	1145	654
	S.D.	202	125

No significant difference in any treated groups from control group.

Table 2-96 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Grip strength of male rats (Recovery group, Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1624	902
	S.D.	139	70
1000	No.	5	5
	Mean	1549	914
	S.D.	173	141

No significant difference between treated group and control group.

Table 2-97 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Grip strength of female rats (Recovery group, Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1096	835
	S.D.	96	226
1000	No.	5	5
	Mean	999	675
	S.D.	152	157

No significant difference between treated group and control group.

Table 2-98 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Grip strength of male rats (Recovery group, Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1490	948
	S.D.	202	51
1000	No.	5	5
	Mean	1621	1010
	S.D.	158	125

No significant difference between treated group and control group.