

Table 2-15

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

Detailed clinical signs in male rats: home cage observations (Recovery group, Week 2 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-16

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

Detailed clinical signs in male rats: home cage observations (Recovery group, Week 3 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-17

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

Detailed clinical signs in male rats: home cage observations (Recovery group, Week 4 of administration)

Parameter	Dose (mg/kg)	
	No. of animals	
	0	1000
	5	5
Posture		
Normal	5	5
Convulsion		
None	5	5
Abnormal behavior		
None	5	5

Table 2-18

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

Detailed clinical signs in male rats: home cage observations (Recovery group, Week 5 of administration)

Parameter	Dose (mg/kg)	
	No. of animals	
	0	1000
	5	5
Posture		
Normal	5	5
Convulsion		
None	5	5
Abnormal behavior		
None	5	5

Table 2-19

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

Detailed clinical signs in male rats: home cage observations (Recovery group, Week 6 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-20

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

Detailed clinical signs in male rats: home cage observations (Recovery group, Week 1 of recovery)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-21 A combined repeated-dose/reproductive-development toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in male rats: home cage observations (Recovery Group, Week 2 of recovery)

Parameter	Dose (mg/kg)	
	0	1000
No. of animals	5	5
Posture		
Normal	5	5
Convulsion	5	5
None	5	5
Abnormal behavior	5	5
None	5	5

Table 2-22 A combined repeated-dose/reproductive-development toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: home cage observations (Recovery Group, Week 1 of administration)

Parameter	Dose (mg/kg)	
	0	1000
No. of animals	5	5
Posture		
Normal	5	5
Convulsion	5	5
None	5	5
Abnormal behavior	5	5
None	5	5

Table 2-23

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

Detailed clinical signs in female rats: home cage observations (Recovery group, Week 2 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-24

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

Detailed clinical signs in female rats: home cage observations (Recovery group, Week 3 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-25

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

Detailed clinical signs in female rats: home cage observations (Recovery group, Week 4 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-26

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

Detailed clinical signs in female rats: home cage observations (Recovery group, Week 5 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-27 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: home cage observations (Recovery group, Week 6 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-28 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: home cage observations (Recovery group, Week 1 of recovery)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-29

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

Detailed clinical signs in female rats: home cage observations (Recovery group, Week 2 of recovery)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-30

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

Detailed clinical signs in male rats: in-the-hand observations (Main group, Week 1 of administration)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		12	12	12	12
Ease of removal from cage					
Easy		12	12	11	11
Some resistance/avoidance		0	0	1	1
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		11	9	9	10
Soft		1	2	3	1
Moderate		0	1	0	1
Reactivity to handling					
Easy		10	11	12	10
Slightly awkward		2	1	0	2

Table 2-31 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in male rats: in-the-hand observations (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	9	11	9
Soft		0	3	1	3
Reactivity to handling					
Easy		12	12	12	12

Table 2-32 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in male rats: in-the-hand observations (Main group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	11	12
Some resistance/avoidance		0	1	1	0
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	6	10	10
Soft		2	6	2	2
Reactivity to handling					
Easy		12	12	11	12
Slightly awkward		0	0	1	0

Table 2-33

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

Detailed clinical signs in male rats: in-the-hand observations (Main group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	8	11	12
Some resistance/avoidance		0	4	1	0
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	6	7	10
Soft		2	4	4	1
Moderate		0	2	1	1
Reactivity to handling					
Easy		11	10	10	11
Slightly awkward		1	2	2	1

R-944

Table 2-34

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

Detailed clinical signs in male rats: in-the-hand observations (Main group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	11	12
Some resistance/avoidance		0	1	1	0
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		9	9	10	11
Soft		3	3	2	1
Reactivity to handling					
Easy		12	12	12	12

Table 2-35

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

Detailed clinical signs in male rats: in-the-hand observations (Main group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	12	12
Some resistance/avoidance		0	1	0	0
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	8	10	11
Soft		2	3	2	1
Moderate		0	1	0	0
Reactivity to handling					
Easy		12	12	12	12

R-944

Table 2-36

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

Detailed clinical signs in female rats: in-the-hand observations (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	12	12
Some resistance/avoidance		0	1	0	0
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	11	10	9
Soft		2	1	2	3
Reactivity to handling					
Easy		10	10	10	11
Slightly awkward		2	2	2	1

Table 2-37

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

Detailed clinical signs in female rats: in-the-hand observations (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage		12	11	12	12
Easy		0	1	0	0
Some resistance/avoidance					
Fur condition		12	12	12	12
Normal					
Skin		12	12	12	12
Normal					
Secretions-Eye, Nose		12	12	12	12
Absent					
Exophthalmos		12	12	12	12
Absent					
Palpebral closure		12	12	12	12
Normal					
Mucosal membranes		12	12	12	12
Normal					
Lacrimation		12	12	12	12
Normal					
Piloerection		12	12	12	12
Absent					
Pupil size		12	12	12	12
Normal					
Salivation		12	12	12	12
None					
Abnormal respiration		12	12	12	12
Absent					
Vocalization		12	11	12	11
None		0	1	0	1
Soft					
Reactivity to handling		12	11	12	12
Easy		0	1	0	0
Slightly awkward					

Table 2-38

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

Detailed clinical signs in female rats: in-the-hand observations (Main group, Day 1 of gestation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	11
Ease of removal from cage		12	11	12	9
Easy		0	1	0	2
Some resistance/avoidance					
Fur condition		12	12	12	11
Normal					
Skin		12	12	12	11
Normal					
Secretions-Eye, Nose		12	12	12	11
Absent					
Exophthalmos		12	12	12	11
Absent					
Palpebral closure		12	12	12	11
Normal					
Mucosal membranes		12	12	12	11
Normal					
Lacrimation		12	12	12	11
Normal					
Piloerection		12	12	12	11
Absent					
Pupil size		12	12	12	11
Normal					
Salivation		12	12	12	11
None					
Abnormal respiration		12	12	12	11
Absent					
Vocalization		11	11	12	10
None		1	1	0	1
Soft					
Reactivity to handling		10	11	12	9
Easy		2	1	0	2
Slightly awkward					

Table 2-39

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

Detailed clinical signs in female rats: in-the-hand observations (Main group, Day 7 of gestation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	11
Ease of removal from cage					
Easy		12	12	12	11
Fur condition					
Normal		12	12	12	11
Skin					
Normal		12	12	12	11
Secretions-Eye, Nose					
Absent		12	12	12	11
Exophthalmos					
Absent		12	12	12	11
Palpebral closure					
Normal		12	12	12	11
Mucosal membranes					
Normal		12	12	12	11
Lacrimation					
Normal		12	12	12	11
Piloerection					
Absent		12	12	12	11
Pupil size					
Normal		12	12	12	11
Salivation					
None		12	12	12	11
Abnormal respiration					
Absent		12	12	12	11
Vocalization					
None		12	11	11	11
Soft		0	1	1	0
Reactivity to handling					
Easy		11	12	12	11
Slightly awkward		1	0	0	0

Table 2-40

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

Detailed clinical signs in female rats: in-the-hand observations (Main group, Day 14 of gestation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	11
Ease of removal from cage					
Easy		12	12	12	11
Fur condition					
Normal		12	12	12	11
Skin					
Normal		12	12	12	11
Secretions-Eye, Nose					
Absent		12	12	12	11
Exophthalmos					
Absent		12	12	12	11
Palpebral closure					
Normal		12	12	12	11
Mucosal membranes					
Normal		12	12	12	11
Lacrimation					
Normal		12	12	12	11
Piloerection					
Absent		12	12	12	11
Pupil size					
Normal		12	12	12	11
Salivation					
None		12	12	12	11
Abnormal respiration					
Absent		12	12	12	11
Vocalization					
None		12	10	11	11
Soft		0	2	1	0
Reactivity to handling					
Easy		12	11	12	11
Slightly awkward		0	1	0	0

Table 2-41

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

Detailed clinical signs in female rats: in-the-hand observations (Main group, Day 20 of gestation)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		12	12	12	11
Ease of removal from cage					
Easy		12	10	12	11
Some resistance/avoidance		0	2	0	0
Fur condition					
Normal		12	12	12	11
Skin					
Normal		12	12	12	11
Secretions-Eye, Nose					
Absent		12	12	12	11
Exophthalmos					
Absent		12	12	12	11
Palpebral closure					
Normal		12	12	12	11
Mucosal membranes					
Normal		12	12	12	11
Lacrimation					
Normal		12	12	12	11
Piloerection					
Absent		12	12	12	11
Pupil size					
Normal		12	12	12	11
Salivation					
None		12	12	12	11
Abnormal respiration					
Absent		12	12	12	11
Vocalization					
None		12	11	12	11
Moderate		0	1	0	0
Reactivity to handling					
Easy		12	10	12	10
Slightly awkward		0	2	0	1

R-944

Table 2-42

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

Detailed clinical signs in female rats: in-the-hand observations (Main group, Day 4 of lactation)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		12	12	12	10
Ease of removal from cage					
Easy		11	12	11	9
Some resistance/avoidance		1	0	1	1
Fur condition					
Normal		12	12	12	10
Skin					
Normal		12	12	12	10
Secretions-Eye, Nose					
Absent		12	12	12	10
Exophthalmos					
Absent		12	12	12	10
Palpebral closure					
Normal		12	12	12	10
Mucosal membranes					
Normal		12	12	12	10
Lacrimation					
Normal		12	12	12	10
Piloerection					
Absent		12	12	12	10
Pupil size					
Normal		12	12	12	10
Salivation					
None		12	12	12	10
Abnormal respiration					
Absent		12	12	12	10
Vocalization					
None		12	11	12	10
Soft		0	1	0	0
Reactivity to handling					
Easy		12	11	11	9
Slightly awkward		0	1	1	1

Table 2-43

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

Detailed clinical signs in male rats: in-the-hand observations (Recovery group, Week 1 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		2	5
Soft		3	0
Reactivity to handling			
Easy		4	5
Slightly awkward		1	0

Table 2-44

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

Detailed clinical signs in male rats: in-the-hand observations (Recovery group, Week 2 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		4	5
Soft		1	0
Reactivity to handling			
Easy		5	5

Table 2-45

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

Detailed clinical signs in male rats: in-the-hand observations (Recovery group, Week 3 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		4	5
Some resistance/avoidance		1	0
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		3	4
Soft		1	1
Moderate		1	0
Reactivity to handling			
Easy		5	5

Table 2-46

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

Detailed clinical signs in male rats: in-the-hand observations (Recovery group, Week 4 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		4	4
Soft		1	1
Reactivity to handling			
Easy		5	5

Table 2-47

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

Detailed clinical signs in male rats: in-the-hand observations (Recovery group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-48

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

Detailed clinical signs in male rats: in-the-hand observations (Recovery group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		4	5
Some resistance/avoidance		1	0
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		2	4
Soft		3	1
Reactivity to handling			
Easy		5	5

Table 2-49

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

Detailed clinical signs in male rats: in-the-hand observations (Recovery group, Week 1 of recovery)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		3	5
Some resistance/avoidance		2	0
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		3	4
Soft		0	1
Moderate		2	0
Reactivity to handling			
Easy		5	5

Table 2-50

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

Detailed clinical signs in male rats: in-the-hand observations (Recovery group, Week 2 of recovery)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		3	5
Some resistance/avoidance		2	0
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		3	3
Soft		1	2
Moderate		1	0
Reactivity to handling			
Easy		5	4
Slightly awkward		0	1

Table 2-51 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 1 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy	5	5	
Fur condition			
Normal	5	5	
Skin			
Normal	5	5	
Secretions-Eye, Nose			
Absent	5	5	
Exophthalmos			
Absent	5	5	
Palpebral closure			
Normal	5	5	
Mucosal membranes			
Normal	5	5	
Lacrimation			
Normal	5	5	
Piloerection			
Absent	5	5	
Pupil size			
Normal	5	5	
Salivation			
None	5	5	
Abnormal respiration			
Absent	5	5	
Vocalization			
None	5	5	
Reactivity to handling			
Easy	5	4	
Slightly awkward	0	1	

Table 2-52 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 2 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy	5	5	
Fur condition			
Normal	5	5	
Skin			
Normal	5	5	
Secretions-Eye, Nose			
Absent	5	5	
Exophthalmos			
Absent	5	5	
Palpebral closure			
Normal	5	5	
Mucosal membranes			
Normal	5	5	
Lacrimation			
Normal	5	5	
Piloerection			
Absent	5	5	
Pupil size			
Normal	5	5	
Salivation			
None	5	5	
Abnormal respiration			
Absent	5	5	
Vocalization			
None	5	5	
Reactivity to handling			
Easy	5	5	

Table 2-53

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

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 3 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-54

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

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 4 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-55 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 5 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-56 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 6 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-57

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

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-58

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

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-58

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 (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	1	2	1
Normal		12	11	10	11
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		3± 2	3± 2	3± 2	3± 2
Defecation count (Mean±S.D.)		1± 1	0± 0	0± 0	1± 2
Urination					
None		12	9	11	10
Small amount		0	3	1	2

No significant difference in any treated groups from control group.

Table 2-60

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 (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	0	1	0
Normal		12	12	11	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		3± 2	3± 2	3± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 1	0± 1
Urination					
None		12	10	12	11
Small amount		0	2	0	1

No significant difference in any treated groups from control group.

Table 2-61 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 (Main group, Week 3 of administration)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	2	2	0
Normal		12	10	10	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		3± 2	3± 3	3± 2	3± 2
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 0	0± 0
Urination					
None		10	7	11	11
Small amount		2	3	1	1
Moderate amount		0	2	0	0

No significant difference in any treated groups from control group.

Table 2-62 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 (Main group, Week 4 of administration)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	1	0	0
Normal		12	11	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	4± 2	4± 2	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 0	0± 0
Urination					
None		10	7	11	11
Small amount		2	4	1	1
Moderate amount		0	1	0	0

No significant difference in any treated groups from control group.

Table 2-63

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 (Main group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	1	0	0
Normal		12	11	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	4± 2	5± 2	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	7	11	12
Small amount		1	5	1	0

No significant difference in any treated groups from control group.

Table 2-64

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 (Main group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	0	0	1
Normal		12	12	12	11
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	4± 2	5± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 0	0± 0
Urination					
None		10	7	9	12
Small amount		2	4	3	0
Moderate amount		0	1	0	0

No significant difference in any treated groups from control group.

Table 2-65 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 (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		6± 2	5± 2	6± 3	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	12
Small amount		0	0	1	0

No significant difference in any treated groups from control group.

Table 2-66 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 (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		8± 3	7± 2	7± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	12

No significant difference in any treated groups from control group.

Table 2-67

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 (Main group, Day 1 of gestation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	11
Arousal					
Normal		12	12	12	11
Convulsion					
None		12	12	12	11
Abnormal behavior					
None		12	12	12	11
Stereotypy					
None		12	12	12	11
Gait					
Normal		12	12	12	11
Posture					
Normal		12	12	12	11
Grooming					
None		12	12	12	11
Rearing (Mean±S.D.)		7± 2	6± 1	7± 2	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	11

No significant difference in any treated groups from control group.

Table 2-68

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 (Main group, Day 7 of gestation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	11
Arousal					
Normal		12	12	12	11
Convulsion					
None		12	12	12	11
Abnormal behavior					
None		12	12	12	11
Stereotypy					
None		12	12	12	11
Gait					
Normal		12	12	12	11
Posture					
Normal		12	12	12	11
Grooming					
None		12	12	12	11
Rearing (Mean±S.D.)		6± 2	7± 2	8± 2	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	10
Small amount		0	0	0	1

No significant difference in any treated groups from control group.

Table 2-69

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 (Main group, Day 14 of gestation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	11
Arousal					
Normal		12	12	12	11
Convulsion					
None		12	12	12	11
Abnormal behavior					
None		12	12	12	11
Stereotypy					
None		12	12	12	11
Gait					
Normal		12	12	12	11
Posture					
Normal		12	12	12	11
Grooming					
None		12	12	12	11
Rearing (Mean±S.D.)		5± 1	6± 2	5± 2	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	11

No significant difference in any treated groups from control group.

Table 2-70

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 (Main group, Day 20 of gestation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	11
Arousal					
Normal		12	12	12	11
Convulsion					
None		12	12	12	11
Abnormal behavior					
None		12	12	12	11
Stereotypy					
None		12	12	12	11
Gait					
Normal		12	12	12	11
Posture					
Normal		12	12	12	11
Grooming					
None		12	12	12	11
Rearing (Mean±S.D.)		6± 2	5± 2	5± 1	4± 2*D
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	11

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

Table 2-71 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 (Main group, Day 4 of lactation)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	10
Arousal					
Normal		12	12	12	10
Convulsion					
None		12	12	12	10
Abnormal behavior					
None		12	12	12	10
Stereotypy					
None		12	12	12	10
Gait					
Normal		12	12	12	10
Posture					
Normal		12	12	12	10
Grooming					
None		12	12	12	10
Rearing (Mean±S.D.)		7± 2	7± 1	6± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	10

No significant difference in any treated groups from control group.

Table 2-72 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 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			
No/minimal location		0	2
Normal		5	3
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		3± 1	2± 2
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 2-73

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 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	3± 2
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 2-74

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 3 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.)		3± 1	3± 2
Defecation count (Mean±S.D.)		0± 0	0± 1
Urination			
None		5	5

No significant difference between treated group and control group.

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)	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.)		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)	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± 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.

Table 2-99 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 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1054	791
	S.D.	157	85
1000	No.	5	5
	Mean	1110	704
	S.D.	217	164

No significant difference between treated group and control group.

Table 2-100 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Motor activity of male rats (Main group, Week 6 of administration)

Dose mg/kg		Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
0	No.	5	5	5	5	5	5	5
	Mean	390	185	77	118	100	63	934
	S.D.	40	69	51	67	169	111	416
100	No.	5	5	5	5	5	5	5
	Mean	362	238	169	171	111	87	1135
	S.D.	56	111	139	89	87	88	294
300	No.	5	5	5	5	5	5	5
	Mean	327	256	110	83	58	44	878
	S.D.	114	101	91	52	44	47	247
1000	No.	5	5	5	5	5	5	5
	Mean	343	276	146	126	59	26	977
	S.D.	45	58	57	62	51	12	138

No significant difference in any treated groups from control group.

Table 2-101 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Motor activity of female rats (Main group, Day 4 of lactation)

Dose mg/kg		Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
0	No.	5	5	5	5	5	5	5
	Mean	176	59	30	13	37	39	354
	S.D.	109	104	45	16	67	52	362
100	No.	5	5	5	5	5	5	5
	Mean	168	52	22	13	54	44	353
	S.D.	60	63	17	9	41	88	118
300	No.	5	5	5	5	5	5	5
	Mean	261	112	124*	103*	114	20	733
	S.D.	75	84	79D	61DT	56	11	267
1000	No.	5	5	5	5	5	5	5
	Mean	108	17	38	17	11	39	230
	S.D.	70	12	39	10	14	45	102

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

Table 2-102 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Motor activity of male rats (Recovery group, Week 6 of administration)

Dose mg/kg		Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
0	No.	5	5	5	5	5	5	5
	Mean	265	208	64	35	48	50	670
	S.D.	171	148	65	22	71	39	334
1000	No.	5	5	5	5	5	5	5
	Mean	386	254	93	26	75	34	867
	S.D.	42	93	74	27	100	27	149

No significant difference between treated group and control group.

Table 2-103

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

Dose mg/kg		Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
0	No.	5	5	5	5	5	5	5
	Mean	365	271	62	35	51	149	932
	S.D.	57	87	74	42	79	151	208
1000	No.	5	5	5	5	5	5	5
	Mean	363	273	222*	245*	227**	232	1562**
	S.D.	53	133	88T	127AT	71T	132	343T

* : p<0.05 ; ** : p<0.01 (Significant difference from control group)
T: Student's t-test
AT: Aspin-Welch t-test

Table 2-104

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

Dose mg/kg		Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
0	No.	5	5	5	5	5	5	5
	Mean	311	217	224	123	127	110	1112
	S.D.	87	96	88	92	99	87	223
1000	No.	5	5	5	5	5	5	5
	Mean	305	283	265	205	146	144	1349
	S.D.	89	78	98	170	162	141	639

No significant difference between treated group and control group.

Table 2-105

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

Motor activity of female rats (Recovery group, Week 2 of recovery)

Dose mg/kg		Interval (minutes)							Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60		
0	No.	5	5	5	5	5	5	5	
	Mean	265	228	168	163	126	107	1057	
	S.D.	91	117	128	123	122	129	513	
1000	No.	5	5	5	5	5	5	5	
	Mean	271	210	177	185	165	86	1092	
	S.D.	54	65	56	58	133	85	336	

No significant difference between treated group and control group.

Table 3-1

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

Body weight of male rats (Main group)

Dose mg/kg		Pre-mating period					Mating period				Post-mating period				Gain 1-42
		1	4	8	11	15	18	22	25	29	32	36	39	42a)	
0	No.	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	Mean	361.8	374.8	390.4	405.5	416.1	424.8	439.4	449.8	461.9	474.4	486.6	496.6	502.9	141.1
	S.D.	15.9	17.4	20.8	23.1	27.2	28.2	29.6	30.2	31.6	32.7	31.0	33.1	33.9	23.3
100	No.	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	Mean	360.9	375.6	390.3	402.3	414.3	419.3	433.4	442.1	457.3	468.3	481.5	490.8	495.3	134.4
	S.D.	12.6	13.9	17.5	20.0	23.1	24.3	25.6	27.0	28.7	31.0	33.2	32.5	33.1	26.4
300	No.	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	Mean	359.6	371.0	385.1	398.5	411.3	417.8	431.8	444.8	457.1	465.6	480.3	487.8	493.3	133.7
	S.D.	15.1	16.4	18.8	19.5	19.8	22.7	23.6	21.5	23.5	25.9	26.9	27.3	27.0	19.2
1000	No.	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	Mean	360.8	382.4	371.0*	383.2*	389.3*	392.6*	406.8*	415.1**	424.7**	432.3**	441.5**	442.7**	447.5**	86.7**
	S.D.	14.8	17.3	20.0D	23.4D	26.0D	28.6D	28.3D	28.0D	29.0D	30.7D	33.4D	34.9D	35.0D	26.1D

Unit: g

No.: No. of animals

a): Day of administration

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

D: Dunnett's test

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

Dose mg/kg		Administration					Gain 1-15
		1	4	8	11	15a)	
0	No.	12	12	12	12	12	12
	Mean	224.3	233.2	240.9	246.6	252.8	28.5
	S.D.	8.9	9.6	9.6	10.8	11.1	6.9
100	No.	12	12	12	12	12	12
	Mean	225.6	233.7	244.8	250.7	257.3	31.8
	S.D.	7.3	7.0	9.5	11.7	12.7	7.4
300	No.	12	12	12	12	12	12
	Mean	223.7	230.5	236.2	239.8	244.4	20.8
	S.D.	12.3	11.3	12.7	14.0	15.6	9.1
1000	No.	12	12	12	12	12	12
	Mean	223.8	224.1*	224.1**	223.7**	240.2	16.4**
	S.D.	9.8	7.6D	14.5D	17.5D	12.4	8.7D

Unit: g
No.: No. of animals
a): Day of administration
*: p<0.05; **: p<0.01 (Significant difference from control group)
D: Dunnett's test

Table 3-3 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Body weight of dams during the gestation period (Main group)

Dose mg/kg		Administration							Gain 0-20
		0	4	7	11	14	17	20a)	
0	No.	12	12	12	12	12	12	12	12
	Mean	254.8	277.9	290.8	314.3	329.0	360.8	407.3	152.5
	S.D.	10.9	13.8	17.6	20.1	24.0	23.0	24.8	19.8
100	No.	12	12	12	12	12	12	12	12
	Mean	259.3	276.7	291.2	313.7	329.8	361.0	408.2	148.9
	S.D.	13.8	14.2	15.3	17.2	17.3	19.1	22.3	16.2
300	No.	12	12	12	12	12	12	12	12
	Mean	251.7	273.2	281.1	304.0	318.4	348.8	396.6	144.9
	S.D.	18.2	16.3	18.7	18.0	19.5	23.0	26.3	11.0
1000	No.	11	11	11	11	11	11	11	11
	Mean	236.1*	254.2**	265.7**	280.8**	286.6**	317.8**	351.5**	115.4**
	S.D.	14.8D	20.7D	18.2D	21.1D	27.2D	29.3D	33.9D	23.5D

Unit: g
No.: No. of dams
a): Day of gestation
*: p<0.05; **: p<0.01 (Significant difference from control group)
D: Dunnett's test

Table 3-4 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Body weight of dams during the lactation period (Main group)

Dose mg/kg		Administration		Gain 0-4
		0	4a)	
0	No.	12	12	12
	Mean	309.9	328.8	18.8
	S.D.	31.8	26.0	19.3
100	No.	12	12	12
	Mean	316.4	325.3	8.9
	S.D.	21.3	20.9	13.1
300	No.	12	12	12
	Mean	300.2	299.8*	-0.4
	S.D.	27.6	28.1D	22.4
1000	No.	11	10 ^{b)}	10
	Mean	268.8**	274.4**	3.2
	S.D.	33.0D	35.3D	26.7

Unit: g
No.: No. of dams
a): Day of lactation
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 3-5 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Body weight of male rats during the administration period (Recovery group)

Dose mg/kg		Day of administration												Gain 1-42	
		1	4	8	11	15	18	22	25	29	32	36	39		42
0	No.	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Mean	355.0	363.6	377.2	390.8	400.8	408.6	422.8	430.8	444.2	454.8	469.0	478.6	476.4	121.4
	S.D.	13.5	17.9	20.1	26.0	26.8	29.8	32.6	37.9	38.0	39.1	40.0	40.3	45.9	38.2
1000	No.	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Mean	357.4	356.4	363.6	377.4	386.2	393.0	405.0	414.4	422.2	430.0	438.0	442.8	447.8	90.4
	S.D.	17.9	18.9	17.7	24.2	25.7	28.6	29.6	28.3	29.8	28.1	32.2	35.9	31.6	16.6

Unit: g
No.: No. of animals
No significant difference between treated group and control group.

Table 3-6 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Body weight of female rats during the administration period (Recovery group)

Dose mg/kg		Day of administration												Gain 1-42	
		1	4	8	11	15	18	22	25	29	32	36	39		42
0	No.	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Mean	218.8	230.6	239.2	241.8	248.0	248.4	250.2	259.0	263.6	266.8	272.0	274.4	270.4	51.6
	S.D.	8.3	9.0	10.4	13.5	19.0	20.1	18.9	25.6	23.4	18.3	21.7	22.0	21.1	17.9
1000	No.	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Mean	224.6	226.2	229.8	231.8	234.6	240.4	246.0	249.8	253.8	253.4	259.2	257.4	258.2	33.6
	S.D.	11.4	15.7	14.4	16.9	17.7	12.8	17.9	18.6	16.2	24.1	20.8	19.7	21.8	12.7

Unit: g

No.: No. of animals

No significant difference between treated group and control group.

Table 3-7 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Body weight of male rats during the recovery period (Recovery group)

Dose mg/kg		Day of recovery					Gain 1-14
		1	4	8	11	14	
0	No.	5	5	5	5	5	5
	Mean	482.2	491.4	496.8	501.4	504.8	22.6
	S.D.	42.5	44.1	44.3	44.5	48.4	7.2
1000	No.	5	5	5	5	5	5
	Mean	450.0	456.4	471.8	486.0	486.6	36.6**
	S.D.	32.6	30.1	35.5	29.7	32.2	5.9T

Unit: g

No.: No. of animals

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

T: Student's t-test

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

Dose mg/kg		Day of recovery					Gain 1-14
		1	4	8	11	14	
0	No.	5	5	5	5	5	5
	Mean	278.6	275.2	277.0	282.2	279.4	0.8
	S.D.	24.1	21.5	25.4	25.4	23.6	6.7
1000	No.	5	5	5	5	5	5
	Mean	259.4	261.0	268.2	275.8	272.4	13.0*
	S.D.	25.0	19.6	20.9	23.1	27.9	8.6T

Unit: g
No.: No. of animals
*: p<0.05 (Significant difference from control group)
T: Student's t-test

Table 4-1 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Food consumption of male rats (Main group)

Dose mg/kg		Pre-mating period					Post-mating period			
		1	4	8	11	15	32	36	39	42a)
0	No.	12	12	12	12	12	12	12	12	12
	Mean	26.8	24.9	25.0	21.5	24.1	23.9	23.6	22.7	25.3
	S.D.	2.8	1.9	2.9	2.5	2.7	2.2	1.7	2.8	2.0
100	No.	12	12	12	12	12	12	12	12	12
	Mean	25.3	24.2	22.5	21.2	23.6	22.5	22.2	22.4	22.9
	S.D.	2.1	2.7	2.8	2.7	2.4	4.1	2.0	2.4	2.6
300	No.	12	12	12	12	12	12	12	12	12
	Mean	25.7	22.3	23.8	20.8	25.1	23.2	23.9	21.9	25.4
	S.D.	4.1	2.7	2.6	2.7	2.5	4.5	3.7	3.7	2.2
1000	No.	12	12	12	12	12	12	12	12	12
	Mean	26.1	16.8**	24.1	21.6	26.5	24.7	23.7	22.1	26.6
	S.D.	3.2	5.4DT	3.7	2.8	4.3	4.5	4.3	4.1	4.4

Unit: g/rat/day
No.: No. of animals
a): Day of administration
**: p<0.01 (Significant difference from control group)
DT: Dunnett-type rank test

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

Dose mg/kg		Administration				
		1	4	8	11	15a)
0	No.	12	12	12	12	12
	Mean	17.7	18.8	18.6	14.3	19.4
	S.D.	3.1	2.2	1.6	2.4	3.1
100	No.	12	12	12	12	12
	Mean	18.8	17.9	18.0	15.0	19.4
	S.D.	2.4	1.5	2.3	1.4	2.7
300	No.	12	12	12	12	12
	Mean	17.3	16.5*	18.5	14.7	18.8
	S.D.	2.1	1.8D	2.7	3.6	3.1
1000	No.	12	12	12	12	12
	Mean	18.5	10.8**	14.7	12.4	24.9*
	S.D.	3.1	3.0D	7.9	5.4	7.8DT

Unit: g/rat/day

No.: No. of animals

a): Day of administration

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

D: Dunnett's test

DT: Dunnett-type rank test

Table 4-3 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Food consumption of dams during the gestation period (Main group)

Dose mg/kg		Administration						
		1	4	7	11	14	17	20a)
0	No.	12	12	12	12	12	12	12
	Mean	17.4	20.1	21.1	23.2	22.7	24.7	21.2
	S.D.	2.2	3.0	3.3	3.3	3.1	4.1	3.6
100	No.	12	12	12	12	12	12	12
	Mean	17.8	20.8	21.2	21.9	22.4	24.8	20.1
	S.D.	2.6	3.1	2.3	2.4	3.3	2.4	2.5
300	No.	12	12	12	12	12	12	12
	Mean	17.2	22.1	20.4	22.2	21.9	25.5	19.9
	S.D.	2.6	3.4	3.7	3.0	3.3	3.6	3.8
1000	No.	11	11	11	11	11	11	11
	Mean	18.2	22.1	20.5	18.8	19.0	23.8	14.0**
	S.D.	4.8	4.7	4.9	6.5	7.7	4.5	4.8D

Unit: g/rat/day

No.: No. of dams

a): Day of gestation

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

D: Dunnett's test

Table 4-4

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

Food consumption of dams during the lactation period (Main group)

Dose mg/kg		Administration	
		2	4a)
0	No.	12	12
	Mean	22.7	37.3
	S.D.	6.5	8.1
100	No.	12	12
	Mean	19.2	38.2
	S.D.	3.9	6.7
300	No.	12	12
	Mean	13.5**	35.0
	S.D.	6.2D	11.7
1000	No.	10 ^{b)}	10
	Mean	12.7**	31.4
	S.D.	8.8D	12.6

Unit: g/rat/day

No.: No. of dams

a): Day of lactation

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

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

D: Dunnett's test

Table 4-5

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

Food consumption of male rats during the administration period (Recovery group)

Dose mg/kg		Day of administration								
		1	4	8	11	15	32	36	39	42
0	No.	5	5	5	5	5	5	5	5	5
	Mean	24.0	22.4	24.0	19.8	25.0	22.6	23.0	23.6	22.0
	S.D.	3.2	2.6	2.7	0.8	2.3	3.1	2.1	1.9	2.8
1000	No.	5	5	5	5	5	5	5	5	5
	Mean	25.6	14.0**	23.4	22.0	25.0	22.4	23.4	24.2	25.8*
	S.D.	4.6	3.7T	6.1	3.7	2.8	2.2	2.5	4.6	1.8T

Unit: g/rat/day

No.: No. of animals

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

T: Student's t-test

Table 4-6 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Food consumption of female rats during the administration period (Recovery group)

Dose mg/kg		Day of administration								
		1	4	8	11	15	32	36	39	42
0	No.	5	5	5	5	5	5	5	5	5
	Mean	15.8	18.2	19.4	14.6	18.4	16.6	15.8	17.4	11.4
	S.D.	2.8	0.4	1.9	3.8	2.8	3.1	1.9	2.8	2.7
1000	No.	5	5	5	5	5	5	5	5	5
	Mean	19.0	12.0*	19.4	10.2	19.6	16.4	16.0	16.4	16.0
	S.D.	3.5	4.4AT	3.6	3.4	3.8	8.4	3.2	1.8	4.6

Unit: g/rat/day
No.: No. of animals
*: p<0.05 (Significant difference from control group)
AT: Aspin-Welch t-test

Table 4-7 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Food consumption of male rats during the recovery period (Recovery group)

Dose mg/kg		Day of recovery				
		1	4	8	11	14
0	No.	5	5	5	5	5
	Mean	22.6	27.0	25.6	27.6	28.4
	S.D.	2.1	2.8	1.9	1.9	3.4
1000	No.	5	5	5	5	5
	Mean	22.2	30.6	32.0*	33.0*	27.8
	S.D.	5.2	3.2	4.2T	3.1T	2.8

Unit: g/rat/day
No.: No. of animals
*: p<0.05 (Significant difference from control group)
T: Student's t-test

Table 4-8 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Food consumption of female rats during the recovery period (Recovery group)

Dose mg/kg		Day of recovery				
		1	4	8	11	14
0	No.	5	5	5	5	5
	Mean	15.4	14.4	18.2	21.0	17.6
	S.D.	2.7	1.3	2.4	2.1	0.9
1000	No.	5	5	5	5	5
	Mean	15.8	23.0**	19.8	23.2	18.8
	S.D.	4.0	3.1T	2.2	1.8	5.4

Unit: g/rat/day
No.: No. of animals
*: p<0.01 (Significant difference from control group)
T: Student's t-test

Table 5-1 A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone
Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	pH										1) Protein					2) Ketone body					3) Glucose						
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0	-	+	++	+++	++++	-	+	++	+++	++++	-	+	++	+++	++++			
0	17	0	0	0	1	0	1	4	10	1	3	6	8	0	0	0	5	5	7	0	0	0	17	0	0	0	0	0
100	12	0	0	0	0	1	1	4	6	0	0	1	11	0	0	0	0	3	9	0	0	0	12	0	0	0	0	0
300	12	0	0	0	0	2	3	4	3	0	3	4	5	0	0	0	2	3	7	0	0	0	12	0	0	0	0	0
1000	17	0	0	0	3	5	7	2	0	0	4	9	4	0	0	0	3	7	7	0	0	0	17	0	0	0	0	0

1) -: <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL
2) -: <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL
3) -: <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL