

Figure 1-2 Changes of body weight in rats

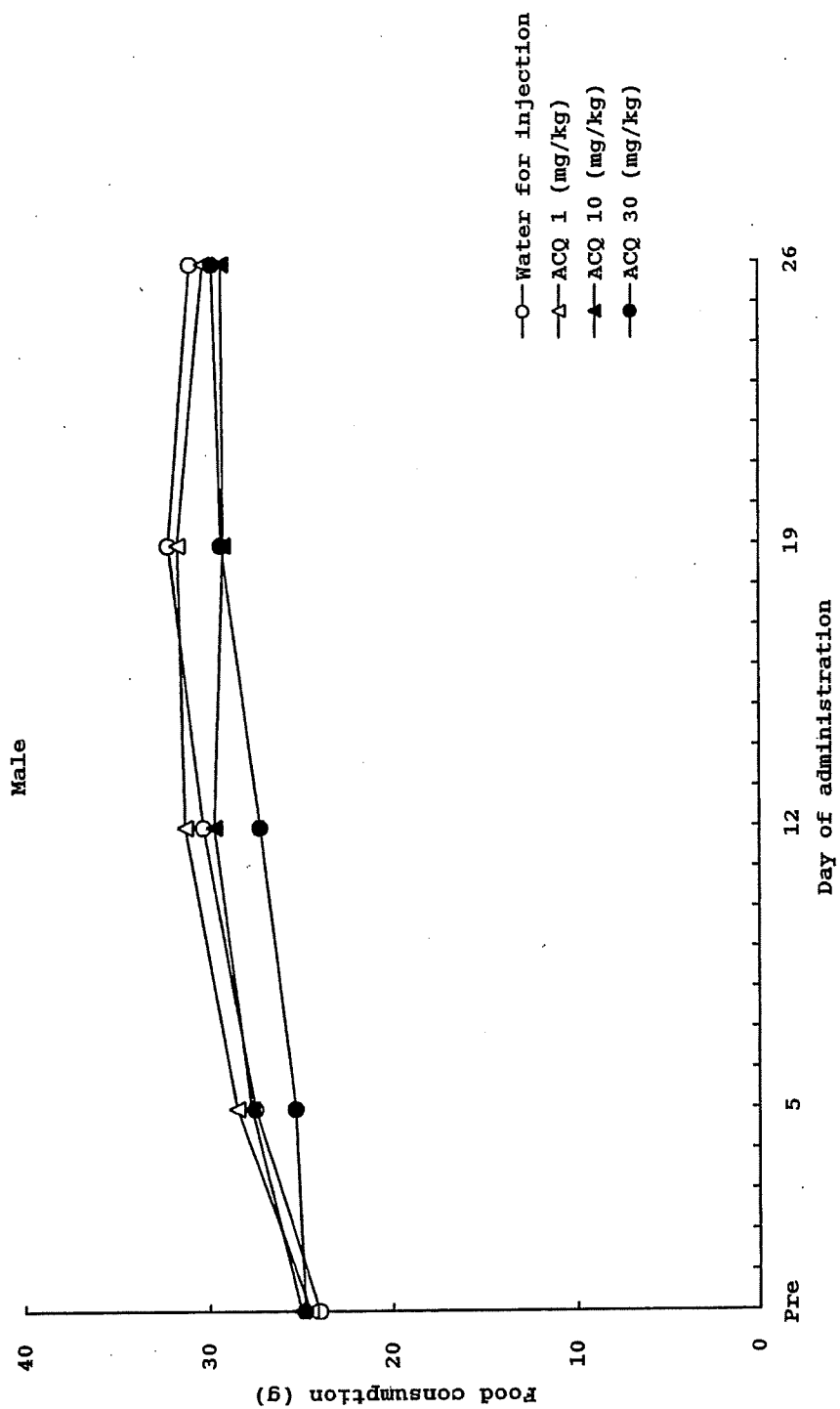


Figure 2-1 Changes of food consumption in rats

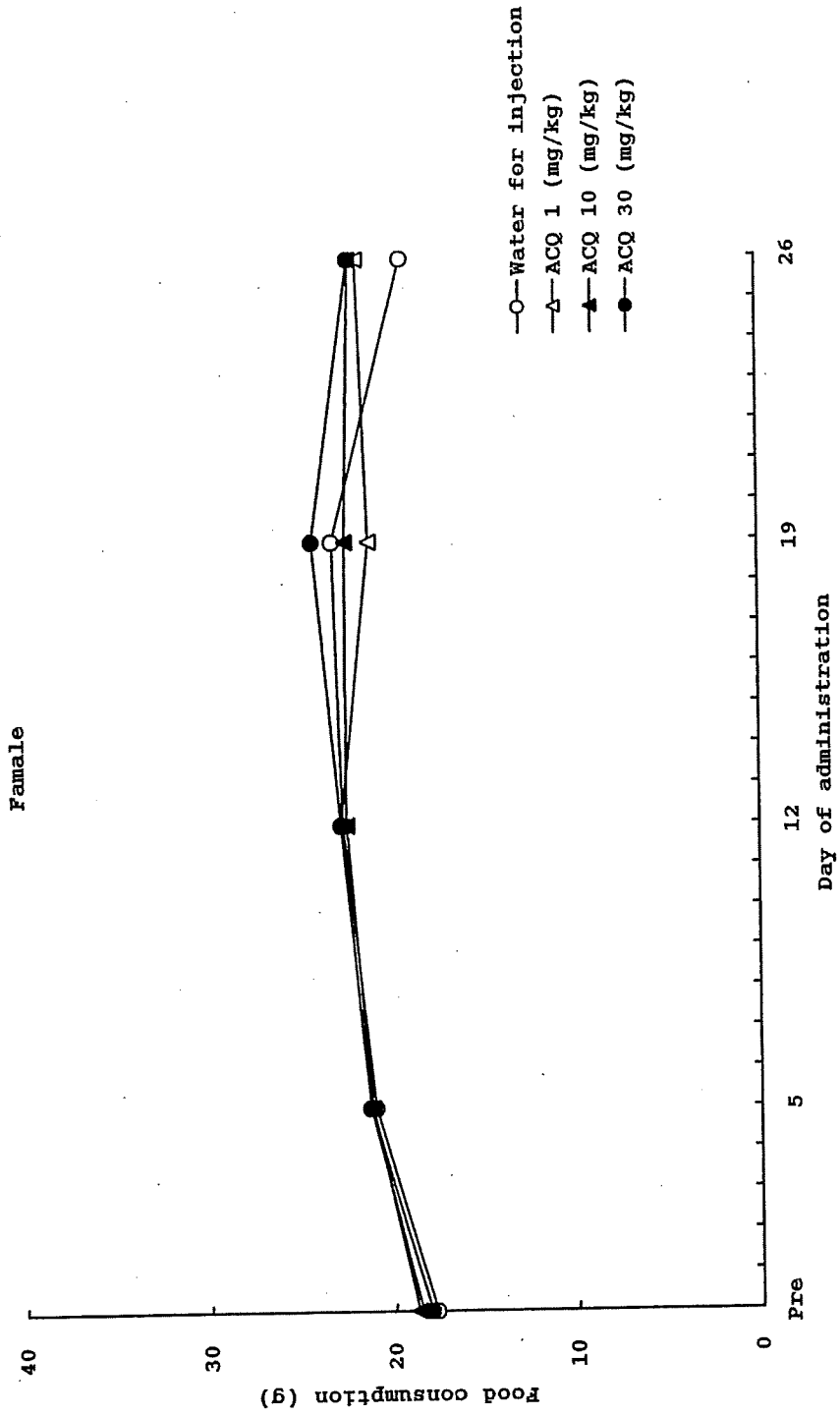


Figure 2-2 Changes of food consumption in rats

Clinical Sign

Grade

- 0 : No abnormal signs
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- + : Non-graded clinical signs

Table 1-1 Clinical signs in male rats

Group	Dose (mg/kg)	Day	Item	Grade			Water for injection			ACQ			ACQ		
				0	1	2 3 +	0	1	2 3 +	0	1	2 3 +	0	1	2 3 +
0	No abnormal signs	0	No abnormal signs	6	6	6	6	6	6	6	6	6	6	6	6
1	No abnormal signs	1	No abnormal signs	6	6	6	6	6	6	6	6	6	6	6	6
2	No abnormal signs	2	No abnormal signs	6	6	6	6	6	6	6	6	6	6	6	6
3	No abnormal signs	3	No abnormal signs	6	6	6	6	6	6	6	6	6	6	6	6
4	No abnormal signs	4	No abnormal signs	6	6	6	6	6	6	6	6	6	6	6	6
5	No abnormal signs	5	No abnormal signs	6	6	6	6	6	6	6	6	6	6	6	6
6	No abnormal signs	6	No abnormal signs	6	6	6	6	6	6	6	6	6	6	6	6
7	Abnormal injection site	7	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
8	Abnormal injection site	8	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
9	Abnormal injection site	9	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
10	Abnormal injection site	10	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
11	Abnormal injection site	11	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
12	Abnormal injection site	12	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
13	Abnormal injection site	13	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
14	Abnormal injection site	14	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
15	Abnormal injection site	15	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
16	Abnormal injection site	16	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
17	Abnormal injection site	17	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
18	Abnormal injection site	18	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
19	Abnormal injection site	19	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
20	Abnormal injection site	20	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
21	Abnormal injection site	21	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
22	Abnormal injection site	22	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6
23	Abnormal injection site	23	Abnormal injection site	6	6	6	6	6	6	6	6	6	6	6	6

Numerals represent the number of animals.

Table 1-2 Clinical signs in male rats

Group	Dose (mg/kg)	Grade	Water for injection			ACQ			ACQ			
			0	1	2 3 +	0	1	2 3 +	0	1	2 3 +	
Day	Item											
24	Abnormal injection site	6	0	0	6	0	5	1	0	6		
25	Abnormal injection site	6	0	0	6	0	4	2	0	6		
26	Abnormal injection site	6	0	0	6	0	4	2	0	6		
27	Abnormal injection site	6	0	0	6	0	3	3	0	6		
28	Abnormal injection site	6	0	0	6	0	3	3	0	6		

Numerals represent the number of animals.

Table 1-3 Clinical signs in female rats

Group	Dose(mg/kg)	Day	Item	Water for injection			ACQ			ACQ			ACQ		
				0	1	2 3 +	0	1	2 3 +	0	1	2 3 +	0	1	2 3 +
0	No abnormal signs	6	6	0	6	6	0	6	6	0	6	6	0	6	6
1	No abnormal signs	6	6	0	6	6	0	6	6	0	6	6	0	6	6
2	No abnormal signs	6	6	0	6	6	0	6	6	0	6	6	0	6	6
3	No abnormal signs	6	6	0	6	6	0	6	6	0	6	6	0	6	6
4	No abnormal signs	6	6	0	6	6	0	6	6	0	6	6	0	6	6
5	No abnormal signs	6	6	0	6	6	0	6	6	0	6	6	0	6	6
6	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
7	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
8	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
9	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
10	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
11	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
12	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
13	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
14	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
15	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
16	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
17	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
18	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
19	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
20	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
21	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
22	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6
23	Abnormal injection site	6	6	0	6	6	0	6	6	0	6	6	0	6	6

Numerals represent the number of animals.

Table 1-4 Clinical signs in female rats

Group	Dose (mg/kg)	Grade	Water for injection	ACQ	ACQ	ACQ	ACQ				
Day	Item	0	1	2	3	+	0	1	2	3	+
24	Abnormal injection site	6	0	6	0	2	4	0	0	6	
25	Abnormal injection site	6	0	6	0	1	5	0	0	6	
26	Abnormal injection site	6	0	6	0	0	6	0	0	6	
27	Abnormal injection site	6	0	6	0	0	6	0	0	6	
28	Abnormal injection site	6	0	6	0	0	6	0	0	6	

Numerals represent the number of animals.

Table 1-5 Clinical signs in male rats (Administration site)

Group	Number of animals	Item	Day of administration (Before administration)																													
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27		
Water for injection	6		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
ACQ (1 mg/kg)	6		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
ACQ (10 mg/kg)	6	Crust	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2	2	3
ACQ (30 mg/kg)	6	Crust	0	0	0	0	0	0	0	0	2	3	4	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	

Numerals represent the number of animals.

Table 1-6 Clinical signs in female rats (Administration site)

Study No.: SBL101-002

Group	Number of animals	Item	Day of administration (Before administration)																											
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
Water for injection	6		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ACQ (1 mg/kg)	6		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ACQ (10 mg/kg)	6	Crust	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	3	3	4	5	6
ACQ (30 mg/kg)	6	Crust	0	0	0	0	0	0	1	2	3	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6

Numerals represent the number of animals.

Table 2-1 Body weight (g) in male rats

Group	Water for injection	ACQ		
		1	10	30
Day Pre	190.5± 8.3(6)	190.3± 8.2(6)	190.2± 7.1(6)	190.2± 7.9(6)
6	253.0±11.0(6)	253.0±13.0(6)	245.5±13.1(6)	237.7±12.3(6)
13	306.2±24.3(6)	306.3±17.0(6)	296.2±15.5(6)	280.8±17.4(6)
20	347.0±32.5(6)	346.5±27.4(6)	329.8±20.9(6)	316.7±24.8(6)
27	374.2±37.4(6)	378.8±34.7(6)	361.3±26.4(6)	345.3±29.3(6)

Values are expressed as the mean ± S.D. (N).
Not significantly different from Water for injection.

Table 2-2 Body weight (g) in female rats

Group	Water for injection	Body weight (g)		
		ACQ	ACQ	ACQ
Dose (mg/kg)		1	10	30
Day Pre				
	154.2± 6.8(6)	152.8± 5.7(6)	154.0± 6.8(6)	154.5± 6.0(6)
6	183.2± 9.0(6)	181.0± 8.8(6)	178.2± 9.3(6)	180.5± 8.6(6)
13	209.8±13.1(6)	206.7±10.0(6)	200.8±11.5(6)	203.3± 8.0(6)
20	227.5±19.0(6)	225.2±13.2(6)	220.5±15.2(6)	223.3±10.2(6)
27	238.5±22.5(6)	244.2±18.8(6)	231.7±13.0(6)	236.5±12.6(6)

Values are expressed as the mean ± S.D. (N).
Not significantly different from Water for injection.

Table 2-3 Body weight gain (g) in male rats

Group	Water for injection	ACQ		
		1	10	30
Day				
6	62.5± 6.3(6)	62.7± 6.7(6)	55.3± 9.4(6)	47.5± 6.0(6)**
13	53.2±14.8(6)	53.3± 8.6(6)	50.7± 5.5(6)	43.2± 7.0(6)
20	40.8±10.5(6)	40.2±11.0(6)	33.7± 9.3(6)	35.8± 7.7(6)
27	27.2± 6.4(6)	32.3± 8.2(6)	31.5± 6.9(6)	28.7± 7.9(6)

Values are expressed as the mean ± S.D. (N).

** P<0.01 : Significantly different from Water for injection.

Table 2-4 Body weight gain (g) in female rats

Group	Water for injection	Body weight gain (g)		
		1	10	30
Day 6	29.0± 2.6 (6)	28.2± 4.9 (6)	24.2± 3.7 (6)	26.0± 5.4 (6)
13	26.7± 4.5 (6)	25.7± 5.7 (6)	22.7± 6.0 (6)	22.8± 2.7 (6)
20	17.7± 6.1 (6)	18.5± 6.0 (6)	19.7± 6.8 (6)	20.0± 5.0 (6)
27	11.0± 5.3 (6)	19.0± 6.4 (6)	11.2± 4.0 (6)	13.2± 6.9 (6)

Values are expressed as the mean ± S.D. (N).
 Not significantly different from Water for injection.

Table 3-1 Food consumption (g/day) in male rats

Group	Water for injection	ACQ		
		1	10	30
Day Pre	24.0± 3.1(6)	24.5± 2.9(6)	25.0± 1.1(6)	24.8± 5.2(6)
5	27.5± 1.5(6)	28.5± 2.1(6)	27.7± 1.6(6)	25.3± 2.2(6)
12	30.3± 4.3(6)	31.3± 3.4(6)	29.7± 2.3(6)	27.2± 2.3(6)
19	32.2± 3.9(6)	31.7± 3.1(6)	29.2± 2.1(6)	29.3± 3.3(6)
26	31.0± 4.4(6)	30.3± 1.9(6)	29.3± 2.7(6)	29.8± 3.1(6)

Values are expressed as the mean ± S.D. (N).
Not significantly different from Water for injection.

Table 3-2 Food consumption (g/day) in female rats

Group	Water for injection	ACQ		
		1	10	30
Day Pre	17.7± 3.5(6)	18.5± 1.5(6)	18.7± 1.4(6)	18.0± 3.7(6)
5	21.0± 3.8(6)	21.3± 1.2(6)	21.2± 1.5(6)	21.3± 1.8(6)
12	22.7± 0.5(6)	22.8± 1.3(6)	22.5± 1.9(6)	22.8± 1.2(6)
19	23.2± 2.4(6)	21.2± 1.5(6)	22.5± 2.7(6)	24.3± 1.9(6)
26	19.3± 3.0(6)	21.8± 2.3(6)	22.2± 2.4(6)	22.2± 1.7(6)

Values are expressed as the mean ± S.D. (N).
Not significantly different from Water for injection.

Gross ophthalmological examination

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- U : Unexamined

Table 4-1 Gross ophthalmological examination in male rats

Group	Water for injection	ACQ	ACQ	ACQ
Dose (mg/kg)		1	10	30
Day	Item	Grade		
Pre	No abnormal changes	6	6	6
25	No abnormal changes	6		6

Numerals represent the number of animals.

Table 4-2 Gross ophthalmological examination in female rats

Group	Dose(mg/kg)	Item	Grade	Water for injection	ACQ	ACQ	ACQ
Pre		No abnormal changes		6	6	6	6
25		No abnormal changes		6	6	10	30

Numerals represent the number of animals.

Slit-lamp examination

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- U : Unexamined