

Table 1. LD 50 of NK-621 in Mice and Rats (mg/kg)

Route	Species		Mouse		Rat	
	Sex	Male	Female	Male	Female	Vehicle
p.o.		2484 (1779-3468)	2313 (1644-3266)	1495 (1221-1829)	1464 (1158-1851)	0.5% CMC
i.p.		675 (531- 850)	839 (655-1076)	560 (492- 638)	580 (494- 682)	0.5% CMC + 0.5% Tween 80
s.c.		>10000	>10000	>10000	>10000	0.5% CMC

Parentheses indicate 95% confidence limits

Fig.1 Average growth curve of per os administration of NK-621 for 90 days upon male rat

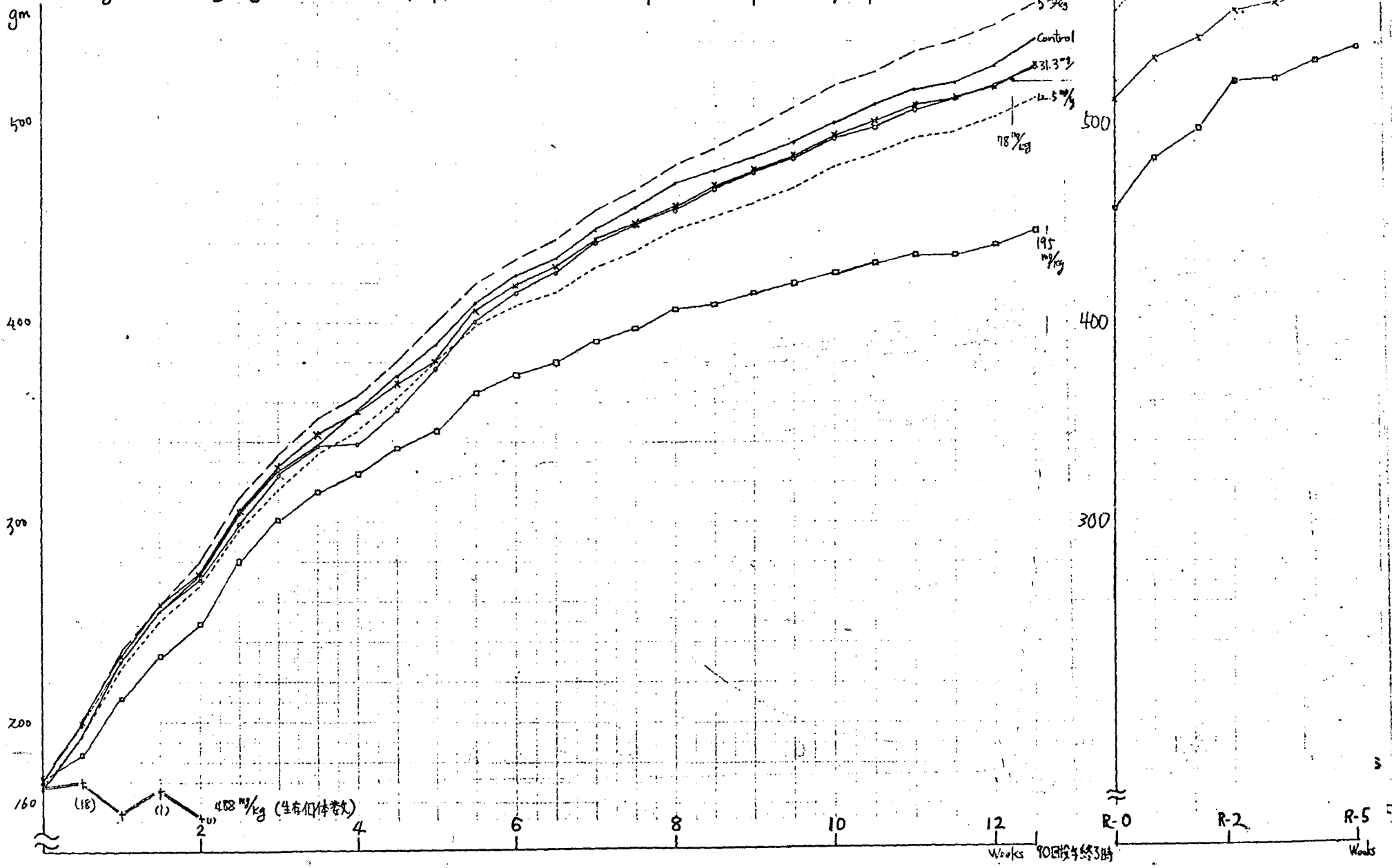


Fig. 2 Average growth curve of ²per as administration of NK-62-1 for 90 days upon female rat

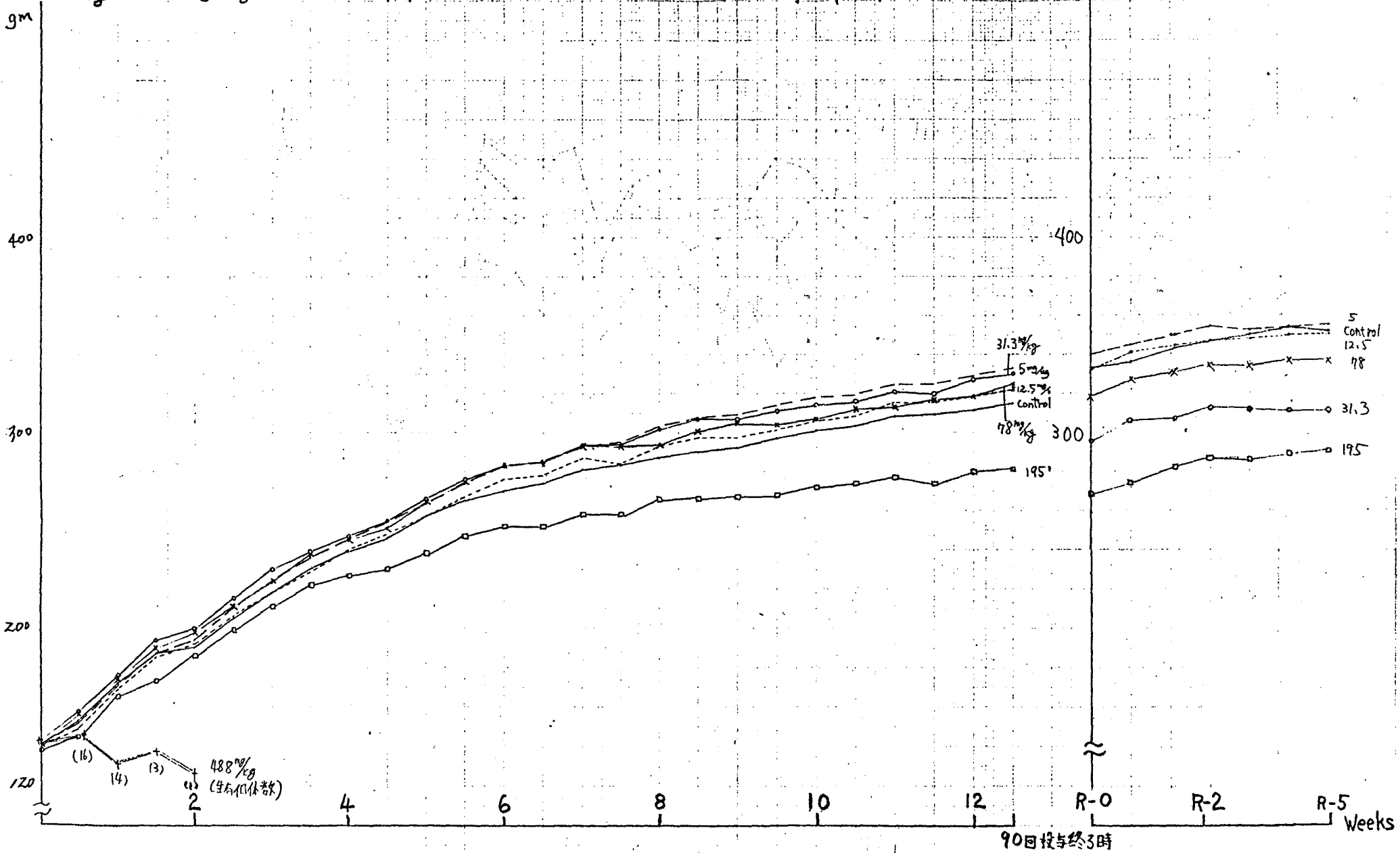


Table 3 Hematological and Biochemical analysis in moribund sacrificed rats (488 mg/kg)

	Rat No.	Sacrificed days *	Hemolysis	RBC (10 ⁶ /mm ³)	WBC (10 ³ /mm ³)	Hemoglobin (g/dl)	Hematocrit (%)	Platelets (10 ⁹ /mm ³)	GPT (K.U.)	Al-ph (K.A.U.)	BIL (mg/dl)	Chol. (mg/dl)	Glu. (mg/dl)	T-P (g/g)	Na (mEq/l)	K (mEq/l)
Male	170	7	++	732	53	9.8	56.5	51.5	122	44.9	-	54	14.0	6.6	168.6	8.88
	154	9	+	-	-	-	-	-	250	63.0	4.9	66	50.6	6.6	158.7	5.31
	160	9	-	-	-	-	-	-	250	58.2	3.9	55	127.8	5.4	155.5	3.63
	163	9	-	-	-	-	-	-	250	71.6	7.0	71	71.7	-	-	-
	151	18	-	722	286	11.1	48.7	56.5	54	31.2	4.6	61	39.6	5.4	165.4	6.12
	Mean	10		727	170	10.4	52.6	54.0	185.2	53.8	5.1	61	60.7	6.0	162.1	5.87
SD	4		7	165	1.1	5.5	3.5	91.9	15.9	1.3	7	42.9	0.7	6.0	2.31	
Female	328	8	±	-	-	-	-	-	62	26.7	0.2	56	85.7	5.4	151.2	4.52
	337	10	-	-	-	-	-	-	49.5	36.8	1.6	46	63.7	5.5	164.0	2.51
	341	13	-	-	-	-	-	-	70	41.1	2.3	43	65.7	5.4	167.3	3.35
	330	14	±	637	172	10.8	47.7	59.9	93	53.3	2.8	54	43.1	5.0	160.3	4.41
	338	17	+	-	-	-	-	-	162	3.8	2.9	92	10.5	6.7	178.0	23.72
	mean	12		637	172	10.8	47.7	59.9	87.3	32.3	2.0	58	53.7	5.6	164.2	7.70
SD	4		0	0	0	0	0	44.7	18.6	1.1	20	28.5	0.6	9.8	8.99	

* : days from treatment start to moribund sacrificed

Table 4 Hemogram of moribund sacrificed rats

	Rat No.	Sacrificed days *	Ba	Eo	St	Se	Ly	Mo	Oth ₁	Oth ₂	
Female	170	7	0	1	17	39	43	0	0	0	Se : 過分葉が多い WBC : 全体的に核周辺不明瞭 RBC : 形態不規則, ばらけている
	151	18	0	0	6	18	24	0	48	4	RBC : 形態不規則, 大小不同軽度 nucleated erythrocyte : 2 / 100 normal Rf
	330	14	0	0	8	56	34	2	0	0	Se : 過分葉が多い RBC : 多染性多し, 大小不同 nucleated erythrocyte : 3 / 100 normal Rf

* : days from treatment start to moribund sacrificed

Oth₁ : perhaps broken Ly.

Oth₂ : perhaps broken nucleated erythrocyte

Table 5 Hematological and Biochemical analysis

		(after 30 times) (n=5)						
		RBC (10 ⁶ /mm ³)	Hemoglobin (g/dl)	Hematocrit (%)	WBC (10 ³ /mm ³)	GPT (KU)	Al-ph (KAU)	
Male	Control	886±26	16.6±0.4	57.4±1.8	193±32	84± 5	20.4±2.8	
	5 mg/kg	863±22	16.5±0.3	57.0±1.7	173±60	87± 6	19.4±3.7	
	12.5	867±43	16.0±0.6	57.7±1.4	134±24*	81±11	19.3±2.9	
	31.3	788±42**	14.8±0.7**	55.5±2.9	134±13**	83± 3	18.4±3.9	
	78	756±81*	13.8±1.2**	57.0±5.2	152±37	86± 6	19.4±2.2	
	195	680±43***	13.2±0.9***	56.8±3.4	138±17*	101±21	20.3±3.2	
	(after 60 times) (n=5)							
	Control	922±41	16.2±0.4	54.6±1.5	141±51	94± 3	12.5±1.7	
	5 mg/kg	922±27	16.2±0.5	55.1±1.7	156±23	91± 5	12.2±1.0	
	12.5	895±32	15.8±0.8	54.3±3.0	158±42	97± 8	12.6±1.6	
31.3	812±30**	15.0±0.4**	53.0±1.1	146±40	88± 5	10.8±2.1		
78	725±38***	13.9±0.5***	50.1±1.9**	146±17	87± 5*	10.9±1.9		
195	708±39***	13.6±0.5***	52.3±2.5	156±31	96± 5	12.7±1.1		

		(after 30 times) (n=5)						
		RBC	Hemoglobin	Hematocrit	WBC	GPT	Al-ph	
Female	Control	815±72	15.7±1.2	55.4±4.3	104±21	78± 9	11.6±2.7	
	5 mg/kg	809±59	15.8±1.0	53.1±3.6	153±35*	74± 9	12.7±0.7	
	12.5	831±42	16.0±0.6	55.2±2.7	96± 8	71± 8	13.4±3.3	
	31.3	765±25	14.9±0.7	53.1±2.7	140±37	81±16	10.6±1.1	
	78	731±60	14.4±0.6	53.1±3.4	144±24*	76±19	10.9±1.6	
	195	709±16**	13.7±0.7**	53.5±1.3	141±42	99±25	13.2±4.3	
	(after 60 times) (n=5)							
	Control	848±54	15.8±0.4	51.4±3.0	150±13	97± 5	8.2±2.3	
	5 mg/kg	887±50	16.1±1.0	53.4±3.0	110±20**	96±12	6.4±1.0	
	12.5	829±43	15.8±0.4	52.1±2.0	170±37	97± 7	7.0±1.0	
31.3	837±22	15.6±0.3	53.0±2.0	115±28*	91± 7	7.5±1.3		
78	766±86	14.4±1.0**	49.8±3.1	152±36	97± 7	7.0±0.8		
195	681±34***	13.6±0.4***	48.9±1.2	86±11***	94±10	7.1±0.9		

* : Significantly different from control mean, P 0.05
 ** : P 0.01
 *** : P 0.001

Table 6 Hemogram

		(after 30 times) (n=5)	Ba	Eo	St	Se	Ly	Mo	oth	
Male		control	0	0.9±0.23	2.4±1.67	5.3±2.60	89.8±2.60	1.4±0.88	0.1±0.33	
		5	0	1.3±1.11	1.9±1.46	4.1±2.61	91.0±4.36	1.6±1.51	0.1±0.38	
		12.5	0	1.6±0.55	2.2±1.64	5.6±1.52	88.2±2.59	1.8±1.30	0.4±0.55	
		31.3	0	1.2±0.45	4.0±2.74	5.4±1.82	88.2±3.83	1.2±0.84	0	
		78	0	2.7±1.07	3.7±1.21	4.9±4.02	90.1±4.98	1.3±0.95	0	
		195	0	0.3±0.82	5.0±4.24	4.3±2.88	87.5±4.85	2.7±1.37	0.17±0.41	
		(after 60 times) (n=5)								
		control	0	1.0±0.71	5.2±2.59	2.8±2.77	90.0±4.95	0.8±1.30	0.2±0.45	
		5	0	0.6±1.34	5.4±2.70	4.0±2.12	88.0±4.30	1.2±1.30	0.8±0.84	
		12.5	0	0.8±1.10	5.6±3.13	2.6±2.19	90.0±4.73	0.8±0.84	0.2±0.45	
		31.3	0	0.8±1.50	4.5±1.73	2.8±2.87	91.0±3.37	1.0±0.82	0	
		78	0	0.6±0.55	5.2±2.05	3.0±2.35	90.4±4.67	0.8±0.84	0	
		195	0	0.9±1.29	6.9±3.63	4.4±3.53	86.5±7.09	1.0±1.15	0.3±0.48	
	Female		(after 30 times) (n=5)							
		Control	0	1.3±1.37	3.2±2.32	3.5±2.26	90.5±4.72	1.0±0.63	0.5±0.84	
		5	0	0.6±0.79	2.6±1.72	4.4±3.82	91.0±5.13	1.4±0.79	0	
		12.5	0	1.0±0.71	2.4±1.52	2.8±2.17	92.8±2.25	0.6±0.55	0.4±0.55	
		31.3	0	0.8±0.75	1.5±1.52	2.5±1.97	93.5±1.64	1.7±0.82	0	
		78	0	0.4±0.55	3.4±1.95	5.0±4.80	89.0±5.87	1.8±0.84	0.4±0.89	
		195	0	0.7±0.52	6.0±5.29	5.8±4.26	84.5±8.89	2.7±1.51	0.3±0.82	
		(after 60 times) (n=5)								
		Control	0	0.4±0.89	3.6±2.07	1.4±1.67	94.4±2.97	0.2±0.45	0	
		5	0	0.8±0.84	3.4±0.89	2.8±1.79	93.0±2.24	0	0	
		12.5	0	1.2±0.84	2.4±2.07	1.4±1.14	94.4±3.51	0.4±0.55	0.2±0.45	
		31.3	0	1.0±1.00	6.2±2.77	3.6±2.07	87.6±5.13	1.6±1.14	0	
		78	0	1.4±1.52	9.6±2.51*	6.4±5.27	81.2±5.36**	1.2±0.84	0.2±0.45	
		195	0	1.0±1.73	7.2±3.56	3.4±1.67	87.4±4.72*	0.6±0.55	0.4±0.55	

* : Significantly different from control mean, P 0.05
 ** : P 0.01
 *** : P 0.001

Table 7 Hematological analysis

	(after 90 times) (n=7-10) Ret.(n=5) Ca-C.T (n=5)							
	RBC (10 ⁹ /mm ³)	Hemoglobin (g/dl.)	Ret. (%)	Hematocrit (%)	WBC (10 ⁹ /mm ³)	Platelets (10 ⁹ /mm ³)	Ca-C.T (sec.)	
M a t e	Control	879±41	16.4±0.5	8.4± 2.6	51.7±2.8	76±25	70.2± 4.0	42.3± 4.4
	5 mg/kg	857±54	16.1±0.5	10.6± 3.6	50.3±3.5	88±17	69.4± 7.5	43.1± 3.9
	12.5	844±99	15.8±0.7	10.8± 4.5	50.2±4.1	81±20	64.8± 4.8*	44.9±12.2
	31.3	760±69***	14.9±0.4***	23.8± 6.7**	48.5±3.3*	89±43	69.8± 9.6	48.6± 4.5
	78	692±53***	13.9±0.5***	27.0± 9.9**	47.0±2.9*	86±26	72.2± 4.6	49.4± 8.5
	195	637±29***	13.5±0.4***	39.8±16.0**	47.0±2.5*	72±18	77.3±10.1	42.0± 7.2
		(5 week recovery) (n=5)						
	Control	816±44	15.8±0.7	21.8± 5.0	44.5±3.6	106±29	52.8± 7.7	-
	5 mg/kg	840±54	15.9±1.2	16.6± 3.0	47.0±3.5	107±28	38.2±14.0	-
	12.5	849±33	16.0±0.5	16.2± 7.4	47.0±2.7	111±30	44.1±12.5	-
31.3	870±43	16.6±0.5	11.8± 3.7*	48.1±2.5	113±23	42.1± 4.5*	-	
78	922±49*	17.1±0.5*	17.6± 6.3	51.8±0.9**	99±30	47.8±10.1	-	
195	886±62	17.1±1.0	16.4± 6.6	49.9±4.5	89±28	59.9± 5.0	-	
F e m a l e	(after 90 times) (n=7-10) Ret.&Ca-C.T (n=5)							
	Control	737±88	15.8±0.4	12.8± 3.7	47.4±3.0	58±10	69.4± 9.9	37.5± 8.5
	5 mg/kg	748±88	15.6±0.6	12.8± 4.5	46.4±4.4	72±22	71.1± 6.0	39.6± 6.8
	12.5	725±42	15.6±0.6	18.4±12.0	45.5±2.8	65± 5	70.1± 6.1	41.8± 9.4
	31.3	649±66	14.5±0.7**	24.0±14.3	42.0±2.8**	67±26	74.5± 8.7	39.2± 6.4
	78	597±65**	13.5±0.7***	35.2±12.0**	39.6±3.1***	115±75	79.0± 5.4*	38.8± 8.6
	195	540±29***	12.5±0.7***	60.4±19.1**	38.8±2.6***	91±56	76.4± 7.8	38.9± 5.9
		(5 week recovery) (n=5)						
	Control	773±61	15.1±0.3	16.8±8.3	43.0±3.2	75±21	55.3±15.1	-
	5 mg/kg	795±56	15.9±0.7	23.0±8.8	46.0±2.2	102±16	69.2±10.8	-
12.5	772±45	16.2±0.7*	22.6±6.7	44.3±2.1	96±24	65.6± 5.5	-	
31.3	821±36	16.4±0.5**	16.6±5.0	48.3±2.8*	86±12	73.4± 9.0	-	
78	787±85	15.8±0.9	14.6±6.6	45.3±4.6	97± 9	65.5± 8.1	-	
195	774±34	16.2±0.6*	12.0±8.2	44.9±2.4	95±20	57.4±11.0	-	

* : Significantly different from control mean, P 0.05
 ** : P 0.01
 *** : P 0.001

Table 8 Hemogram

(after 90 times) (n=7-10)

	Ba	Ho	St	Se	Ly	Mo	Oth
Control	0.0	1.3 ± 1.25	2.6 ± 1.78	7.9 ± 3.78	87.5 ± 4.93	0.7 ± 0.67	0.0
5 mg/kg	0.0	0.8 ± 0.63	4.0 ± 2.21	10.1 ± 5.67	83.5 ± 7.18	1.5 ± 0.97	0.1 ± 0.32
12.5 mg/kg	0.0	0.7 ± 0.87	2.9 ± 1.90	7.6 ± 4.19	87.8 ± 3.53	1.3 ± 0.71	0.0
31.3 mg/kg	0.0	0.9 ± 0.78	4.0 ± 2.65	8.1 ± 5.18	85.4 ± 5.70	1.6 ± 1.59	0.0
78.0 mg/kg	0.0	0.1 ± 0.32*	3.6 ± 3.41	6.8 ± 3.12	88.5 ± 4.58	0.9 ± 0.99	0.1 ± 0.32
195.0 mg/kg	0.0	0.7 ± 1.12	5.3 ± 4.64	8.3 ± 3.74	83.9 ± 3.37	1.7 ± 1.58	0.1 ± 0.33
Male							
(after 5 week recovery) (n=5)							
Control	0.0	1.8 ± 0.84	2.8 ± 1.64	3.0 ± 3.54	80.4 ± 4.88	1.6 ± 1.52	0.4 ± 0.55
5 mg/kg	0.0	1.2 ± 1.30	1.2 ± 0.84	6.4 ± 3.21*	89.4 ± 3.51*	1.6 ± 0.89	0.2 ± 0.45
12.5 mg/kg	0.0	1.4 ± 1.14	1.4 ± 0.55	8.2 ± 4.66	87.2 ± 5.54	1.8 ± 1.10	0.0
31.3 mg/kg	0.0	1.0 ± 0.71	0.8 ± 1.10	4.6 ± 2.51**	92.8 ± 4.32**	0.8 ± 0.84	0.0
78.0 mg/kg	0.0	1.0 ± 1.73	1.4 ± 1.52	5.6 ± 4.28*	90.8 ± 6.14*	1.0 ± 1.00	0.2 ± 0.45
195.0 mg/kg	0.0	0.6 ± 0.55*	1.2 ± 1.30	9.6 ± 9.94	86.8 ± 11.5	1.8 ± 1.30	0.0
Female							
(after 90 times) (n=7-10)							
Control	0.0	0.6 ± 0.92	2.1 ± 1.55	9.8 ± 6.39	86.9 ± 8.74	0.5 ± 0.76	0.0
5 mg/kg	0.0	0.9 ± 1.10	0.7 ± 0.67*	7.6 ± 2.37	90.2 ± 2.94	0.6 ± 0.70	0.0
12.5 mg/kg	0.0	1.0 ± 0.58	1.9 ± 1.86	8.7 ± 4.15	87.4 ± 4.96	0.8 ± 0.90	0.3 ± 0.49
31.3 mg/kg	0.0	1.0 ± 1.13	1.4 ± 1.13	8.6 ± 2.99	88.3 ± 2.78	0.4 ± 0.53	0.3 ± 0.76
78.0 mg/kg	0.0	0.7 ± 0.71	2.0 ± 0.87	7.8 ± 4.97	88.8 ± 5.56	0.4 ± 0.73	0.3 ± 0.50
195.0 mg/kg	0.0	0.8 ± 0.83	2.0 ± 0.87	10.8 ± 6.28	84.8 ± 6.61	1.1 ± 1.05	0.3 ± 0.50
(after 5 week recovery) (n=5)							
Control	0.0	0.6 ± 1.34	1.8 ± 1.30	5.8 ± 7.29	79.8 ± 9.15	1.6 ± 1.52	0.4 ± 0.55
5 mg/kg	0.0	1.0 ± 0.71	0.4 ± 0.89	4.6 ± 4.16	92.2 ± 6.34	1.8 ± 1.92	0.0
12.5 mg/kg	0.0	0.8 ± 0.84	1.2 ± 1.30	5.0 ± 4.00	91.4 ± 4.10*	1.4 ± 1.34	0.2 ± 0.45
31.3 mg/kg	0.0	0.8 ± 0.84	2.0 ± 1.87	4.0 ± 2.55	91.0 ± 3.39	2.2 ± 1.79	0.0
78.0 mg/kg	0.2 ± 0.45	1.0 ± 0.71	1.8 ± 1.30	7.6 ± 2.61	87.0 ± 4.00	2.4 ± 0.89	0.0
195.0 mg/kg	0.0	0.4 ± 0.55	1.4 ± 0.89	6.0 ± 4.30	90.8 ± 4.97	1.4 ± 0.55	0.0

* : Significantly different from control mean, P 0.05
 ** : P 0.01
 *** : P 0.001

Table 9 Biochemical analysis

		(after 90 times) (n=12-15)														
		GOT	GPT	Al-ph	BIL(mg/dl)	LAP	LDH	Chol.	TGL	Glu.	BUN	Creatinine	Na	K	Cl	TP
Male	Control	141±28	34± 9	242±30	0.60±0.04	65.0±6.7	2304±773	51± 8	115±24	253±41	19.5±2.9	0.89±0.13	148±3	5.6±0.2	108±2	7.0±0.2
	5mg/kg	119±21*	32± 5	252±31	0.62±0.03	60.4±6.0	1621±504*	56±10	97±24	339±39***	19.8±1.7	0.95±0.09	148±6	5.8±1.1	106±3*	7.2±0.7
	12.5	128±18	36±10	269±41	0.62±0.04	61.8±8.2	1718±655*	55± 8	94±29*	335±66**	20.3±2.3	0.97±0.10	146±3	5.6±0.5	107±2	7.0±0.3
	31.3	118±26*	32± 8	250±43	0.62±0.03	57.0±5.3*	1740±568*	64± 9***	94±26*	278±54	18.5±2.6	0.84±0.15	146±2	5.1±0.4***	106±2*	7.3±0.4*
	78	108±20**	37± 8	245±31	0.63±0.06	55.5±4.5***	1558±558**	64±10***	68±21***	248±54	20.3±2.7	0.81±0.13	147±3	4.9±0.5***	105±3**	7.6±0.2***
195	126±16	54±29*	292±58**	0.71±0.07***	62.8±5.0	2005±378	56±14	74±30**	156±51***	20.8±2.9	0.78±0.12*	148±2	4.9±0.8**	105±3**	7.8±0.4***	
		(5 week recovery) (n=5)														
		GOT	GPT	Al-ph	BIL	LAP	LDH	Chol.	TGL	Glu.	BUN	Creatinine	Na	K	Cl	TP
Male	Control	134± 5	47± 6	176±15	0.23±0.04	59.9±1.4	1418±723	45± 9	91±60	328±57	19.7±1.0	0.93±0.05	146±5	5.9±1.7	105±2	6.5±0.9
	5 mg/kg	120±32	40±20	202±65	0.22±0.06	61.2±11.4	1171±458	46±7	104±31	308±48	19.1±1.6	0.83±0.10	147±6	5.6±1.6	105±2	6.8±0.7
	12.5	113±17*	38±17	171±29	0.22±0.06	56.8±2.2*	1593±407	45±11	88±15	286±42	19.5±2.3	0.84±0.06	146±3	5.3±0.9	104±1	6.6±0.3
	31.3	110± 7***	44±12	170±40	0.23±0.04	56.1±3.9	1369±259	47± 8	82±22	307±16	20.2±1.3	0.89±0.08	146±3	5.5±0.4	105±1	6.5±0.1
	78	110±13**	31± 6**	199±16	0.22±0.02	59.7±3.2	1268±194	41± 7	70±25	286±26	19.1±1.9	0.77±0.10*	148±3	4.7±0.3	106±3	6.5±0.3
195	124±12	44±10	202±49	0.22±0.04	58.8±9.8	1274±309	46± 9	85±31	333±27	19.0±1.5	0.90±0.03	146±6	5.8±1.5	107±2	6.6±0.8	
		(after 90 times) (n=12-15)														
		GOT	GPT	Al-ph	BIL	LAP	LDH	Chol.	TGL	Glu.	BUN	Creatinine	Na	K	Cl	TP
Female	Control	168±74	69±48	103±32	0.61±0.03	56.0±6.5	1667±402	61±11	96±15	230±49	18.5±2.4	0.88±0.10	149±3	4.7±0.5	108±3	7.9±0.6
	5 mg/kg	127±43	41±22	104±16	0.60±0.04	53.6±5.6	1372±290*	62±10	85±21	228±46	19.2±2.1	0.87±0.10	150±2	4.9±0.3	108±2	7.7±0.5
	12.5	152±51	58±43	93±13	0.62±0.03	51.0±4.8*	1592±352	65±11	84±10*	260±76	20.2±2.1	0.97±0.10*	148±2	4.7±0.3	108±2	7.7±0.5
	31.3	128±37	42±27	93±31	0.62±0.05	49.2±5.5*	1395±393	82±12***	76±12**	248±69	20.6±1.7*	0.91±0.07	149±3	4.6±0.9	107±2	8.3±0.6
	78	156±76	63±43	96±20	0.69±0.09**	50.5±5.3*	1574±529	94±22***	79±21*	225±52	22.1±2.9**	0.89±0.12	147±2	4.5±0.6	105±3*	8.3±0.7
195	155±69	58±39	190±80**	0.72±0.05***	57.3±6.8	1733±574	106±16***	88±25	165±45**	21.0±2.8*	0.83±0.06	149±3	4.8±0.7	107±2	8.1±0.4	
		(5 week recovery) (n=5)														
		GOT	GPT	Al-ph	BIL	LAP	LDH	Chol.	TGL	Glu.	BUN	Creatinine	Na	K	Cl	TP
Female	Control	157±46	57±20	75±16	0.21±0.05	51.8±3.9	1123±241	49±12	69±14	200±22	17.3±3.3	0.87±0.13	145±4	4.4±0.2	107±2	6.8±0.4
	5 mg/kg	161±57	55±21	68± 7	0.21±0.03	52.4±2.6	1092±324	62± 8	71± 7	200±21	20.1±1.6	0.92±0.02	148±1	4.6±0.3	108±2	7.5±0.2*
	12.5	117±15	35± 8	72±11	0.21±0.01	55.7±9.3	953±283	54±12	69± 4	196±29	16.5±1.5	0.85±0.11	147±3	4.3±0.3	106±1	7.3±0.7
	31.3	184±26	72±19	69±20	0.20±0.03	54.6±6.6	1216±549	60±11	71±12	177±29	16.5±1.2	0.90±0.09	146±3	4.3±0.3	107±2	7.3±0.3
	78	120±28	40±11	59±12	0.20±0.02	44.8±3.9*	1039± 89	72±16	76±11	197±19	16.7±3.0	0.81±0.13	146±2	4.4±0.4	105±2	7.8±0.4**
195	149±43	46±12	85±25	0.20±0.03	52.8±7.6	1232±215	70±22	63± 9	226±54	17.5±2.6	0.82±0.05	143±3	4.3±0.3	105±2	7.3±0.7	

* : Significantly different from control mean, P 0.05
 ** : P 0.01
 *** : P 0.001

Table 12 NK-621 ラット亜急性毒性 剖検所見

剖検所見	投与量		Control		5 mg/kg		12.5 mg/kg		31.3 mg/kg		78 mg/kg		195 mg/kg		計
	性別		M	F	M	F	M	F	M	F	M	F	M	F	
胸腔内検体出現								1		1		1	1	2	6
肺 充血						1									1
腎 貧血					1					1	1	1			4
胃 出血									1	1					2
胃 充血								1							1
小腸 出血						2			1		1		2		6
小腸 充血					3	1			1	2	1				8
副腎 腫大										1		3		5	9
副腎 貧血										3	1	5		7	16
肝 辺縁鈍							1				2	1	2		6
肝 貧血					4		1		1				5		11
肝 黄変					4		4	2	8	5	11	16	18	16	84
肝 肥大							3		6	6	15	14	19	18	81
個体数	20	18	20	20	20	18	19	18	20	19	19	19	19	19	230

Fig.8

Faecal occult blood
(n = 10)
Treatment
Days

Recovery (n = 5)
Weeks

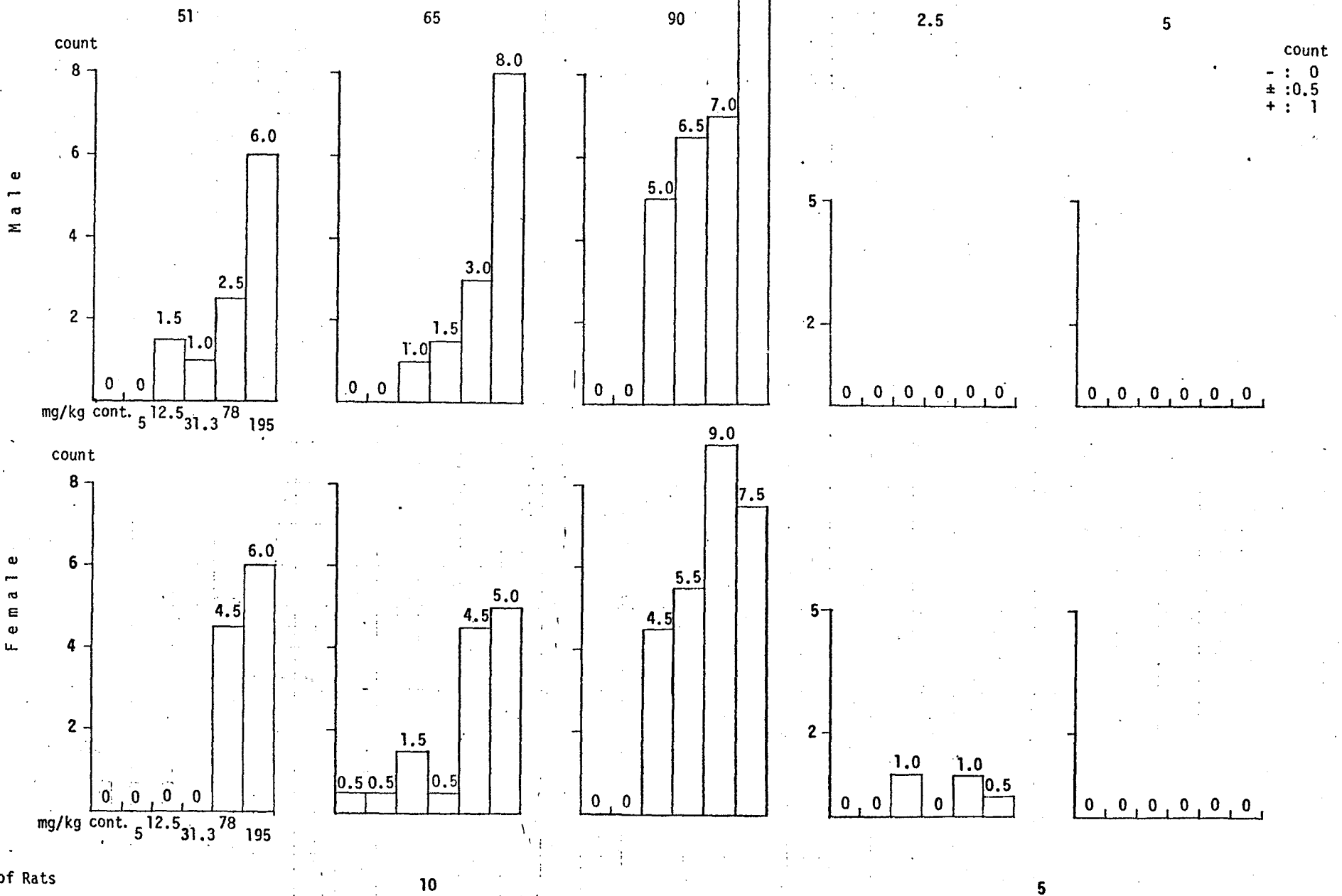


Table 16

Subacute toxicity in rats following per os administration of NK-621

Histopathological grade of fatty change in the liver

dose mg/kg/day	male		female	
	subacute	recovery	subacute	recovery
0	1.20	1.00	0.60	1.40
5	0.60	1.00	0.75	1.20
12.5	0.60	0.60	1.80	2.00
31.3	1.50	0.80	4.00	1.50
78	2.00	2.80	3.60	2.40
195	5.20	3.25	5.60	3.60
488	1.60	-	1.80	-

grade of fatty change, 0: normal, 1: negligible, 2: slight,
4: moderate, 6: severe

Table 17

Subacute toxicity in rats following per os administration of NK-621
 Histopathological grade of vacuolation in the zona fasciculata of adrenal cortex

dose mg/kg/day	male		female	
	subacute	recovery	subacute	recovery
0	0.0	0.0	0.0	0.0
5	0.6	0.0	0.0	0.0
12.5	0.2	0.4	0.0	0.0
31.3	0.2	0.6	0.0	0.0
78	1.8	1.0	0.0	0.0
195	3.0	3.6	1.0	0.6
488	1.6	-	1.8	-

vacuolation grade, 0: normal, 1: negligible, 2: slight, 4: moderate