

Figure 1 Study schedule of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

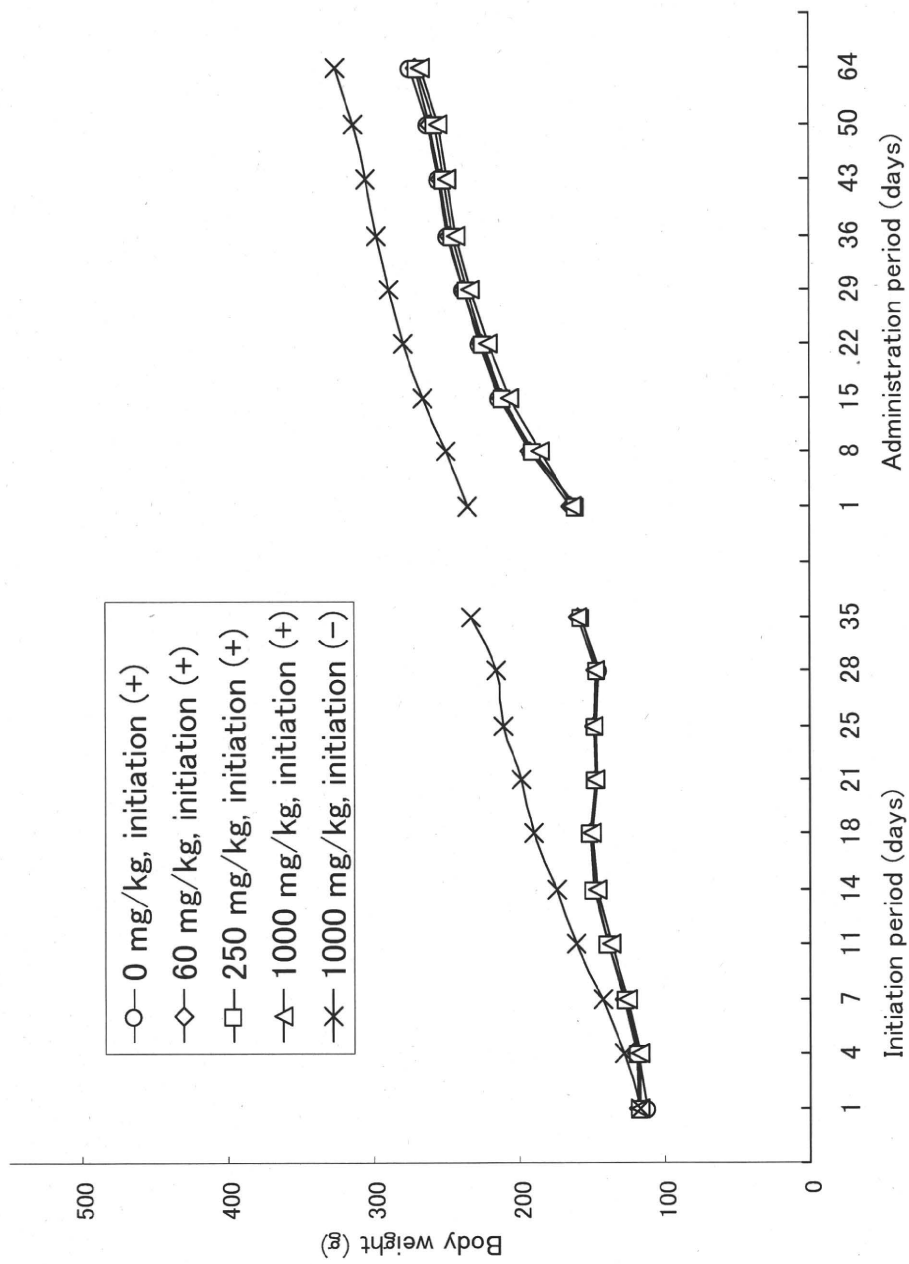


Figure 2 Body weight of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

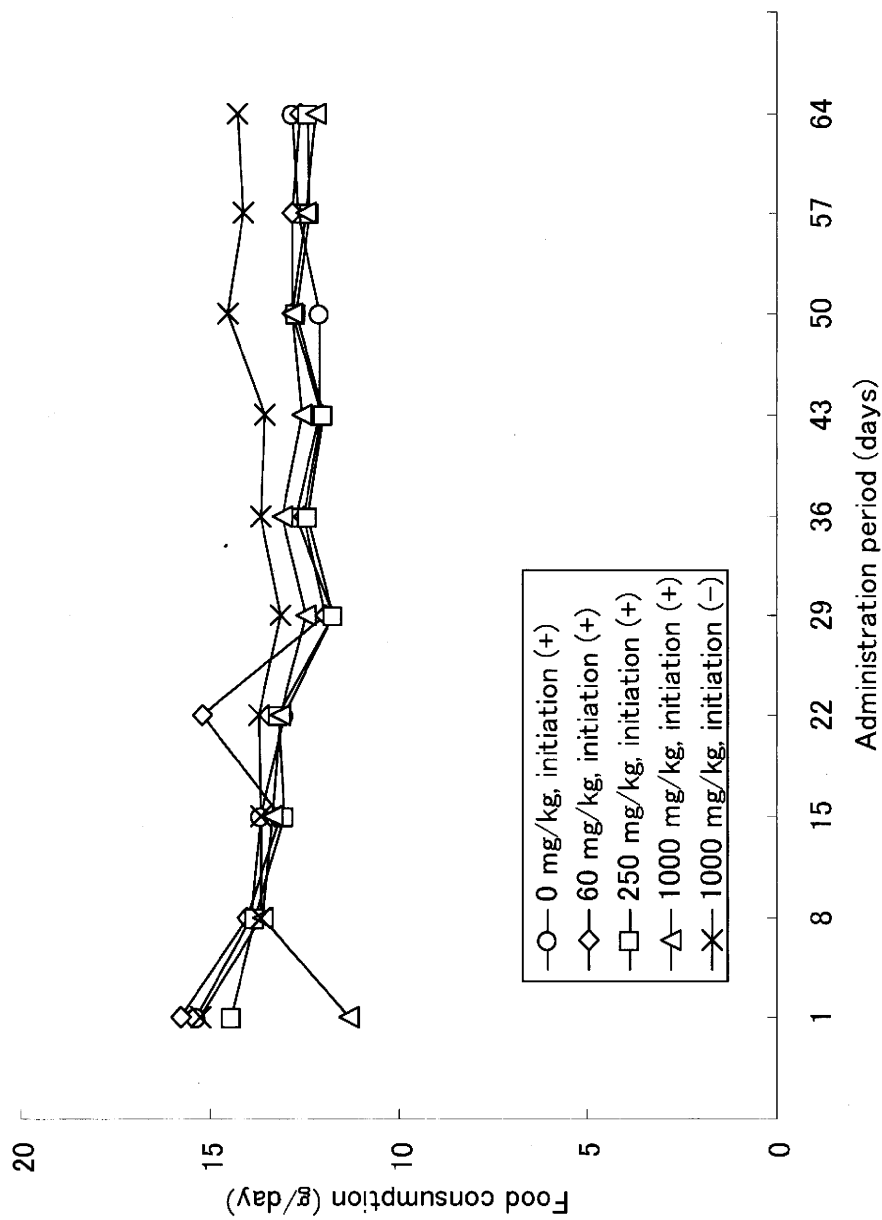


Figure 3 Food intake of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Table 1-1 Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose (mg/kg)	Initiation	Initiation period (days)									
		1	4	7	11	14	18	21	25	28	35
0	(+)	112.3	118.1	126.6	138.8	148.7	150.2	146.5	147.0	145.7	157.7
		±21.5	±4.8	±5.7	±5.5	±6.1	±6.6	±7.0	±8.2	±8.3	±11.7
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
60	(+)	118.6	119.8	127.9	139.4	148.1	151.0	147.4	148.5	147.0	160.0
		±4.7	±5.3	±8.7	±7.6	±7.5	±7.5	±6.7	±8.3	±8.2	±12.6
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
250	(+)	117.5	118.7	127.4	139.2	148.6	151.0	147.0	147.0	146.6	157.5
		±4.5	±5.2	±5.9	±6.5	±6.5	±7.4	±7.6	±9.1	±9.9	±13.7
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
1000	(+)	116.5	117.0	125.6	137.0	146.9	150.5	147.1	148.4	147.7	159.4
		±5.4	±5.7	±6.1	±7.1	±7.1	±7.3	±8.9	±8.9	±9.6	±14.6
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
1000	(-)	116.6	127.5 **	142.9 **	160.8 **	174.7 **	189.9 **	199.1 **	210.5 **	215.9 **	233.1 **
		±4.8	±4.8	±5.9	±6.8	±7.5	±8.4	±8.5	±8.9	±10.3	±9.9
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)

Mean±SD (N)

** , significant difference from the negative control, p<0.01

Table 1-2 Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose (mg/kg)	Initiation	Administration period (days)								
		1	8	15	22	29	36	43	50	64
0	(+)	161.2	191.4	213.3	227.2	238.2	248.6	255.1	262.8	274.6
		±12.9	±11.9	±10.2	±9.5	±10.2	±10.0	±10.6	±10.9	±12.1
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
60	(+)	164.1	192.3	212.7	225.6	237.4	247.0	253.8	260.5	271.1
		±12.7	±12.0	±10.6	±9.5	±9.9	±9.9	±10.6	±10.7	±10.6
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
250	(+)	160.7	189.9	211.2	224.1	235.5	245.6	250.8	257.7	269.0
		±14.0	±12.2	±12.0	±11.8	±11.5	±11.7	±12.1	±12.0	±14.5
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
1000	(+)	163.2	185.0	205.8	220.8	232.4	242.7	248.6	255.5	267.2
		±14.2	±15.0	±13.0	±11.7	±10.8	±9.7	±9.5	±8.8	±8.8
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
1000	(-)	234.8 **	249.9 **	266.2 **	278.7 **	288.6 **	297.6 **	304.7 **	313.4 **	325.7 **
		±10.1	±11.3	±12.3	±12.7	±13.6	±12.6	±12.9	±12.7	±12.7
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)

Mean±SD (N)

** , significant difference from the negative control, p<0.01

Table 2 Water intake (mL/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose (mg/kg)	Initiation	Initiation period (days)								
		1	4	7	11	14	18	21	25	28
0	(+)	13.6	15.1	14.7	17.7	18.4	14.6	18.8	19.6	20.6
		±6.8 (20)	±2.2 (20)	±2.6 (20)	±2.5 (20)	±2.5 (20)	±4.9 (20)	±4.8 (20)	±4.6 (20)	±4.7 (20)
60	(+)	15.7	16.5	16.1	17.9	19.0	16.8	18.5	19.5	22.0
		±4.6 (20)	±8.0 (20)	±2.8 (20)	±2.6 (20)	±4.0 (20)	±5.6 (20)	±4.7 (20)	±4.5 (20)	±4.4 (20)
250	(+)	14.4	13.8	15.1	18.3	19.9	16.3	20.3	21.2	20.1
		±3.6 (20)	±3.4 (20)	±2.3 (20)	±2.7 (20)	±2.5 (20)	±5.5 (20)	±4.6 (20)	±6.1 (20)	±3.4 (20)
1000	(+)	12.0	13.4	14.2	18.3	18.6	15.7	19.2	20.3	20.9
		±5.0 (20)	±2.6 (20)	±2.8 (20)	±5.3 (20)	±2.3 (20)	±4.3 (20)	±3.7 (20)	±4.2 (20)	±3.8 (20)
1000	(-)	19.2 **	17.2 **	18.3 **	20.1 **	20.7 **	22.1 **	22.1 **	22.7	25.4 **
		±9.2 (20)	±3.1 (20)	±2.6 (20)	±2.0 (20)	±1.6 (20)	±1.4 (20)	±1.8 (20)	±2.3 (20)	±3.3 (20)

Mean±SD (N)

** , significant difference from the negative control, p<0.01

Table 3 Food intake (g/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose (mg/kg)	Initiation	Administration period (days)									
		1	8	15	22	29	36	43	50	57	64
0	(+)	15.4	13.9	13.7	13.0	11.7	12.7	12.1	12.1	12.7	12.8
		±2.0 (20)	±1.3 (20)	±1.0 (20)	±1.1 (20)	±0.9 (20)	±1.2 (20)	±1.0 (20)	±0.9 (20)	±1.1 (20)	±2.8 (20)
60	(+)	15.7	14.0	13.2	15.2	11.9	12.5	12.1	12.8	12.8	12.6
		±2.2 (20)	±1.0 (20)	±1.1 (20)	±6.1 (20)	±1.0 (20)	±0.9 (20)	±1.0 (20)	±0.9 (20)	±1.2 (20)	±0.9 (20)
250	(+)	14.4	13.8	13.0	13.2	11.7	12.4	12.0	12.7	12.3	12.4
		±1.5 (20)	±1.2 (20)	±0.8 (20)	±1.0 (20)	±0.9 (20)	±1.0 (20)	±1.2 (20)	±1.1 (20)	±1.1 (20)	±1.0 (20)
1000	(+)	11.3 **	13.6	13.3	13.1	12.5	13.1	12.5	12.8	12.5	12.2
		±2.1 (20)	±1.7 (20)	±1.4 (20)	±1.1 (20)	±1.2 (20)	±1.2 (20)	±1.2 (20)	±1.3 (20)	±1.2 (20)	±1.3 (20)
1000	(-)	15.3	13.6	13.7	13.7	13.1 **	13.6 *	13.6 **	14.5 **	14.1 **	14.3 **
		±1.8 (20)	±1.3 (20)	±0.9 (20)	±0.8 (20)	±1.0 (20)	±1.1 (20)	±0.7 (20)	±1.0 (20)	±1.2 (20)	±0.8 (20)

Mean±SD (N)

* , significant difference from the negative control, p<0.05

** , significant difference from the negative control, p<0.01

Table 4 Arachidonic acid intake (mg/kg/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose (mg/kg)	Initiation	Administration period (days)								
		1	8	15	22	29	36	43	50	64
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	±0.0	±0.0	±0.0	±0.0	±0.0
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
60	(+)	133.2	101.2	86.0	94.1	69.8	70.4	66.2	68.3	64.6
		±15.1	±6.5	±7.1	±40.1	±4.9	±5.2	±5.9	±5.3	±4.2
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
250	(+)	526.9	424.8	359.3	343.0	289.9	294.6	278.8	287.7	268.6
		±75.6	±44.1	±30.6	±25.6	±24.9	±23.2	±30.3	±25.7	±19.9
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
1000	(+)	1616.0	1717.2	1519.3	1390.9	1257.4	1258.8	1180.0	1171.9	1066.3
		±224.0	±202.6	±167.5	±144.8	±149.2	±112.4	±115.5	±121.8	±120.5
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)
1000	(-)	1519.2	1273.3	1198.5	1147.8	1063.2	1070.2	1040.4	1081.1	1023.3
		±159.5	±98.2	±61.7	±62.4	±69.5	±81.9	±55.0	±67.0	±62.9
		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)

Mean±SD (N)

Appendix 1-1 Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)									
			1	4	7	11	14	18	21	25	28	35
0 mg/kg	(+)	M01001	115.1	116.3	129.4	141.8	150.9	152.6	147.5	148.8	151.7	166.2
		M01002	114.8	115.0	123.9	136.6	146.5	144.8	141.0	133.3	131.9	140.2
		M01003	121.4	123.7	135.1	144.4	154.5	155.6	150.9	149.6	145.8	153.9
		M01004	118.6	122.6	131.8	144.5	156.1	156.8	149.5	153.6	154.7	171.0
		M01005	111.2	113.2	120.6	130.7	145.3	150.6	143.1	143.9	141.6	150.8
		M01006	113.9	114.8	124.2	136.9	143.9	149.9	146.1	151.9	149.1	162.7
		M01007	125.8	127.7	137.4	150.1	160.2	164.7	160.7	162.1	158.5	174.2
		M01008	111.6	110.2	118.8	128.8	137.0	136.1	132.3	134.7	132.9	140.1
		M01009	121.0	122.0	130.5	143.2	151.9	155.6	149.5	151.9	146.9	164.3
		M01010	117.5	117.7	126.6	140.0	149.5	145.3	147.5	145.9	146.1	164.5
		M01011	118.3	119.1	122.6	132.5	139.3	139.0	133.7	132.4	130.1	136.3
		M01012	117.8	123.3	130.9	141.7	151.5	152.5	147.8	145.3	143.9	156.0
		M01013	120.3	121.1	115.6	139.2	147.8	152.4	153.4	159.7	159.0	174.8
		M01014	121.7	118.7	127.4	137.3	148.2	147.1	142.3	139.3	143.4	148.6
		M01015	118.5	123.6	134.6	146.7	159.2	153.8	149.0	149.6	146.6	159.6
		M01016	114.7	117.5	125.9	136.5	149.0	152.5	150.6	153.0	150.7	166.2
		M01017	117.0	115.1	125.5	136.6	147.7	152.3	150.2	148.6	149.0	150.8
		M01018	110.3	111.5	121.4	134.9	141.8	145.9	143.4	142.7	143.8	157.7
		M01019	116.9	116.2	127.9	140.8	150.5	154.4	154.8	154.3	152.8	170.8
		M01020	111.3	112.0	121.6	132.2	143.5	142.9	136.4	139.8	135.0	144.7
N		20	20	20	20	20	20	20	20	20	20	
Mean		112.3	118.1	126.6	138.8	148.7	150.2	146.5	147.0	145.7	157.7	
SD		±21.5	±4.8	±5.7	±5.5	±6.1	±6.6	±7.0	±8.2	±8.3	±11.7	

Appendix 1-1 (continued) Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)									
			1	8	15	22	29	36	43	50	64	
0 mg/kg	(+)	M01001	170.5	203.3	219.6	231.0	243.4	250.3	253.2	259.3	270.4	
		M01002	138.9	172.8	201.6	214.9	228.1	238.5	246.9	256.2	271.6	
		M01003	158.2	187.9	211.8	225.9	236.9	252.1	257.7	267.7	282.2	
		M01004	175.1	205.1	224.9	237.2	250.9	256.3	260.7	267.0	282.3	
		M01005	154.7	185.9	209.6	223.8	233.0	243.9	252.2	255.9	269.7	
		M01006	167.8	195.5	220.9	237.2	250.8	262.6	269.8	280.8	292.3	
		M01007	179.0	205.4	225.2	238.0	245.4	255.6	262.4	267.6	274.6	
		M01008	141.0	173.2	197.4	211.7	223.2	233.2	241.6	249.7	264.1	
		M01009	166.8	197.5	217.0	228.3	238.5	250.1	259.5	265.2	278.6	
		M01010	170.3	198.4	216.4	231.1	241.6	249.4	256.1	263.9	273.0	
		M01011	143.5	170.1	194.2	208.9	218.5	229.4	235.6	245.5	256.0	
		M01012	157.3	187.6	207.9	225.2	236.0	249.4	254.1	264.9	277.1	
		M01013	180.3	206.0	223.6	235.2	246.5	256.3	261.5	268.8	281.8	
		M01014	149.7	183.1	205.3	217.4	226.4	238.9	245.7	256.6	268.3	
		M01015	161.8	195.7	219.6	233.0	248.0	259.5	270.3	277.6	292.5	
		M01016	170.5	200.1	220.0	235.7	247.0	258.7	266.1	273.3	286.4	
		M01017	155.4	188.6	212.0	227.9	239.7	251.3	260.0	265.7	273.7	
		M01018	161.1	191.2	211.7	225.3	233.6	241.3	244.8	253.2	263.6	
		M01019	177.3	205.8	230.0	241.1	252.7	262.2	268.5	277.4	289.4	
		M01020	145.5	174.5	197.4	214.8	224.4	233.9	236.0	238.7	243.8	
N		20	20	20	20	20	20	20	20	20		
Mean		161.2	191.4	213.3	227.2	238.2	248.6	255.1	262.8	274.6		
SD		±12.9	±11.9	±10.2	±9.5	±10.2	±10.	±10.6	±10.9	±12.1		

Appendix 1-2 Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)									
			1	4	7	11	14	18	21	25	28	35
60 mg/kg	(+)	M02021	119.4	118.5	127.5	138.1	147.2	147.2	139.9	142.7	138.7	158.7
		M02022	118.5	122.6	130.1	142.8	128.8	154.6	155.8	161.0	161.1	183.4
		M02023	118.6	117.6	101.2	131.3	142.1	142.7	137.8	137.1	134.6	139.9
		M02024	109.7	112.7	121.1	120.1	142.6	148.2	146.6	145.8	143.0	151.5
		M02025	109.8	112.3	121.2	131.5	141.1	132.8	140.5	144.8	143.5	165.4
		M02026	121.9	125.0	130.5	142.0	149.5	149.5	147.3	143.8	140.8	146.4
		M02027	123.5	123.0	133.6	145.4	151.6	153.1	149.5	146.1	144.7	159.8
		M02028	122.6	124.6	136.7	147.9	158.6	159.8	157.9	160.4	161.3	179.1
		M02029	124.9	126.3	133.2	141.9	152.1	153.0	146.8	142.8	142.3	145.4
		M02030	120.7	122.1	132.5	142.9	151.1	154.2	151.2	153.2	149.0	162.8
		M02031	117.0	119.8	128.5	139.9	149.4	152.0	146.5	159.4	157.6	174.7
		M02032	117.4	115.4	122.7	133.8	146.3	148.7	142.7	141.7	139.9	150.3
		M02033	115.5	115.5	124.8	137.4	149.0	150.6	146.5	153.3	151.1	163.5
		M02034	117.3	121.5	131.4	140.2	149.2	152.0	149.5	150.7	148.6	164.8
		M02035	109.6	106.2	114.2	127.1	134.4	134.6	131.1	130.5	134.1	138.7
		M02036	121.8	124.5	134.5	145.1	154.9	157.9	152.8	154.8	153.3	162.8
		M02037	117.0	118.1	129.4	138.7	148.2	155.8	150.1	151.2	153.8	170.3
		M02038	121.6	123.0	132.1	142.0	150.5	152.2	145.9	141.0	139.7	148.4
		M02039	121.1	122.3	134.3	147.0	155.7	157.5	150.2	151.2	148.2	163.7
		M02040	125.0	125.5	138.8	152.1	159.3	162.8	158.4	158.8	154.5	170.4
N		20	20	20	20	20	20	20	20	20		
Mean		118.6	119.8	127.9	139.4	148.1	151.0	147.4	148.5	147.0	160.0	
SD		±4.7	±5.3	±8.7	±7.6	±7.5	±7.5	±6.7	±8.3	±8.2	±12.6	

Appendix 1-2 (continued) Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)								
			1	8	15	22	29	36	43	50	64
60 mg/kg	(+)	M02021	166.3	195.7	211.7	221.3	231.3	238.4	243.0	248.9	264.5
		M02022	185.3	207.2	222.7	230.9	242.8	249.4	256.4	264.4	275.0
		M02023	145.4	179.8	207.9	219.4	231.1	241.9	246.3	257.6	271.9
		M02024	154.4	181.2	206.0	218.8	228.3	240.0	243.3	250.3	261.2
		M02025	170.9	193.5	212.1	219.5	230.0	237.9	244.6	248.7	257.2
		M02026	151.4	175.5	201.2	217.4	232.0	241.4	248.1	253.1	265.6
		M02027	164.4	195.4	217.0	230.3	243.9	253.3	262.6	269.4	281.1
		M02028	184.2	209.8	227.0	238.2	251.4	258.6	263.2	270.4	280.3
		M02029	149.5	178.8	199.3	211.9	222.1	232.9	239.5	248.1	254.7
		M02030	165.8	194.8	217.2	227.2	237.7	247.9	254.3	259.7	268.5
		M02031	180.4	203.2	221.4	231.9	242.7	252.4	258.6	266.0	272.4
		M02032	154.2	179.4	202.0	219.7	230.1	240.8	248.0	255.4	269.4
		M02033	169.4	194.8	215.3	229.9	243.5	254.4	265.4	271.0	285.8
		M02034	164.0	190.5	208.6	218.2	230.0	240.2	245.8	256.6	265.3
		M02035	140.5	167.8	185.8	205.7	219.4	228.1	239.2	243.7	252.8
		M02036	164.5	201.6	221.7	236.4	248.9	261.4	267.5	271.8	280.2
		M02037	175.5	202.3	217.4	231.5	242.7	251.6	258.8	264.6	275.9
		M02038	154.5	186.2	208.1	224.5	235.2	245.8	249.1	253.6	264.5
		M02039	165.8	202.1	220.6	238.3	247.9	258.0	268.7	272.8	284.2
		M02040	176.3	206.5	230.0	241.9	256.4	265.2	274.2	284.5	290.8
N		20	20	20	20	20	20	20	20	20	
Mean		164.1	192.3	212.7	225.6	237.4	247.0	253.8	260.5	271.1	
SD		±12.7	±12.	±10.6	±9.5	±9.9	±9.9	±10.6	±10.7	±10.6	

Appendix 1-3 Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)									
			1	4	7	11	14	18	21	25	28	35
250 mg/kg	(+)	M03041	112.4	114.0	120.9	130.9	139.1	142.7	138.7	133.0	133.6	141.2
		M03042	125.0	124.4	132.0	141.0	149.6	153.9	150.1	148.7	150.7	162.2
		M03043	118.7	125.3	134.7	146.2	154.4	157.5	152.9	155.4	154.6	169.5
		M03044	114.1	115.5	120.7	132.0	139.8	144.3	136.9	133.1	131.2	134.5
		M03045	119.6	118.1	126.4	134.1	146.1	148.0	144.5	147.5	149.8	159.5
		M03046	122.2	120.5	128.2	140.5	151.9	157.6	155.4	159.0	159.5	179.3
		M03047	110.2	107.6	117.0	128.3	139.6	139.9	134.6	134.0	127.7	137.9
		M03048	118.7	118.3	128.4	140.1	149.9	153.9	147.1	149.2	149.2	159.1
		M03049	119.0	124.0	134.3	147.7	147.8	159.2	155.5	156.2	155.2	169.2
		M03050	121.9	122.2	134.0	145.2	155.4	152.6	145.5	145.4	143.9	150.1
		M03051	118.6	120.1	128.9	141.8	150.2	154.4	153.2	149.9	151.0	162.7
		M03052	121.6	125.1	133.3	147.4	157.5	161.5	160.4	162.7	161.9	179.5
		M03053	110.7	110.2	117.9	130.8	139.4	140.9	135.0	134.7	133.7	133.6
		M03054	114.6	119.8	131.8	143.1	153.8	155.5	149.7	147.5	150.0	162.7
		M03055	120.1	118.3	124.0	136.7	146.7	147.2	146.1	148.8	150.8	165.1
		M03056	111.7	113.3	121.0	132.6	142.2	146.7	141.4	142.2	140.9	149.5
		M03057	114.7	117.2	127.2	140.4	151.3	139.2	142.3	140.4	140.9	152.6
		M03058	124.4	126.7	137.1	151.7	162.4	165.0	158.5	161.5	160.2	172.9
		M03059	113.3	113.5	123.9	135.3	145.0	148.3	143.2	142.1	140.3	149.2
		M03060	118.2	119.6	125.9	137.4	149.5	152.3	149.8	148.6	147.8	158.7
N		20	20	20	20	20	20	20	20	20	20	
Mean		117.5	118.7	127.4	139.2	148.6	151.0	147.0	147.0	146.6	157.5	
SD		±4.5	±5.2	±5.9	±6.5	±6.5	±7.4	±7.6	±9.1	±9.9	±13.7	

Appendix 1-3 (continued) Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)								
			1	8	15	22	29	36	43	50	64
250 mg/kg	(+)	M03041	141.3	178.0	201.8	216.8	226.5	234.4	235.2	242.5	249.0
		M03042	169.9	196.2	218.7	227.1	238.9	249.7	253.5	262.7	278.2
		M03043	176.4	204.1	224.6	240.5	252.8	263.9	267.5	272.6	289.3
		M03044	137.6	166.7	188.6	202.7	215.6	223.1	226.6	233.2	243.5
		M03045	165.4	190.7	210.9	224.5	232.6	241.2	243.9	252.3	264.3
		M03046	181.7	203.3	221.4	234.8	242.6	250.6	257.7	263.3	274.7
		M03047	143.7	171.8	192.6	205.4	214.4	223.7	227.8	234.8	244.6
		M03048	163.3	192.3	215.9	225.4	235.7	250.1	250.9	258.5	267.9
		M03049	171.2	204.0	226.5	237.2	247.4	257.7	262.2	270.1	283.0
		M03050	150.6	181.4	209.4	222.7	239.2	252.8	260.6	265.9	279.1
		M03051	166.8	193.8	212.9	225.5	238.0	244.6	249.7	257.7	270.7
		M03052	182.3	208.3	223.1	236.3	249.3	255.7	262.1	269.5	280.4
		M03053	134.8	167.9	187.5	201.0	216.3	225.4	234.5	240.8	256.2
		M03054	168.1	195.4	214.5	221.4	233.1	242.8	247.9	254.0	264.0
		M03055	163.8	196.1	219.7	235.2	247.1	255.1	261.4	267.9	281.2
		M03056	152.8	183.6	203.8	217.9	229.0	241.5	245.7	254.4	267.0
		M03057	158.2	188.0	208.3	223.2	231.8	244.3	251.1	255.7	245.3
		M03058	172.7	201.9	226.7	239.3	250.1	259.9	266.5	273.9	285.8
		M03059	153.7	185.5	202.1	215.1	227.7	242.9	255.0	264.1	278.5
		M03060	160.1	189.4	215.9	230.6	241.7	251.6	256.3	260.1	277.2
	N	20	20	20	20	20	20	20	20	20	
	Mean	160.7	189.9	211.2	224.1	235.5	245.6	250.8	257.7	269.0	
	SD	±14.	±12.2	±12.	±11.8	±11.5	±11.7	±12.1	±12.	±14.5	

Appendix 1-4 Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)									
			1	4	7	11	14	18	21	25	28	35
1000 mg/kg	(+)	M04061	123.4	123.8	132.3	143.6	153.3	159.1	156.5	161.9	164.9	180.8
		M04062	113.5	111.5	121.7	132.7	140.1	146.8	141.7	139.6	139.6	141.5
		M04063	115.3	113.4	119.1	132.3	140.7	149.0	146.0	149.2	148.2	160.8
		M04064	119.7	123.8	133.1	142.5	156.1	159.7	158.9	158.9	156.8	167.8
		M04065	115.4	113.1	121.4	132.7	143.8	146.4	140.7	136.8	137.2	145.5
		M04066	112.3	112.4	118.8	129.1	140.6	144.4	137.3	139.6	139.1	152.7
		M04067	124.0	125.5	132.5	141.9	154.8	158.0	156.9	157.1	158.5	177.7
		M04068	109.2	108.2	117.2	126.8	134.8	138.2	132.8	135.6	130.6	137.7
		M04069	115.6	116.7	127.4	140.4	150.1	154.3	150.7	152.2	152.4	160.9
		M04070	123.9	122.3	129.9	143.5	155.0	155.7	152.1	153.6	152.7	169.4
		M04071	108.9	110.9	118.9	126.7	138.5	142.0	137.8	140.5	145.2	146.1
		M04072	112.8	113.1	123.3	132.6	142.2	144.9	144.2	148.4	150.6	161.4
		M04073	124.7	128.3	138.3	152.1	160.0	164.2	163.8	165.3	164.6	195.7
		M04074	113.6	117.4	125.3	136.6	148.0	147.0	140.2	139.4	137.1	142.4
		M04075	113.5	113.8	121.5	132.4	143.7	148.2	144.5	145.0	145.7	157.6
		M04076	114.0	115.2	123.2	136.4	146.1	149.2	148.8	152.2	147.6	165.8
		M04077	120.5	116.5	125.1	134.6	144.1	145.1	137.8	141.4	138.1	151.3
		M04078	125.6	124.6	134.7	149.8	156.0	161.5	158.1	154.2	155.0	159.0
		M04079	112.4	117.1	128.3	140.6	149.4	152.8	154.5	156.0	152.1	166.6
		M04080	111.3	113.3	120.0	132.0	140.4	142.5	138.8	140.7	138.2	148.0
	N	20	20	20	20	20	20	20	20	20		
	Mean	116.5	117.0	125.6	137.0	146.9	150.5	147.1	148.4	147.7	159.4	
	SD	±5.4	±5.7	±6.1	±7.1	±7.1	±7.3	±8.9	±8.9	±9.6	±14.6	

Appendix 1-4 (continued) Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)								
			1	8	15	22	29	36	43	50	64
1000 mg/kg	(+)	M04061	184.1	203.6	220.3	235.1	244.6	252.2	257.8	265.7	279.4
		M04062	147.4	168.4	193.3	211.3	222.2	236.8	240.3	246.7	257.4
		M04063	166.1	183.7	206.7	225.3	238.3	253.6	258.2	262.6	267.3
		M04064	172.3	195.8	219.1	222.4	233.0	242.3	252.2	259.4	268.2
		M04065	148.9	164.4	188.0	206.5	221.8	237.2	243.4	252.4	265.7
		M04066	155.5	182.8	205.2	218.0	233.2	241.5	246.8	255.3	270.0
		M04067	180.4	204.4	218.4	233.7	245.6	255.9	260.3	268.4	280.7
		M04068	140.9	156.5	179.1	193.3	210.9	227.3	236.3	248.9	261.9
		M04069	160.9	185.4	209.0	221.3	231.9	242.0	247.5	252.4	264.0
		M04070	174.5	200.7	222.4	241.5	252.2	262.0	269.5	276.9	287.3
		M04071	155.1	178.4	199.1	216.5	226.3	236.5	243.2	249.8	265.4
		M04072	161.9	187.0	208.7	222.8	232.4	239.0	245.2	250.0	260.0
		M04073	197.4	213.4	226.4	236.7	244.8	250.4	252.7	256.1	267.6
		M04074	146.0	165.0	184.6	203.5	218.7	229.5	236.6	246.9	262.7
		M04075	163.5	183.9	206.6	224.2	235.5	244.8	251.6	260.6	272.2
		M04076	171.5	193.7	211.7	220.9	229.1	235.1	239.6	246.6	257.9
		M04077	156.0	181.6	201.6	216.8	224.3	234.7	240.9	247.7	254.8
		M04078	159.9	180.6	203.7	222.7	240.6	251.6	259.4	261.0	276.5
		M04079	171.0	197.4	215.9	229.9	242.6	251.3	255.6	260.3	269.7
		M04080	150.7	173.5	195.4	213.5	220.4	229.7	235.7	242.0	254.4
N		20	20	20	20	20	20	20	20	20	
Mean		163.2	185.0	205.8	220.8	232.4	242.7	248.6	255.5	267.2	
SD		±14.2	±15.	±13.	±11.7	±10.8	±9.7	±9.5	±8.8	±8.8	

Appendix 1-5 Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)									
			1	4	7	11	14	18	21	25	28	35
1000 mg/kg	(-)	M05081	114.8	129.1	147.1	165.0	181.4	195.0	204.0	214.3	220.7	235.7
		M05082	112.1	118.0	130.1	147.5	159.6	174.2	184.1	195.8	190.5	215.7
		M05083	118.6	130.4	145.2	162.4	174.7	191.6	200.4	214.1	219.8	232.7
		M05084	117.8	129.0	143.6	162.3	174.4	187.7	199.3	209.1	215.6	231.1
		M05085	112.9	125.6	138.0	154.5	165.4	178.0	185.9	196.0	202.0	219.4
		M05086	112.2	124.8	143.0	162.9	179.0	196.5	207.2	217.2	223.8	238.5
		M05087	109.3	120.8	134.1	149.7	163.6	176.7	185.2	194.2	202.9	219.7
		M05088	115.4	122.8	137.8	154.5	168.9	187.1	195.6	210.2	216.7	229.3
		M05089	114.4	127.2	142.2	160.7	175.4	190.5	197.0	209.3	217.0	236.3
		M05090	117.5	129.1	143.7	160.6	176.7	192.0	201.1	213.4	223.5	243.1
		M05091	120.6	133.4	150.9	169.5	183.9	198.7	205.1	213.2	221.6	227.0
		M05092	116.8	127.1	144.4	161.3	175.8	187.9	199.0	209.4	215.0	226.1
		M05093	120.2	128.4	144.0	158.0	170.7	186.7	192.6	204.1	209.2	226.5
		M05094	110.1	123.8	141.0	160.3	175.3	193.3	203.7	216.8	222.4	241.0
		M05095	125.6	132.4	146.8	165.2	180.0	199.4	209.4	222.8	231.4	249.3
		M05096	116.0	129.9	146.0	166.3	181.4	197.8	206.5	220.1	211.3	245.2
		M05097	122.6	134.1	152.1	171.2	185.1	199.8	210.6	220.4	227.8	242.2
		M05098	122.8	132.4	148.4	170.1	182.0	197.9	206.7	219.2	227.2	241.8
		M05099	109.4	118.2	132.3	148.9	161.7	174.2	185.3	196.1	202.5	219.2
		M05100	122.5	132.9	146.9	164.4	179.1	193.2	203.2	214.5	218.0	241.3
N		20	20	20	20	20	20	20	20	20	20	
Mean		116.6	127.5 **	142.9 **	160.8 **	174.7 **	189.9 **	199.1 **	210.5 **	215.9 **	233.1 **	
SD		±4.8	±4.8	±5.9	±6.8	±7.5	±8.4	±8.5	±8.9	±10.3	±9.9	

** , significant difference from the negative control, p<0.01

Appendix 1-5 (continued) Body weight (g) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)									
			1	8	15	22	29	36	43	50	64	
1000 mg/kg	(-)	M05081	237.3	251.2	265.9	280.8	287.0	294.4	297.1	309.6	320.8	
		M05082	216.2	230.8	243.8	253.9	264.4	277.8	286.3	295.1	302.7	
		M05083	235.9	251.0	270.9	285.9	300.0	308.0	317.3	325.8	336.0	
		M05084	234.4	248.7	267.9	280.6	288.3	299.6	306.8	316.7	330.2	
		M05085	220.4	236.8	252.2	267.4	273.8	287.1	293.0	302.0	316.1	
		M05086	241.6	257.8	279.0	292.3	307.5	312.8	319.7	332.6	343.0	
		M05087	220.2	232.9	250.5	263.5	272.6	280.7	284.2	293.5	309.4	
		M05088	233.4	249.4	261.2	272.4	282.6	287.6	294.8	302.8	315.6	
		M05089	237.0	253.2	271.1	283.6	291.5	305.0	312.2	320.3	336.3	
		M05090	244.3	261.0	278.0	290.9	302.0	309.0	316.5	322.4	338.0	
		M05091	232.5	242.3	256.7	270.7	279.6	290.4	296.2	306.3	315.7	
		M05092	226.9	239.3	257.3	265.8	275.5	283.3	292.5	300.1	310.7	
		M05093	227.0	240.8	254.5	263.1	272.1	284.5	293.7	299.6	316.8	
		M05094	245.0	256.0	270.2	283.9	290.8	297.9	305.2	312.4	321.8	
		M05095	249.9	269.5	286.9	298.2	309.9	318.9	326.2	335.9	345.0	
		M05096	246.4	264.6	278.8	289.5	300.3	309.5	317.0	324.5	337.6	
		M05097	242.8	258.9	276.0	290.6	300.2	306.9	315.7	319.9	330.6	
		M05098	243.7	262.9	281.9	292.6	304.2	313.2	319.0	325.1	338.7	
		M05099	218.8	234.6	249.6	263.0	273.8	283.6	290.6	302.6	313.9	
		M05100	241.5	256.7	272.4	284.7	295.5	302.4	310.9	320.7	334.8	
N		20	20	20	20	20	20	20	20	20		
Mean		234.8 **	249.9 **	266.2 **	278.7 **	288.6 **	297.6 **	304.7 **	313.4 **	325.7 **		
SD		±10.1	±11.3	±12.3	±12.7	±13.6	±12.6	±12.9	±12.7	±12.7		

** , significant difference from the negative control, p<0.01

Appendix 2-1 Water intake (mL/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)									
			1	4	7	11	14	18	21	25	28	
0 mg/kg	(+)	M01001	12.7	14.5	14.3	19.6	17.7	4.1	16.6	21.7	22.5	
		M01002	19.8	18.3	15.6	15.4	20.2	21.7	23.6	23.5	26.9	
		M01003	12.6	14.8	13.1	16.5	20.6	12.1	23.6	23.4	31.4	
		M01004	10.4	12.7	16.0	19.0	16.6	13.6	17.1	20.5	20.8	
		M01005	11.9	15.6	16.8	18.1	17.9	11.9	14.1	16.3	14.4	
		M01006	7.7	11.7	12.1	15.6	15.5	9.9	16.5	17.1	15.1	
		M01007	36.3	16.5	16.1	21.5	16.7	15.8	19.1	21.2	25.2	
		M01008	7.6	15.9	12.5	15.5	14.9	12.5	15.3	4.2	18.1	
		M01009	13.0	15.6	16.7	15.9	16.6	19.6	16.9	22.6	18.1	
		M01010	9.5	11.6	13.1	14.2	16.0	13.5	12.4	16.0	21.2	
		M01011	14.4	12.2	14.0	19.8	18.6	14.8	20.0	22.9	20.7	
		M01012	16.5	16.4	17.8	19.1	19.0	13.6	21.6	18.1	19.2	
		M01013	12.8	13.3	12.7	16.3	16.0	14.4	13.1	16.0	17.6	
		M01014	12.3	15.9	15.0	20.3	21.2	14.9	17.4	21.7	11.3	
		M01015	18.5	20.1	8.4	22.7	21.6	28.2	34.3	22.6	27.5	
		M01016	11.5	12.6	11.3	15.6	15.2	11.8	19.2	21.0	23.0	
		M01017	15.9	15.2	16.6	19.5	24.3	19.7	21.0	17.6	19.7	
		M01018	17.6	16.5	16.1	16.7	19.6	11.6	19.5	25.2	19.9	
		M01019	1.5	14.5	15.6	13.6	18.1	13.0	16.0	22.2	17.8	
		M01020	10.3	17.3	20.1	18.7	20.7	14.5	19.6	18.9	21.2	
N		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)		
Mean		13.6	15.1	14.7	17.7	18.4	14.6	18.8	19.6	20.6		
SD		6.8	2.2	2.6	2.5	2.5	4.9	4.8	4.6	4.7		

Appendix 2-2 Water intake (mL/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)								
			1	4	7	11	14	18	21	25	28
60 mg/kg	(+)	M02021	12.8	14.8	14.9	18.3	17.2	11.9	15.1	20.2	19.4
		M02022	11.3	9.8	13.3	17.2	34.3	13.1	17.0	20.0	27.4
		M02023	19.8	14.1	24.1	14.3	16.1	14.4	14.1	15.6	16.7
		M02024	11.5	14.2	16.2	25.2	18.1	13.1	18.4	21.3	23.0
		M02025	15.3	12.0	14.7	16.7	18.1	18.0	13.3	16.8	17.2
		M02026	18.8	12.6	15.2	17.3	19.0	20.0	21.4	23.6	25.2
		M02027	15.8	49.1	16.0	16.0	17.1	12.6	16.1	17.6	19.5
		M02028	15.2	18.7	19.0	22.3	22.0	24.0	25.7	27.4	27.8
		M02029	15.4	15.2	16.4	18.5	20.0	22.6	29.3	25.2	24.4
		M02030	10.9	15.2	14.7	15.6	17.4	16.9	16.7	17.6	22.3
		M02031	12.1	11.9	9.9	13.1	17.0	10.6	16.6	14.6	21.6
		M02032	14.0	14.1	13.6	19.9	16.4	14.1	17.3	18.4	22.7
		M02033	6.0	14.6	16.6	17.7	17.6	15.8	16.4	20.0	16.2
		M02034	14.8	16.1	16.3	19.4	19.7	34.6	23.5	22.0	33.2
		M02035	20.6	14.3	17.5	19.2	17.7	16.6	20.7	21.5	15.5
		M02036	18.5	18.2	17.7	17.2	15.3	15.7	21.1	21.0	20.8
		M02037	16.3	18.3	15.7	17.3	19.3	14.6	7.2	18.0	20.7
		M02038	23.1	16.5	16.5	17.8	19.1	12.1	19.7	5.9	19.8
		M02039	15.9	14.6	14.8	18.1	17.3	13.4	20.4	19.6	24.9
		M02040	25.8	15.3	19.8	17.4	20.5	22.2	19.5	22.8	21.2
N		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)		
Mean		15.7	16.5	16.1	17.9	19.0	16.8	18.5	19.5	22.0	
SD		4.6	8.0	2.8	2.6	4.0	5.6	4.7	4.5	4.4	

Appendix 2-3 Water intake (mL/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)								
			1	4	7	11	14	18	21	25	28
250 mg/kg	(+)	M03041	20.2	15.3	13.6	20.5	21.8	12.1	16.9	24.8	22.9
		M03042	18.8	14.7	15.7	19.1	18.7	17.3	23.3	26.0	21.3
		M03043	12.7	14.9	16.4	18.1	22.4	14.5	15.7	16.4	20.1
		M03044	19.1	4.5	17.5	18.3	19.7	32.9	27.7	21.0	20.3
		M03045	10.5	13.5	12.6	19.1	17.8	11.6	17.4	16.9	15.4
		M03046	13.4	14.2	16.5	17.8	20.4	18.2	20.2	22.8	23.0
		M03047	12.3	16.9	16.3	21.5	20.5	22.9	17.7	17.5	16.4
		M03048	13.9	14.1	14.1	17.0	18.3	11.6	18.0	21.4	22.4
		M03049	14.5	15.3	13.8	9.6	24.9	24.8	32.7	38.4	24.6
		M03050	17.4	12.5	12.6	19.2	16.4	13.1	18.5	17.0	20.0
		M03051	14.2	4.3	16.1	19.8	20.6	13.9	24.2	24.3	25.4
		M03052	10.8	16.4	16.2	20.1	23.0	15.3	17.4	20.3	19.8
		M03053	10.6	13.0	11.7	17.2	13.3	9.5	15.6	17.9	12.9
		M03054	16.9	15.2	15.8	18.5	17.6	15.3	19.2	18.3	22.8
		M03055	21.2	14.9	14.2	20.6	21.2	16.0	19.9	18.2	18.5
		M03056	9.5	13.2	13.2	17.9	19.7	11.2	16.7	17.1	19.2
		M03057	10.9	15.1	12.9	15.8	19.4	15.1	16.2	8.8	14.7
		M03058	10.6	15.9	22.1	20.6	22.2	13.8	19.5	24.0	22.6
		M03059	13.1	16.1	14.6	15.0	19.7	15.6	23.2	30.0	22.9
		M03060	17.8	16.0	15.1	20.8	19.7	20.9	26.1	22.6	17.1
N		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)		
Mean		14.4	13.8	15.1	18.3	19.9	16.3	20.3	21.2	20.1	
SD		3.6	3.4	2.3	2.7	2.5	5.5	4.6	6.1	3.4	

Appendix 2-4 Water intake (mL/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)								
			1	4	7	11	14	18	21	25	28
1000 mg/kg	(+)	M04061	16.0	16.0	13.4	19.2	18.1	18.0	19.6	24.2	23.4
		M04062	2.9	13.6	9.8	17.6	18.6	13.3	19.4	21.5	19.0
		M04063	6.8	9.4	12.5	16.5	19.4	13.7	17.9	17.5	21.6
		M04064	13.6	12.9	17.2	39.0	23.7	24.9	22.8	25.7	25.2
		M04065	11.3	13.5	14.2	17.5	16.8	12.4	20.2	17.0	18.4
		M04066	9.4	9.9	10.8	16.4	17.1	10.1	14.6	19.8	20.6
		M04067	22.6	16.3	16.0	19.7	18.4	24.6	21.4	23.9	25.3
		M04068	8.6	13.1	15.0	15.7	19.2	14.7	16.8	14.9	20.7
		M04069	20.2	17.5	17.9	19.6	21.9	21.5	26.9	29.7	24.3
		M04070	14.0	16.4	17.3	13.8	16.9	12.8	14.1	19.1	21.8
		M04071	8.9	9.1	9.6	14.9	15.0	13.9	18.8	18.5	17.2
		M04072	8.9	12.9	13.1	16.2	16.5	10.4	17.7	18.7	20.9
		M04073	10.6	14.5	15.0	14.2	21.3	12.8	18.0	21.5	25.0
		M04074	7.5	13.4	15.6	17.4	17.7	12.8	16.5	14.5	15.7
		M04075	9.6	11.0	10.1	15.9	18.7	17.7	17.3	17.9	18.7
		M04076	10.0	10.8	14.7	17.0	15.7	16.5	18.9	28.2	30.1
		M04077	19.6	13.7	13.2	15.9	20.5	11.4	15.1	16.5	17.2
		M04078	9.3	14.4	15.1	18.0	18.3	14.9	28.8	20.8	14.6
		M04079	17.4	17.7	19.8	21.8	21.7	18.0	21.0	19.1	18.3
		M04080	12.8	11.9	13.3	18.8	16.8	19.7	18.8	16.2	19.3
N		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	
Mean		12.0	13.4	14.2	18.3	18.6	15.7	19.2	20.3	20.9	
SD		5.0	2.6	2.8	5.3	2.3	4.3	3.7	4.2	3.8	

Appendix 2-5 Water intake (mL/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Initiation period (days)								
			1	4	7	11	14	18	21	25	28
1000 mg/kg	(-)	M05081	18.1	20.3	18.6	21.2	20.5	21.8	22.3	24.1	26.7
		M05082	19.4	16.3	16.3	18.4	21.2	20.5	20.4	20.7	30.3
		M05083	17.4	16.8	16.4	15.1	20.0	20.9	22.3	23.6	23.8
		M05084	20.4	19.7	20.3	20.0	20.4	23.9	22.9	27.1	25.0
		M05085	1.3	16.5	16.9	19.7	20.2	22.0	21.4	19.0	22.6
		M05086	20.1	18.7	19.3	20.2	21.2	24.8	25.2	25.5	25.8
		M05087	19.0	16.6	16.4	19.6	18.9	20.3	17.9	19.6	22.0
		M05088	17.3	16.8	17.3	18.9	17.6	22.4	22.2	23.7	25.0
		M05089	18.0	17.1	18.4	21.5	23.8	20.6	23.3	22.8	22.6
		M05090	10.9	5.5	15.7	22.6	20.5	22.3	22.4	26.4	24.2
		M05091	19.1	19.4	20.1	21.8	21.1	21.4	22.1	24.9	25.3
		M05092	19.7	19.8	19.6	20.2	19.7	21.8	20.8	21.0	23.2
		M05093	18.7	18.1	19.4	22.1	20.8	22.6	23.2	20.9	24.6
		M05094	15.5	16.4	19.0	21.9	18.2	23.7	25.1	23.8	27.7
		M05095	16.2	18.9	20.0	22.2	23.7	21.0	23.6	20.1	27.4
		M05096	21.1	17.8	20.0	22.0	23.7	24.1	22.7	24.5	35.3
		M05097	18.7	16.7	20.4	16.4	20.4	21.5	19.6	21.3	20.4
		M05098	18.6	18.8	19.8	19.6	20.7	23.1	22.4	22.4	24.5
		M05099	53.5	15.7	22.3	18.7	20.5	20.0	19.0	23.2	23.1
		M05100	20.3	17.7	10.3	20.5	21.3	22.5	22.5	20.0	28.6
N		(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	
Mean		19.2 **	17.2 **	18.3 **	20.1 **	20.7 **	22.1 **	22.1 **	22.7	25.4 **	
SD		9.2	3.1	2.6	2.0	1.6	1.4	1.8	2.3	3.3	

** , significant difference from the negative control, p<0.01

Appendix 3-1 Food intake (g/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)									
			1	8	15	22	29	36	43	50	57	64
0 mg/kg	(+)	M01001	17.1	13.7	13.3	14.1	11.3	12.5	11.7	12.2	12.9	11.7
		M01002	13.4	11.1	12.5	13.3	12.0	13.7	11.5	13.8	13.6	13.5
		M01003	13.3	13.6	14.0	12.9	11.7	11.6	11.1	11.4	13.5	11.6
		M01004	18.4	15.1	14.2	14.6	11.2	12.7	12.3	12.7	12.4	12.9
		M01005	15.7	14.0	13.6	12.3	12.9	13.3	11.5	12.9	13.6	12.0
		M01006	16.5	16.4	13.0	15.2	14.2	14.3	14.2	13.1	14.5	12.1
		M01007	15.0	13.4	13.6	12.8	12.1	13.1	11.4	12.1	11.0	24.1
		M01008	13.2	13.2	11.7	10.8	12.0	13.2	11.7	13.2	12.6	12.1
		M01009	19.5	14.8	14.0	12.7	11.3	11.4	12.0	11.8	12.4	12.0
		M01010	16.0	14.1	14.3	13.0	11.2	12.2	12.3	12.8	12.1	10.8
		M01011	13.1	13.1	11.8	12.4	10.5	13.4	12.8	10.6	11.5	12.1
		M01012	14.5	14.1	14.4	13.5	11.8	12.1	13.3	12.6	13.4	12.6
		M01013	18.2	14.8	14.3	12.8	10.2	12.1	12.4	11.3	13.3	12.8
		M01014	12.9	12.5	13.2	13.3	11.4	11.7	11.4	11.7	11.1	11.2
		M01015	14.5	14.3	14.5	14.6	12.5	16.0	13.7	12.6	14.4	12.6
		M01016	16.1	16.0	14.2	12.6	12.2	12.6	11.3	10.8	13.0	12.3
		M01017	14.9	13.4	15.7	13.4	10.5	12.0	10.9	11.5	12.4	13.3
		M01018	16.4	13.2	14.1	10.9	11.1	11.1	12.6	11.6	11.8	11.5
		M01019	16.4	15.1	13.9	13.5	12.6	13.7	13.3	12.0	13.1	13.8
		M01020	12.1	11.7	12.9	12.2	11.6	11.9	10.9	11.2	10.9	11.5
N		20	20	20	20	20	20	20	20	20	20	
Mean		15.4	13.9	13.7	13.0	11.7	12.7	12.1	12.1	12.7	12.8	
SD		2.0	1.3	1.0	1.1	0.9	1.2	1.0	0.9	1.1	2.8	

Appendix 3-2 Food intake (g/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)									
			1	8	15	22	29	36	43	50	57	64
60 mg/kg	(+)	M02021	15.6	13.1	13.1	12.5	11.1	12.8	11.1	14.0	12.4	11.8
		M02022	16.3	14.3	12.8	13.0	12.0	11.7	11.3	12.0	12.9	12.7
		M02023	15.3	15.4	13.9	16.5	12.2	12.5	14.2	13.3	13.2	14.2
		M02024	11.5	13.4	11.4	14.1	12.8	13.1	12.9	14.1	11.9	12.3
		M02025	15.0	13.0	11.9	22.6	10.4	10.5	11.4	10.9	10.9	11.0
		M02026	11.5	13.5	12.7	39.2	10.4	13.0	13.0	13.1	13.1	13.3
		M02027	17.2	14.6	13.8	14.3	12.4	12.3	12.2	13.8	14.3	13.5
		M02028	18.0	15.6	13.9	15.3	12.1	11.9	12.3	12.9	14.1	14.1
		M02029	14.4	13.0	11.5	13.0	12.8	12.3	10.9	11.5	12.6	11.9
		M02030	20.4	14.6	12.9	11.9	12.7	11.8	12.8	13.2	13.4	12.7
		M02031	17.7	16.0	13.3	12.1	12.1	12.2	11.6	12.2	11.2	11.4
		M02032	13.9	13.6	13.7	12.9	10.5	12.5	10.3	12.3	11.5	11.7
		M02033	15.6	13.0	13.1	13.3	11.5	13.2	12.1	13.5	14.5	13.5
		M02034	18.0	13.9	13.1	12.1	11.3	10.7	12.5	11.7	12.4	12.2
		M02035	12.8	12.7	12.2	12.4	10.8	12.9	11.7	13.1	10.8	11.2
		M02036	16.4	14.3	13.4	14.1	13.7	13.1	11.8	11.8	13.7	12.3
		M02037	16.7	13.8	12.6	11.7	12.2	12.5	13.9	12.6	13.6	13.6
		M02038	15.7	13.1	15.8	15.8	12.2	14.0	11.9	13.4	13.7	13.5
		M02039	16.6	14.8	15.0	14.2	11.9	13.8	11.3	13.1	14.1	12.5
		M02040	16.3	14.0	12.9	12.9	13.4	13.3	12.1	13.4	11.8	12.4
N		20	20	20	20	20	20	20	20	20	20	
Mean		15.7	14.0	13.2	15.2	11.9	12.5	12.1	12.8	12.8	12.6	
SD		2.2	1.0	1.1	6.1	1.0	0.9	1.0	0.9	1.2	0.9	

Appendix 3-3 Food intake (g/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)									
			1	8	15	22	29	36	43	50	57	64
250 mg/kg	(+)	M03041	13.0	13.2	13.1	12.3	11.4	11.7	10.2	11.5	10.8	12.1
		M03042	13.7	13.3	11.1	12.0	12.6	12.3	12.9	12.8	12.7	12.3
		M03043	16.5	14.7	13.5	13.2	11.5	12.2	12.5	14.0	14.2	13.3
		M03044	14.1	12.7	13.3	13.9	10.1	10.6	10.6	11.8	12.5	11.1
		M03045	15.8	13.5	13.2	13.2	11.0	12.3	13.1	12.0	12.1	11.7
		M03046	14.1	14.4	12.9	12.0	12.7	11.6	11.1	13.3	12.2	11.8
		M03047	11.7	10.8	12.3	11.5	12.4	11.3	13.3	12.0	11.5	12.2
		M03048	15.7	13.5	13.3	12.8	10.8	12.4	10.3	11.9	13.4	11.4
		M03049	14.4	14.8	12.8	14.5	12.4	13.0	11.8	11.9	13.3	13.9
		M03050	12.9	14.4	12.1	12.1	12.9	12.9	12.4	13.7	12.3	14.0
		M03051	13.3	13.4	12.3	11.6	10.8	10.9	13.5	13.3	12.6	11.1
		M03052	16.3	13.3	13.6	13.7	12.1	13.4	11.3	13.3	12.7	13.7
		M03053	12.5	13.5	12.4	14.3	12.0	13.7	11.2	12.8	13.1	12.7
		M03054	14.8	14.6	12.0	12.8	11.2	11.7	11.0	11.6	11.6	12.4
		M03055	16.4	13.3	13.5	14.6	10.9	12.9	12.0	11.9	11.3	12.2
		M03056	15.7	12.6	13.8	14.1	10.8	12.6	12.9	12.2	12.3	11.1
		M03057	16.5	16.2	14.2	12.9	12.7	12.0	11.5	11.2	9.2	12.5
		M03058	14.4	14.6	12.8	14.4	13.4	14.2	13.4	13.9	14.0	14.0
		M03059	14.3	14.0	13.5	14.0	11.2	14.0	14.4	15.3	12.9	11.2
		M03060	12.6	15.4	14.3	14.0	11.3	12.6	10.5	14.0	12.1	13.4
N		20	20	20	20	20	20	20	20	20	20	
Mean		14.4	13.8	13.0	13.2	11.7	12.4	12.0	12.7	12.3	12.4	
SD		1.5	1.2	0.8	1.0	0.9	1.0	1.2	1.1	1.1	1.0	

Appendix 3-4 Food intake (g/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)									
			1	8	15	22	29	36	43	50	57	64
1000 mg/kg	(+)	M04061	11.0	12.9	10.7	11.8	10.1	13.0	10.9	12.6	11.5	11.8
		M04062	10.0	14.3	13.2	13.4	12.0	11.6	13.1	12.0	11.0	12.8
		M04063	13.9	14.0	13.2	14.4	14.3	14.5	13.0	14.7	13.2	7.7
		M04064	11.1	14.6	13.2	13.1	12.5	13.2	13.6	13.6	14.0	13.1
		M04065	7.1	11.6	10.7	12.9	13.0	14.7	13.1	12.7	12.1	12.1
		M04066	11.3	15.5	15.9	13.9	13.4	13.0	12.6	10.8	14.4	13.4
		M04067	14.7	15.4	15.0	13.5	11.8	13.4	12.9	14.0	13.7	13.6
		M04068	7.9	9.0	12.2	13.3	13.3	12.1	13.0	12.5	12.3	12.9
		M04069	12.3	13.9	13.0	12.5	12.4	11.0	10.4	12.0	10.9	11.9
		M04070	11.8	14.8	14.7	13.6	13.9	13.5	11.6	12.8	11.7	11.0
		M04071	12.1	12.5	13.3	11.5	13.7	12.9	12.4	12.9	11.2	13.0
		M04072	11.4	13.6	11.9	11.9	10.3	12.4	11.8	12.7	11.5	11.3
		M04073	14.8	13.4	12.3	12.4	11.3	13.2	10.1	11.1	11.1	10.9
		M04074	10.3	13.0	13.8	14.9	14.2	14.9	12.4	14.3	13.3	12.9
		M04075	12.4	15.1	13.8	14.1	12.2	12.8	14.0	11.9	12.2	12.4
		M04076	12.4	12.9	13.1	13.5	11.9	11.6	12.4	11.9	11.6	11.9
		M04077	11.5	10.9	13.9	12.8	12.8	12.0	12.4	13.0	14.7	12.6
		M04078	10.3	16.2	15.2	15.0	12.9	15.4	14.4	14.8	14.0	13.1
		M04079	12.8	13.9	14.2	12.0	10.9	12.6	14.2	10.9	12.7	13.6
		M04080	7.7	14.1	13.6	11.6	12.5	13.6	12.6	14.9	12.1	11.7
N		20	20	20	20	20	20	20	20	20	20	
Mean		11.3 **	13.6	13.3	13.1	12.5	13.1	12.5	12.8	12.5	12.2	
SD		2.1	1.7	1.4	1.1	1.2	1.2	1.2	1.3	1.2	1.3	

** , significant difference from the negative control, p<0.01

Appendix 3-5 Food intake (g/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)									
			1	8	15	22	29	36	43	50	57	64
1000 mg/kg	(-)	M05081	14.6	14.5	13.9	13.2	12.5	12.6	13.1	12.8	14.6	14.7
		M05082	14.4	11.0	12.3	12.2	12.9	11.8	13.4	14.1	14.7	14.2
		M05083	12.6	14.2	14.1	14.6	13.3	14.0	13.7	14.8	13.1	14.4
		M05084	13.1	14.0	12.7	13.5	11.6	15.0	14.1	14.5	14.7	15.4
		M05085	14.8	12.8	13.6	12.7	12.0	13.0	14.1	13.3	14.3	14.4
		M05086	16.5	13.9	15.6	14.9	13.4	15.3	14.2	16.0	15.1	14.6
		M05087	14.9	12.6	12.8	13.8	12.5	11.3	13.2	14.0	13.5	13.6
		M05088	13.8	11.7	13.4	13.2	12.2	14.0	12.4	14.7	12.2	13.5
		M05089	17.9	14.4	13.8	14.6	13.6	13.1	13.4	13.2	13.8	13.4
		M05090	15.0	13.9	15.0	13.4	14.3	14.8	14.7	15.9	15.5	13.7
		M05091	13.1	12.8	13.7	13.7	12.2	13.4	14.5	14.9	13.3	14.7
		M05092	14.8	11.8	12.7	13.8	13.5	15.8	12.7	15.3	14.8	15.5
		M05093	15.4	13.9	12.6	12.3	12.7	12.8	13.3	14.1	13.6	13.0
		M05094	13.4	14.0	12.7	13.9	13.7	14.2	12.9	13.9	11.8	14.5
		M05095	18.1	14.5	14.7	13.2	13.4	13.1	14.1	15.3	14.6	14.4
		M05096	18.2	13.0	15.1	15.0	14.8	13.9	14.3	14.3	14.6	15.2
		M05097	15.9	14.0	12.9	13.8	13.0	14.1	12.6	15.2	13.1	13.3
		M05098	15.3	15.9	13.7	13.1	15.6	13.6	13.2	13.9	16.5	14.5
		M05099	15.2	13.3	13.7	14.0	13.3	12.8	13.7	13.4	12.7	12.9
		M05100	18.4	16.5	14.2	14.8	12.1	14.1	13.6	16.4	15.5	15.2
N		20	20	20	20	20	20	20	20	20	20	
Mean		15.3	13.6	13.7	13.7	13.1 **	13.6 *	13.6 **	14.5 **	14.1 **	14.3	
SD		1.8	1.3	0.9	0.8	1.0	1.1	0.7	1.0	1.2	0.8	

* , significant difference from the negative control, p<0.05

** , significant difference from the negative control, p<0.01

Appendix 4-1 Arachidonic acid intake (mg/kg/day) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)									
			1	8	15	22	29	36	43	50	64	
0 mg/kg	(+)	M01001	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01002	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01003	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01004	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01005	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01006	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01007	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01008	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01009	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01010	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01011	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01012	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01013	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01014	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01015	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01016	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01017	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01018	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01019	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		M01020	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
N		20	20	20	20	20	20	20	20	20	20	
Mean		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
SD		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	

Appendix 4-2 Arachidonic acid intake (mg/kg) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)								
			1	8	15	22	29	36	43	50	64
60 mg/kg	(+)	M02021	130.4	93.0	86.0	78.5	66.7	74.6	63.5	78.2	62.0
		M02022	122.3	95.9	79.9	78.2	68.7	65.2	61.2	63.1	64.2
		M02023	146.2	119.0	92.9	104.5	73.4	71.8	80.1	71.8	72.6
		M02024	103.5	102.8	76.9	89.6	77.9	75.9	73.7	78.3	65.4
		M02025	122.0	93.4	78.0	143.1	62.8	61.3	64.8	60.9	59.4
		M02026	105.6	106.9	87.7	250.6	62.3	74.8	72.8	71.9	69.6
		M02027	145.4	103.8	88.4	86.3	70.7	67.5	64.6	71.2	66.7
		M02028	135.8	103.3	85.1	89.3	66.9	64.0	64.9	66.3	69.9
		M02029	133.9	101.0	80.2	85.3	80.1	73.4	63.3	64.4	64.9
		M02030	171.0	104.2	82.5	72.8	74.3	66.2	70.0	70.6	65.7
		M02031	136.4	109.4	83.5	72.5	69.3	67.2	62.3	63.7	58.2
		M02032	125.3	105.4	94.3	81.6	63.4	72.1	57.7	66.9	60.4
		M02033	128.0	92.7	84.6	80.4	65.6	72.1	63.4	69.2	65.6
		M02034	152.5	101.4	87.3	77.1	68.3	61.9	70.7	63.4	63.9
		M02035	126.6	105.2	91.3	83.8	68.4	78.6	68.0	74.7	61.6
		M02036	138.6	98.6	84.0	82.9	76.5	69.6	61.3	60.3	61.0
		M02037	132.2	94.8	80.5	70.2	69.9	69.0	74.6	66.2	68.5
		M02038	141.2	97.8	105.5	97.8	72.1	79.2	66.4	73.4	70.9
		M02039	139.1	101.8	94.5	82.8	66.7	74.3	58.4	66.7	61.1
		M02040	128.5	94.2	77.9	74.1	72.6	69.7	61.3	65.5	59.3
N		20	20	20	20	20	20	20	20	20	
Mean		133.2	101.2	86.0	94.1	69.8	70.4	66.2	68.3	64.6	
SD		15.1	6.5	7.1	40.1	4.9	5.2	5.9	5.3	4.2	

Appendix 4-3 Arachidonic acid intake (mg/kg) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)								
			1	8	15	22	29	36	43	50	64
250 mg/kg	(+)	M03041	478.2	408.6	366.0	320.7	286.2	278.7	236.4	261.7	282.8
		M03042	469.3	394.5	295.4	307.5	306.9	286.7	296.1	283.6	257.3
		M03043	599.8	451.7	363.9	333.1	276.9	282.2	283.8	313.2	267.5
		M03044	502.5	384.3	358.5	358.9	249.4	246.7	245.9	265.7	265.3
		M03045	639.9	457.3	398.9	374.0	298.6	320.0	334.7	297.4	257.6
		M03046	608.7	499.1	400.4	347.4	341.7	299.5	275.5	321.4	250.0
		M03047	405.1	321.7	333.7	302.3	309.6	270.8	312.2	274.9	290.3
		M03048	547.8	405.4	363.6	330.3	264.1	295.0	240.1	268.7	247.6
		M03049	485.2	426.6	328.6	352.6	288.5	291.1	257.7	252.8	285.8
		M03050	488.4	451.8	348.4	327.4	329.7	309.1	283.0	301.9	291.9
		M03051	468.0	408.9	339.4	300.7	270.2	263.0	322.1	306.8	238.6
		M03052	689.4	464.3	419.7	393.3	326.6	349.5	290.2	331.9	284.3
		M03053	444.1	400.6	328.5	353.8	282.6	312.5	249.3	278.1	288.5
		M03054	609.6	477.3	346.1	343.6	287.8	290.5	272.2	278.4	273.3
		M03055	525.3	380.7	354.9	361.9	261.5	299.6	271.0	263.0	252.5
		M03056	598.0	399.4	394.1	376.6	274.5	303.6	305.5	279.1	241.9
		M03057	560.9	462.1	364.9	316.5	298.7	271.0	255.2	241.3	296.6
		M03058	475.1	416.3	331.7	348.5	308.5	313.1	291.5	296.7	285.1
		M03059	456.5	391.1	352.2	344.8	261.5	318.6	319.7	330.4	234.0
		M03060	486.9	494.1	397.4	365.8	274.9	290.1	234.5	306.4	281.3
N		20	20	20	20	20	20	20	20	20	
Mean		526.9	424.8	359.3	343.0	289.9	294.6	278.8	287.7	268.6	
SD		75.6	44.1	30.6	25.6	24.9	23.2	30.3	25.7	19.9	

Appendix 4-4 Arachidonic acid intake (mg/kg) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)								
			1	8	15	22	29	36	43	50	64
1000 mg/kg	(+)	M04061	1395.5	1479.8	1134.4	1172.3	964.4	1203.9	987.5	1107.6	986.4
		M04062	1584.5	1983.3	1594.9	1481.1	1261.3	1144.1	1273.2	1136.1	1161.4
		M04063	1954.5	1780.0	1491.5	1492.8	1401.5	1335.4	1175.9	1307.4	672.8
		M04064	1504.6	1741.5	1407.1	1375.7	1253.0	1272.4	1259.5	1224.5	1140.8
		M04065	1113.7	1648.0	1329.3	1459.0	1368.9	1447.4	1257.0	1175.2	1063.6
		M04066	1697.2	1980.4	1809.7	1489.2	1342.1	1257.2	1192.4	988.0	1159.1
		M04067	1903.2	1759.7	1604.1	1349.2	1122.1	1223.0	1157.5	1218.3	1131.6
		M04068	1309.5	1343.1	1591.0	1607.0	1472.9	1243.3	1284.9	1172.9	1150.4
		M04069	1785.4	1751.0	1452.7	1319.2	1248.9	1061.6	981.4	1110.4	1052.8
		M04070	1579.4	1722.3	1543.7	1315.3	1287.2	1203.4	1005.3	1079.6	894.2
		M04071	1822.1	1636.5	1560.2	1240.6	1413.9	1273.9	1190.8	1206.1	1144.0
		M04072	1644.6	1698.6	1331.7	1247.5	1035.1	1211.8	1124.0	1186.5	1015.1
		M04073	1751.1	1466.6	1268.9	1223.5	1078.1	1231.2	933.5	1012.3	951.3
		M04074	1647.7	1840.1	1746.0	1710.1	1516.5	1516.3	1224.1	1352.7	1146.9
		M04075	1771.3	1917.7	1560.1	1468.8	1209.9	1221.2	1299.6	1066.5	1064.0
		M04076	1688.7	1555.4	1445.3	1427.4	1213.2	1152.4	1208.7	1127.1	1077.7
		M04077	1721.7	1401.9	1610.3	1378.9	1332.8	1194.2	1202.2	1225.8	1155.0
		M04078	1504.5	2095.0	1742.8	1573.1	1252.2	1429.6	1296.5	1324.4	1106.5
		M04079	1748.3	1644.6	1536.1	1219.1	1049.4	1171.0	1297.5	978.0	1177.7
		M04080	1193.4	1898.1	1625.6	1269.0	1324.6	1382.8	1248.5	1438.0	1074.1
	N	20	20	20	20	20	20	20	20	20	
	Mean	1616.0	1717.2	1519.3	1390.9	1257.4	1258.8	1180.0	1171.9	1066.3	
	SD	224.0	202.6	167.5	144.8	149.2	112.4	115.5	121.8	120.5	

Appendix 4-5 Arachidonic acid intake (mg/kg) of medium term multi-organ carcinogenesis study of arachidonic acid in rats.

Dose	Initiation	Animal No	Administration period (days)								
			1	8	15	22	29	36	43	50	64
1000 mg/kg	(-)	M05081	1437.0	1348.2	1220.9	1097.9	1017.2	999.6	1029.8	965.6	1070.2
		M05082	1555.6	1113.1	1178.3	1122.3	1139.5	992.1	1093.1	1115.9	1095.6
		M05083	1247.5	1321.3	1215.6	1192.7	1035.4	1061.6	1008.4	1061.0	1001.0
		M05084	1305.3	1314.8	1107.2	1123.7	939.7	1169.3	1073.4	1069.3	1089.3
		M05085	1568.3	1262.5	1259.5	1109.3	1023.6	1057.6	1123.9	1028.6	1064.0
		M05086	1595.1	1259.3	1305.9	1190.6	1017.8	1142.4	1037.4	1123.5	994.1
		M05087	1580.4	1263.6	1193.4	1223.2	1071.0	940.2	1084.8	1114.1	1026.6
		M05088	1380.9	1095.7	1198.2	1131.8	1008.3	1136.9	982.4	1133.8	999.1
		M05089	1764.0	1328.3	1188.9	1202.4	1089.7	1003.1	1002.5	962.5	930.6
		M05090	1434.0	1243.8	1260.2	1075.9	1105.9	1118.7	1084.8	1151.8	946.7
		M05091	1316.0	1233.8	1246.5	1182.0	1019.1	1077.7	1143.3	1136.1	1087.5
		M05092	1523.4	1151.7	1152.8	1212.6	1144.5	1302.6	1014.1	1190.7	1165.2
		M05093	1584.5	1348.2	1156.3	1091.9	1090.1	1050.8	1057.6	1099.2	958.4
		M05094	1277.4	1277.3	1097.8	1143.5	1100.3	1113.3	987.2	1039.2	1052.4
		M05095	1691.6	1256.6	1196.7	1033.9	1009.9	959.4	1009.6	1063.8	974.8
		M05096	1725.1	1147.5	1265.0	1210.1	1151.1	1048.9	1053.6	1029.2	1051.6
		M05097	1529.5	1263.0	1091.6	1109.1	1011.4	1073.0	932.2	1109.7	939.6
		M05098	1466.3	1412.5	1135.1	1045.7	1197.7	1014.2	966.4	998.6	999.9
		M05099	1622.5	1324.1	1281.9	1243.3	1134.5	1054.1	1101.1	1034.3	959.8
		M05100	1779.5	1501.2	1217.5	1214.1	956.4	1089.0	1021.7	1194.4	1060.4
	N	20	20	20	20	20	20	20	20	20	
	Mean	1519.2	1273.3	1198.5	1147.8	1063.2	1070.2	1040.4	1081.1	1023.3	
	SD	159.5	98.2	61.7	62.4	69.5	81.9	55.0	67.0	62.9	

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「加齢ラットの空間認知機能に及ぼすアラキドン酸長期投与の影響」

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研究要旨

脳内の代表的な多価不飽和脂肪酸であるアラキドン酸の学習・記憶機能への影響を検討するために、魚油抜き飼料で2世代にわたり飼育した21カ月齢のWistar系加齢雄ラットを2群に分け、アラキドン酸群にはアラキドン酸（240 mg/kg BW/day）を、コントロール群には基礎混合油（牛脂：大豆油：菜種油＝2：1：1）を其々13週間にわたり経口投与を行った。

体重は両群間で有意な変化が認められなかった。空間認知機能の評価指標である参照記憶や作業記憶には有意な影響は認められなかったが、アラキドン酸投与ラットではすべての報酬餌をとりきるに要した時間（摂取所要時間）がコントロール群に比べて有意に低値を示した。アラキドン酸投与ラットでは、血漿のHDL・LDLコレステロール、アラキドン酸、ならびにn-6/n-3比は増加し、パルミチン酸、オレイン酸、ならびにリノール酸は有意に低下した。アラキドン酸投与ラットでは、大脳皮質のアラキドン酸が有意に増加し、リノール酸が低下した。海馬ではアラキドン酸の摂取により、リノール酸とDHA/AA比の低下とn-6/n-3比の増加が認められた。

アラキドン酸を摂取した加齢ラットでは、脳内のアラキドン酸が増加し、行動機能に影響を及ぼす可能性が示唆された。

A. 研究目的

脳内の代表的な n-6 系脂肪酸であるアラキドン酸は総脂肪酸の約 10%を占め、少量ではアラキドン酸カスケードを介して生成される生理活性物質が正常な脳機能を営む上で重要な役割を果たしていることがよく知られている。しかしながら、長期的に給与された外因性アラキドン酸による脳機能への影響についてはほとんど未解決のままである。本研究では、アラキドン酸エチルエステルによる老齢ラット認知機能向上効果の有無を検証する。

B. 研究方法

B-1. 加齢ラットとアラキドン酸投与：

F-1魚粉抜き固形飼料（フナバシファーム、船橋市）で2世代飼育した加齢Wistar系雄ラット（21カ

月齢）を、アラキドン酸（240 mg/kg BW/day）と対照基礎混合油（牛脂：大豆油：菜種油＝2：1：1）を其々経口投与するアラキドン酸群（n=15）とコントロール群（n=15）との2群に分け、投与期間中に放射状迷路法により各ラットの空間認知機能を評価した。総投与期間は13週間である。

表1には投与したアラキドン酸豊富油と対照基礎混合油の脂肪酸組成が示されている。アラキドン酸豊富油はCABIO社（中国）から輸入され、アラキドン酸豊富油は対照基礎混合油に比べて、アラキドン酸が多く、パルミチン酸、ステアリン酸、オレイン酸、リノール酸が少ない組成である。

表1 給油脂肪酸組成

	アラキドン酸油	対照基礎混合油
PLA(mol%)	6.95±0.00	13.8±0.01
STA(mol%)	5.91±0.00	13.8±0.01
OLA(mol%)	5.31±0.00	42.5±0.03
LA(mol%)	9.38±0.01	20.0±0.02
AA(mol%)	45.1±0.04	ND
EPA(mol%)	0.52±0.00	0.13±0.01
DPA(mol%)	ND	ND
DHA(mol%)	ND	ND

B-2. 空間認知機能評価法：

アラキドン酸群とコントロール群のラットを其々10匹から行動実験を開始した。評価法としては8走路放射状迷路法を用い、投与開始6週間後から給餌制限（平均体重の77.4%）を行い、2週間の馴化期間の後に8走路のうちの4走路に報酬餌を置き、評価を行った。このとき、放射状迷路法で得られる評価項目としては、Total Time (TT: 摂取所要時間)、Reference Memory Error (RME: 参照記憶エラー)ならびにWorking Memory Error (WME: 作業記憶エラー)があり、RMEは長期記憶、WMEは短期記憶の指標として各々扱われている。

B-3. 血液生化学一般検査項目測定法：

- 1) 血液生化学一般検査項目：医療法人仁寿会加藤病院に検査を依頼。主に酵素法により測定。
- 2) 血漿と脳の脂肪酸測定：ガスクロマト法

C. 研究結果

C-1. 体重と血液生化学一般検査項目への影響

- ・体重には2群間で有意差は認められなかった。
- ・アラキドン酸群ではコントロール群に比べて、血漿の総コレステロールは増加傾向が認められ (P=0.055)、HDLコレステロールとLDLコレステロールは有意に増加した (P<0.05) (表2)。その他の測定項目 (GOT、GTP、 γ -GTP、アルブミン、中性脂肪、血液尿素窒素、クレアチニン、ならびに空腹時血糖) にはアラキドン酸投与の影響は認められなかった。

表2 体重・血液生化学一般検査項目

	Control群(n=15)	AA群(n=15)
体重 (g)	422±10	457±10
GOT (IU/L)	93.7±7.1	96.6±8.8
GTP (IU/L)	52.3±4.3	52.8±4.1
γ -GTP (IU/L)	1.9±0.2	1.6±0.2
ALB(mg/dL)	2.7±0.0	2.8±0.1
Total-C (mg/dL)	105.8±5.8	120.2±4.4*
TG ((mg/dL)	61.6±9.8	68.1±8.6
BUN(mg/dL)	17.2±0.6	18.4±0.6
CRE(mg/dL)	0.30±0.0	0.33±0.0*
BS(mg/dL)	128.9±4.6	140.2±7.3
HDL-C(mg/dL)	60.1±2.7	69.6±2.6**
LDL-C(mg/dL)	30.1±1.6	35.9±2.1**

数値は平均値±標準誤差で表している。

*0.05<P<0.1, **P<0.05.

C-2. 空間認知機能への影響 (図1)

- ・各群はそれぞれ10匹から行動評価実験を開始したが、最終的にはコントロール群は7匹、アラキドン酸群は8匹で行った。この原因としては、21カ月齢である加齢ラットの適応能力差であると思われる。
- ・参照記憶、作業記憶は、群間とブロック間でそれぞれ有意差はあるものの、相互作用には有意差が認められなかった。
- ・アラキドン酸投与ラットではコントロールラットに比べて摂取所要時間が有意に低値を示した (p=0.0011)。

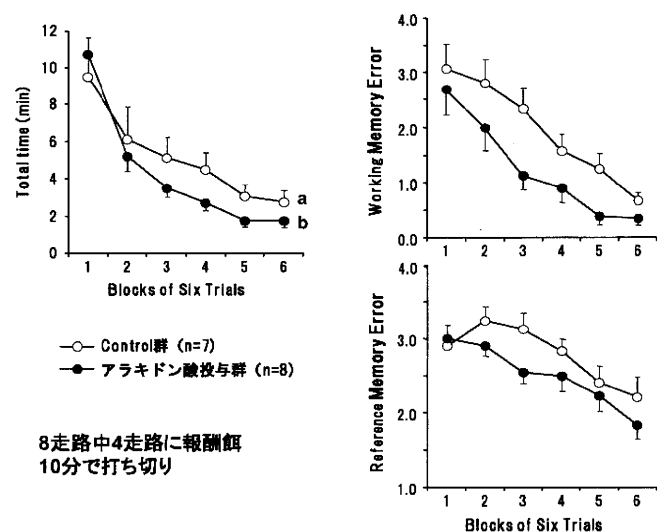


図1 空間認知機能に及ぼす影響