

Figure 7B. Water intake in female F344 rats (2-year carcinogenicity study)

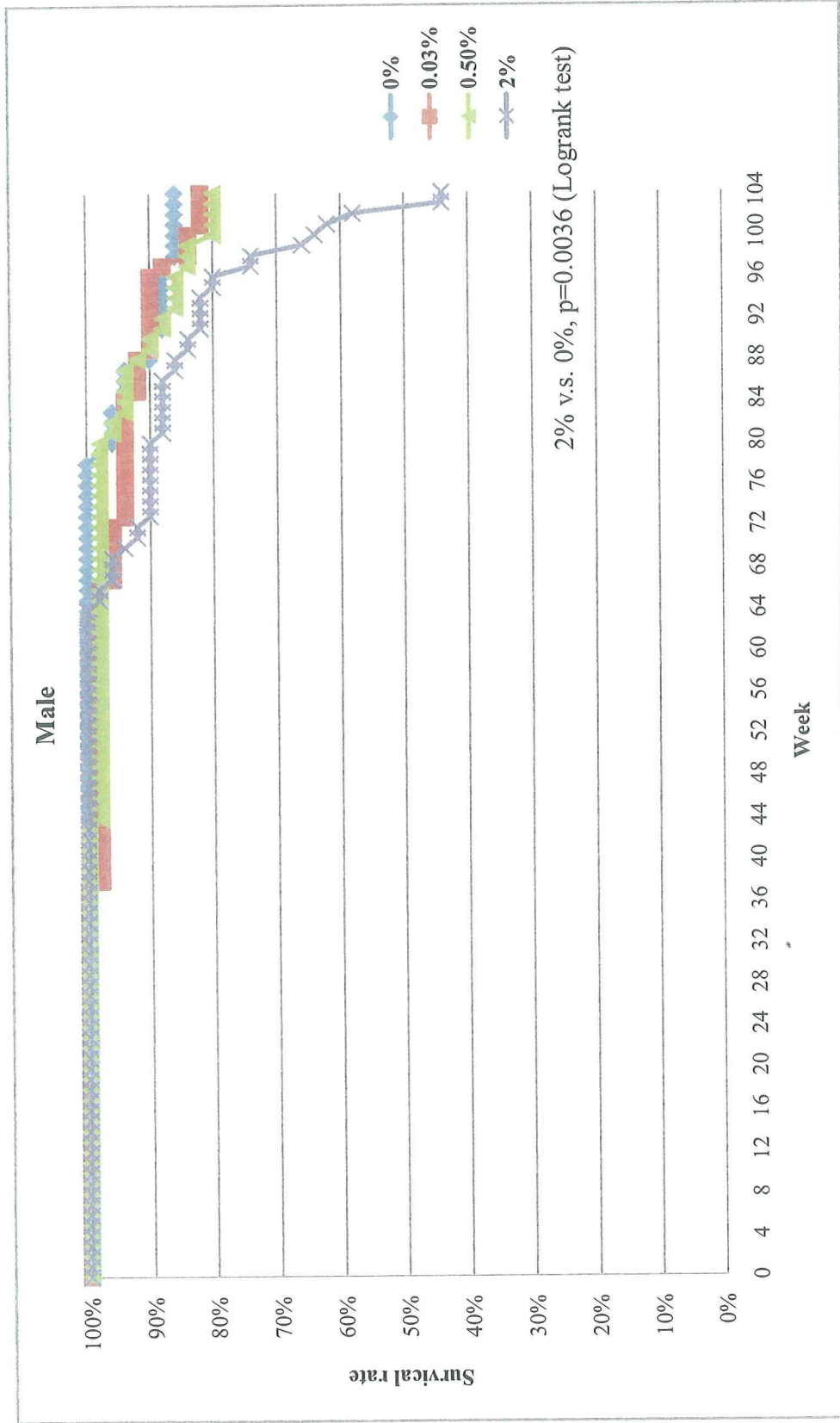


Figure 8A. Survival curves in male F344 rats (2-year carcinogenicity study)

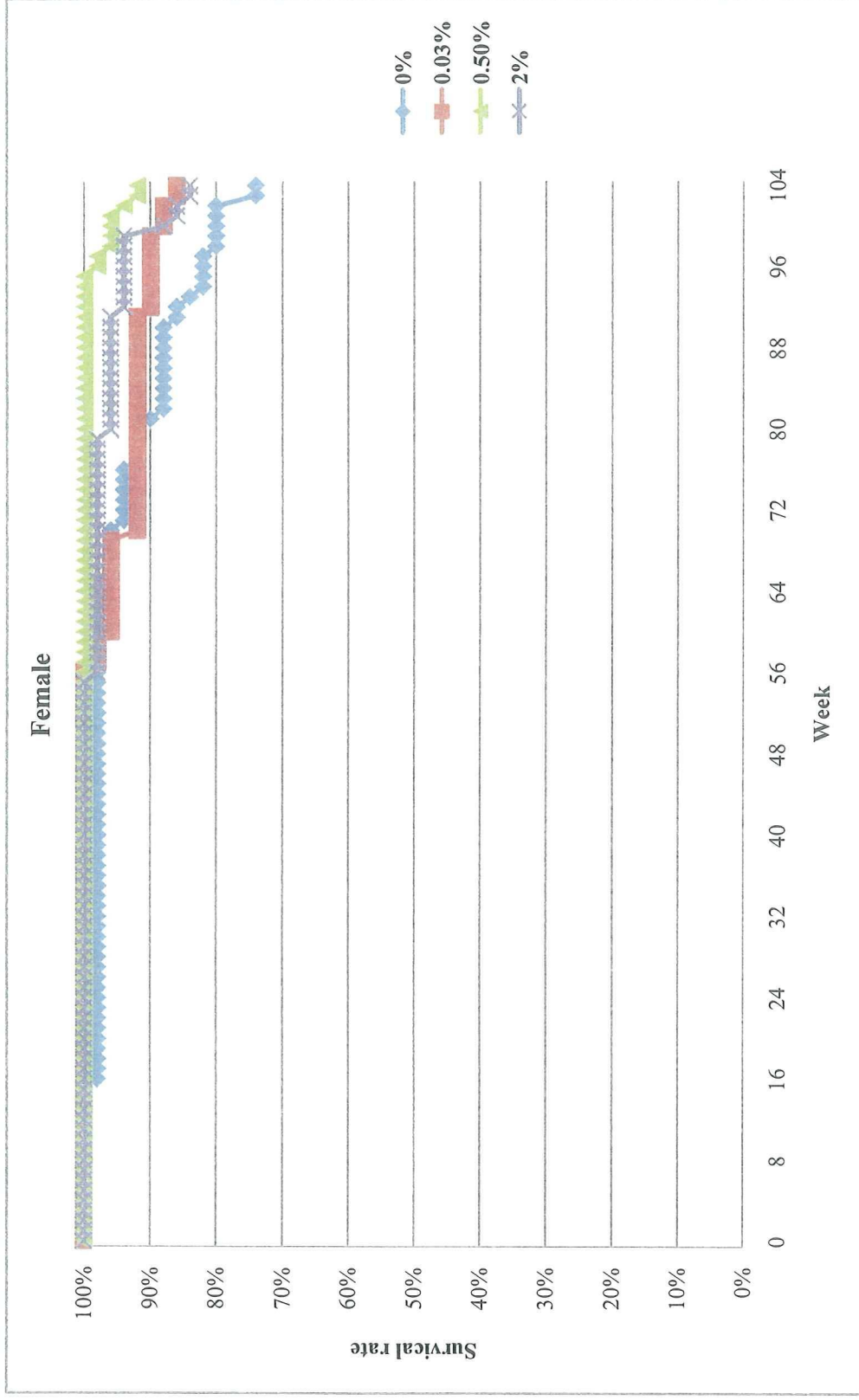


Figure 8B. Survival curves in female F344 rats (2-year carcinogenicity study)

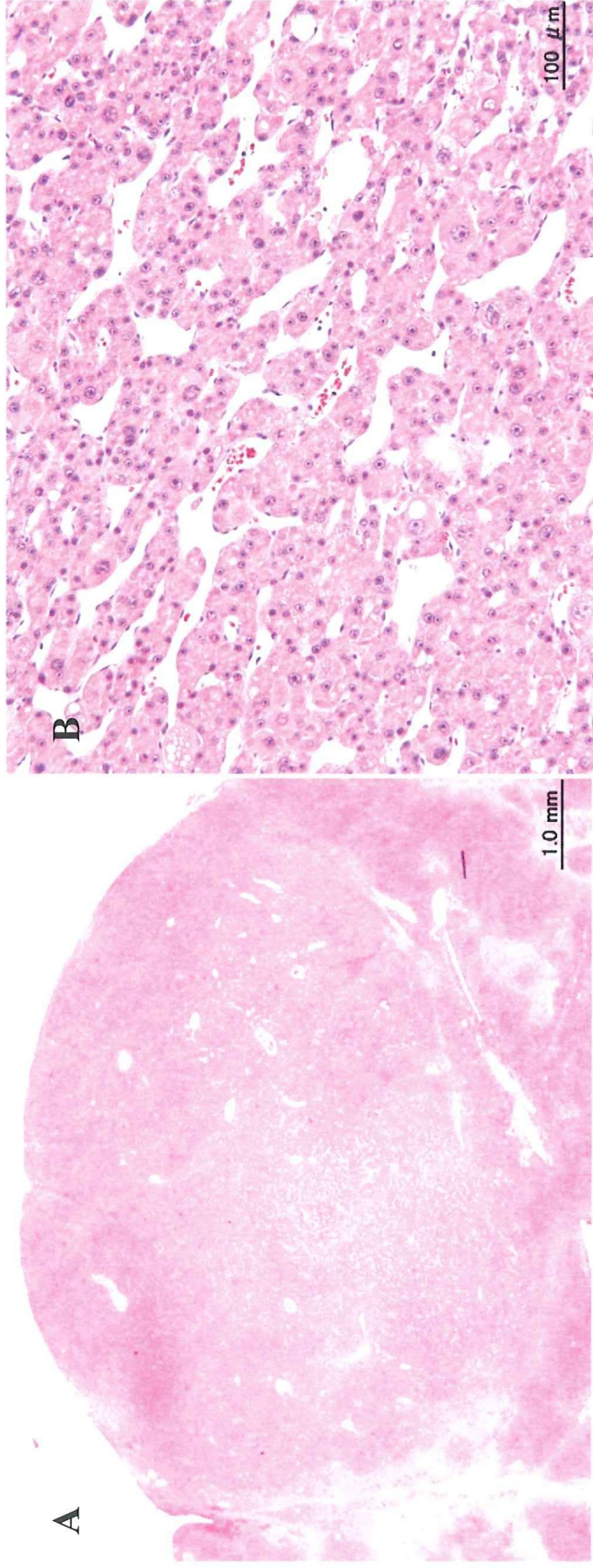


Figure 9. Hepatocellular carcinoma in 2% male group (2-year carcinogenicity study).

A, low magnification; B, high magnification of A.

Table 1
Body weight (g) in 1-year toxicity study

Treatment	No. of animals	Week											
		0	1	2	3	4	5	6	7	8	9	10	11
Male													
Control	10	115.1	163.4	195.3	222.1	237.9	261.4	278.7	290.3	300.8	309.9	318.6	327.0
0.03%	10	115.1	165.5	199.4	227.3	245.2	270.0	287.1	301.2	314.6	326.6*	336.4*	346.0*
0.125%	10	115.6	165.1	198.5	226.9	244.4	269.3	284.9	299.4	310.8	320.7	329.6	338.2
0.5%	10	114.9	162.6	196.4	223.2	240.8	264.6	281.1	294.4	305.0	315.5	325.3	333.1
2%	10	115.9	156.6	184.5*	209.8*	224.5*	247.1*	260.0*	271.0*	280.3*	287.4*	295.1*	302.3*
Female													
Control	10	92.4	117.1	130.0	140.9	146.2	158.3	164.4	168.7	172.1	174.4	179.3	182.2
0.03%	10	93.2	118.0	133.2	142.2	149.2	159.1	167.2	171.1	175.2	179.9*	182.5	185.9
0.125%	10	92.8	116.8	131.4	141.0	148.8	160.8	167.3	171.9	176.5	180.0	183.6	185.9
0.5%	10	92.1	116.4	130.2	141.0	145.9	156.9	164.3	167.8	173.6	176.8	179.4	182.6
2%	10	92.1	112.2	127.7	137.0	141.4	150.4	155.4	159.0*	162.9	166.1*	168.6*	172.8

* Significantly different from control group.

Table 1 (*continued*)

Body weight (g) in 1-year toxicity study

Treatment	Week												
	12	13	17	21	25	29	33	37	41	45	49	51	52
Male													
Dammar resin	12	13	17	21	25	29	33	37	41	45	49	51	52
Control	334.8	338.4	360.0	378.0	394.7	405.4	415.1	425.1	434.3	441.9	449.9	448.4	449.0
0.03%	354.7*	359.4*	384.6*	404.8*	420.4*	434.2*	443.8*	455.3*	463.0*	471.6*	479.7*	477.1*	477.4*
0.125%	346.2	349.2	374.1	392.3	408.4	419.0	426.9	436.4	445.7	454.3	462.6	460.5	460.5
0.5%	340.5	345.9	370.0	386.0	400.6	413.7	424.1	435.3	445.4	454.5	463.2	462.2	460.6
2%	307.9*	311.3*	332.3*	346.3*	361.4*	368.0*	377.1*	385.3*	392.5*	394.8*	404.1*	404.2*	401.7*
Female													
Control	184.9	184.7	190.2	193.9	199.2	201.6	203.9	208.0	212.8	217.3	222.1	223.0	224.0
0.03%	188.7	188.6	197.2	202.7	208.4	210.6*	215.3	219.0*	227.3*	231.9	236.5*	238.4*	240.0*
0.125%	188.1	190.4	197.9	201.5	209.5	212.7*	217.2	223.8	226.2	232.7	237.8	237.9*	240.0*
0.5%	185.1	186.5	192.0	195.7	203.2	208.0	212.5	218.4	220.9	224.6	228.4	232.2	232.8
2%	175.9*	175.3*	181.7*	185.3*	191.7	192.9*	194.7	197.1	202.2	203.5	206.4*	205.5*	207.5*

* Significantly different from control group.

Table 2

Food intake (g/day/rat) in 1-year toxicity study

Treatment	No. of animals	Week											
		1	2	3	4	5	6	7	8	9	10	11	12
Male													
Control	10	12.9	14.0	15.0	15.1	15.2	15.3	13.9	13.9	13.7	13.1	13.5	12.9
0.03%	10	13.4	14.7	15.7	15.1	15.9	14.5	15.1	14.6	14.7	14.0*	14.5*	13.9*
0.125%	10	13.7	14.8	15.5	15.4	15.9	14.8	15.3	14.8	14.0	13.5	14.1	13.2
0.5%	10	13.8	14.5	15.4	15.6	15.9	14.3	15.1*	14.5	14.6	13.5	14.0	13.5
2%	10	13.1	14.5	14.7	15.4	15.0	13.3	14.0	13.7	12.7	12.0*	13.1	12.1
Female													
Control	10	9.8	9.8	10.6	9.3	10.5	9.6	9.5	9.2	9.0	10.2	9.1	8.8
0.03%	10	10.3	10.5	10.8	10.4	10.3	10.3	9.7	9.9	9.4	9.2	9.0	8.8
0.125%	10	9.9	10.2	10.8	10.0	10.8	10.7	10.1	10.6	9.3	9.0	9.0	9.3
0.5%	10	10.7*	10.2	10.9	10.5	10.5	8.6	9.7	9.6	9.6	9.3	9.5	8.9
2%	10	10.0	10.0	10.4	10.5	10.3	9.1	9.2	8.9	8.8	8.9	8.9	8.7

* Significantly different from control group.

Table 2 (continued)
Food intake (g/day/rat) in 1-year toxicity study

Treatment	Week											
	13	14	18	22	26	30	34	38	42	46	50	52
Dammar resin	13.1	12.6	13.5	12.9	13.4	13.2	13.4	13.0	13.2	13.1	13.5	12.5
Control	13.1	12.6	13.5	12.9	13.4	13.2	13.4	13.0	13.2	13.1	13.5	12.5
0.03%	14.3	13.9*	14.4	14.0*	14.4	14.4*	14.3	14.4*	14.2	14.3*	14.7*	13.4
0.125%	13.6	13.1	14.0	13.5	14.0	13.6	13.7	13.9*	14.2	14.0	14.1	12.8
0.5%	12.9	12.5	14.0	13.3	13.8	13.6	13.8	14.1*	14.4*	14.3*	14.6*	13.0
2%	13.2	12.0	13.9	13.2	14.2	13.5	13.9	13.7	13.5	13.8	13.5	12.9
Male												
Control	8.7	8.0	8.5	8.5	8.3	7.9	8.2	8.4	8.6	8.8	9.1	8.5
0.03%	9.4	8.1	9.1	8.6	9.1	8.6	8.3	8.9	9.2	9.2	9.8	8.9
0.125%	9.7	9.2	9.6	8.6	9.1	8.6	8.8	8.5	9.1	8.8	9.3	8.2
0.5%	10.0	8.3	9.1	8.7	9.1	9.3*	8.8	9.0	9.2	8.8	9.7	8.5
2%	9.0	8.3	9.2	8.6	9.0	8.5	8.1	9.0	8.6	8.5	9.0	8.5
Female												

* Significantly different from control group.

Table 3

Intake of dammar resin of F344 rats in 1-year toxicity study

Sex	Treatment Dammar resin	No. of animals	Total intake of dammar resin (mg/kg b.w.)	Average intake of dammar resin (mg/kg b.w./day)
Male	Control	10	0	0
	0.03%	10	4320.75	11.87
	0.125%	10	18050.48	49.59
	0.5%	10	72960.79	200.44
	2%	10	311849.79	856.73
Female	Control	10	0	0
	0.03%	10	5192.11	14.26
	0.125%	10	21558.39	59.23
	0.5%	10	88063.29	241.93
	2%	10	363244.98	997.93

Table 4

Hematology data (1-year toxicity study)

Sex	Treatment	No. of animal	WBC (/□l)	RBC (x10 ⁴ /l)	Hb (g/dl)	Platelet (x10 ⁴ /□l)	Ht (%)
Male	Control	10	3190 ± 606	902 ± 14	15.0 ± 0.4	60.3 ± 3.8	45.3 ± 0.6
	0.03%	10	2790 ± 559	921 ± 15*	14.9 ± 0.2	63.1 ± 2.6	45.8 ± 1.2
	0.125%	10	2610 ± 415*	912 ± 12	14.8 ± 0.2	59.9 ± 3.0	45.6 ± 0.6
	0.5%	10	2250 ± 350*	888 ± 15	14.5 ± 0.4*	67.9 ± 3.2*	44.8 ± 0.9
	2%	10	2630 ± 432*	869 ± 24*	14.1 ± 0.5*	71.6 ± 3.5*	44.7 ± 1.4
	Control	10	2360 ± 832	867 ± 39	15.7 ± 0.7	48.0 ± 8.4	48.2 ± 2.7
	0.03%	10	2150 ± 327	863 ± 40	15.6 ± 0.8	51.1 ± 3.0	48.9 ± 2.7
	0.125%	10	1930 ± 386	856 ± 16	15.3 ± 0.4	52.1 ± 3.5	48.7 ± 1.5
Female	0.5%	10	2400 ± 476	865 ± 45	15.3 ± 1.3*	58.6 ± 5.3*	49.6 ± 2.6
	2%	10	2470 ± 371	833 ± 43	14.3 ± 0.8*	69.7 ± 17.7*	49.0 ± 2.5

* Significantly different from control group.

Table 4 (Continued)

Hematology data (1-year toxicity study)

Sex	Treatment Dammar resin	No. of animal	MCV (fl)	MCH (pg)	MCHC (%)
Male	Control	10	50.23 ± 0.71	16.63 ± 0.35	33.11 ± 0.61
	0.03%	10	49.71 ± 1.30	16.16 ± 0.20*	32.52 ± 0.63*
	0.125%	10	49.96 ± 0.56	16.19 ± 0.19*	32.41 ± 0.29*
	0.5%	10	50.42 ± 0.57	16.32 ± 0.27*	32.38 ± 0.53*
	2%	10	51.41 ± 0.83*	16.20 ± 0.17*	31.51 ± 0.46*
Female	Control	10	55.64 ± 1.41	18.12 ± 0.16	32.59 ± 0.94
	0.03%	10	56.62 ± 1.18	18.09 ± 0.18	31.97 ± 0.55
	0.125%	10	56.83 ± 1.28	17.86 ± 0.17*	31.43 ± 0.66*
	0.5%	10	57.40 ± 1.51*	17.64 ± 0.59*	30.75 ± 1.48*
	2%	10	58.91 ± 1.71*	17.18 ± 0.28*	29.17 ± 0.66*

* Significantly different from control group.

Table 5

Serum chemistry data (1-year toxicity study)

Sex	Treatment	Dammar resin	No. of animal	AST (IU/l)	ALT (IU/l)	ALP (IU/l)	γ -GTP (IU/l)	T-BiL (mg/dl)
Male	Control		10	176.80 \pm 40.94	107.40 \pm 26.31	376.20 \pm 29.53	3.10 \pm 1.85	0.10 \pm 0.00
	0.03%		10	177.00 \pm 50.47	110.30 \pm 22.72	369.90 \pm 49.75	3.00 \pm 1.05	0.10 \pm 0.00
	0.125%		10	148.50 \pm 21.37	89.50 \pm 11.44	332.90 \pm 47.04	3.70 \pm 2.16	0.10 \pm 0.00
	0.5%		10	117.70 \pm 27.68*	62.50 \pm 12.74*	290.90 \pm 38.99*	2.50 \pm 1.27	0.10 \pm 0.00
	2%		10	66.00 \pm 7.32*	49.00 \pm 4.74*	284.40 \pm 14.29*	2.20 \pm 0.63	0.10 \pm 0.00
Female	Control		10	125.10 \pm 35.71	52.50 \pm 11.94	234.10 \pm 56.30	1.10 \pm 0.32	0.10 \pm 0.00
	0.03%		10	103.30 \pm 19.40	47.80 \pm 10.22	205.00 \pm 46.10	1.20 \pm 0.63	0.10 \pm 0.00
	0.125%		10	107.70 \pm 23.37	45.50 \pm 4.88	189.40 \pm 32.07	1.40 \pm 0.52	0.10 \pm 0.00
	0.5%		10	87.10 \pm 16.00*	40.70 \pm 4.85*	148.00 \pm 25.58*	2.50 \pm 0.53*	0.10 \pm 0.00
	2%		10	68.60 \pm 14.77*	43.20 \pm 4.59*	183.60 \pm 38.20*	15.60 \pm 3.92*	0.10 \pm 0.00

* Significantly different from control group.

Table 5 (Continued)

Serum chemistry data (1-year toxicity study)

Sex	Treatment	No. of animal	TP (g/dl)	ALB (g/dl)	A/G	TG (mg/dl)	T-Cho (mg/dl)
Male	Control	10	6.75 ± 0.24	4.52 ± 0.13	2.02 ± 0.13	92.10 ± 17.65	81.70 ± 7.20
	0.03%	10	6.73 ± 0.16	4.52 ± 0.08	2.04 ± 0.10	91.20 ± 29.07	86.30 ± 7.48
	0.125%	10	6.63 ± 0.18	4.45 ± 0.10	2.04 ± 0.14	69.60 ± 17.88	84.10 ± 9.12
	0.5%	10	6.82 ± 0.19	4.51 ± 0.10	1.95 ± 0.14	61.60 ± 19.79*	83.10 ± 8.09
	2%	10	6.88 ± 0.20	4.70 ± 0.21	2.15 ± 0.19	61.50 ± 14.80*	94.00 ± 9.65*
Female	Control	10	6.91 ± 0.60	5.23 ± 0.50	3.16 ± 0.44	84.50 ± 33.22	106.80 ± 16.89
	0.03%	10	7.18 ± 0.35	5.40 ± 0.23	3.06 ± 0.34	119.50 ± 45.25	110.90 ± 12.40
	0.125%	10	7.39 ± 0.38*	5.54 ± 0.32	3.00 ± 0.12	131.00 ± 54.32	119.30 ± 19.07
	0.5%	10	7.71 ± 0.29*	5.72 ± 0.18*	2.90 ± 0.22	138.90 ± 34.47*	139.50 ± 16.53*
	2%	10	7.37 ± 0.29*	5.31 ± 0.21	2.59 ± 0.14*	97.20 ± 49.64	162.00 ± 21.98*

* Significantly different from control group.

Table 5 (Continued)

Serum chemistry data (1-year toxicity study)

Sex	Treatment	Dammar resin	No. of animal	Creatinine (mg/dl)	BUN (mg/dl)	Na (mEq/l)	K (mEq/l)	Cl (mEq/l)
Male	Control		10	0.31 ± 0.04	20.30 ± 4.50	144.70 ± 1.25	4.54 ± 0.32	103.50 ± 1.27
	0.03%		10	0.32 ± 0.05	19.90 ± 3.07	144.50 ± 1.65	4.57 ± 0.22	103.50 ± 1.96
	0.125%		10	0.30 ± 0.05	19.40 ± 2.84	144.00 ± 1.76	4.57 ± 0.42	102.40 ± 1.84
	0.5%		10	0.27 ± 0.03	17.50 ± 2.46	144.70 ± 1.16	4.64 ± 0.35	101.30 ± 1.83*
	2%		10	0.28 ± 0.05	22.30 ± 4.74	145.20 ± 0.79	4.27 ± 0.39	102.10 ± 1.10
Female	Control		10	0.28 ± 0.05	26.30 ± 4.42	144.20 ± 1.69	4.48 ± 0.34	100.90 ± 1.29
	0.03%		10	0.30 ± 0.04	20.80 ± 4.08*	144.60 ± 2.01	4.43 ± 0.53	101.60 ± 1.07
	0.125%		10	0.29 ± 0.04	22.30 ± 3.53	144.30 ± 1.64	4.26 ± 0.24	101.60 ± 1.51
	0.5%		10	0.28 ± 0.03	23.70 ± 4.37	144.90 ± 1.29	4.22 ± 0.38	100.30 ± 1.42
	2%		10	0.26 ± 0.03	26.30 ± 5.79	143.80 ± 1.55	4.48 ± 0.38	100.60 ± 1.07

* Significantly different from control group.

Table 5 (*Continued*)
 Serum chemistry data (1-year toxicity study)

Sex	Treatment	No. of animal	Ca (mg/dl)	P (mg/dl)
Male				
	Control	10	10.31 ± 0.20	5.08 ± 0.75
	0.03%	10	10.39 ± 0.26	5.41 ± 0.56
	0.125%	10	10.21 ± 0.09	5.27 ± 0.61
	0.5%	10	10.35 ± 0.25	5.46 ± 0.45
	2%	10	10.68 ± 0.15*	5.33 ± 0.47
Female				
	Control	10	10.34 ± 0.49	4.44 ± 0.83
	0.03%	10	10.47 ± 0.36	3.99 ± 1.34
	0.125%	10	10.53 ± 0.53	4.14 ± 0.71
	0.5%	10	10.86 ± 0.32	4.56 ± 0.86
	2%	10	10.40 ± 0.38	5.15 ± 0.76

* Significantly different from control group.

Table 6

Urinalysis data (1-year toxicity study)

Treatment	No. of animal	Protein			Glucose			Ketone				
		-	+/-	30mg/dl	100mg/dl	≥ 300 mg/dl	-	100mg/dl	-	+/-	1+	2+
Male												
Control	10	0	0	0	6	4	9	0	0	0	7	3
0.03%	10	0	0	0	6	4	10	0	0	0	8	2
0.125%	10	0	0	0	4	6	10	0	0	0	10	0
0.5%	10	0	0	0	1	9	9	0	0	0	9	1
2%	10	0	0	0	0	10*	9	1	0	1	9	0
Female												
Control	10	0	0	2	7	1	10	0	4	6	0	0
0.03%	10	0	0	5	5	0	10	0	3	7	0	0
0.125%	10	0	0	4	4	2	9	0	0	6	4	0
0.5%	10	0	0	0	5	5	10	0	2	6	2	0
2%	10	0	0	3	5	2	10	0	5	5	0	0

* Significantly different from control group.

Table 6 (Continued)

Urinalysis data (1-year toxicity study)

Treatment	No. of animal	Specific gravity				Occult blood				Bilirubin		
		1.015	1.020	1.025	≥ 1.030	-	+/-	1+	2+	3+	-	1+
Male												
Dammar resin												
Control	10	0	6	1	3	7	0	0	2	1	7	3
0.03%	10	0	9	1	0	9	1	0	0	0	7	3
0.125%	10	0	7	2	1	9	1	0	0	0	7	3
0.5%	10	1	3	5	1	7	2	0	1	0	7	3
2%	10	0	10	0	0	8	2	0	0	0	8	2
Female												
Control	10	0	9	1	0	10	0	0	0	0	8	2
0.03%	10	0	7	2	1	9	0	1	0	0	8	2
0.125%	10	0	6	3	1	8	0	0	0	2	9	0
0.5%	10	1	7	2	0	10	0	0	0	0	9	1
2%	10	3	7	0	0	9	1	0	0	0	10	0

Table 6 (Continued)

Urinalysis data (1-year toxicity study)

Treatment	No. of animal	pH			Urobilinogen		Nitrite		
		7.0	7.5	8.0	8.5	0.1 E.U./dl		1.0 E.U./dl	
Male									
Control	10	3	0	4	3	6	3	8	1
0.03%	10	1	2	6	1	3	7	9	1
0.125%	10	1	4	1	4	2	8	10	0
0.5%	10	1	4	3	2	7	3	9	0
2%	10	0	0	3	7	8	2	10	0
Female									
Control	10	0	3	2	5	2	8	10	0
0.03%	10	0	2	0	8	6	4	10	0
0.125%	10	0	0	1	9	1	9	9	0
0.5%	10	0	1	0	9	2	8	10	0
2%	10	0	1	1	8	7	3	10	0

Table 7

Organ weights (1-year toxicity study)

Sex	Treatment	No. of animal	Liver		Kidney		Spleen		Thymus	
			Absolute (g)	Relative (%)	Absolute (g)	Relative (g)	Absolute (g)	Relative (%)	Absolute (g)	Relative (%)
Male	Control	10	9.33 ± 0.54	2.08 ± 0.17	2.36 ± 0.28	0.53 ± 0.07	0.75 ± 0.04	0.17 ± 0.01	0.048 ± 0.010	0.011 ± 0.002
	0.03%	10	9.92 ± 0.60	2.08 ± 0.09	2.49 ± 0.13	0.52 ± 0.04	0.78 ± 0.06	0.16 ± 0.01	0.050 ± 0.012	0.011 ± 0.002
	0.125%	10	9.82 ± 0.61	2.13 ± 0.06	2.36 ± 0.13	0.51 ± 0.01	0.73 ± 0.04	0.16 ± 0.01	0.049 ± 0.011	0.011 ± 0.003
	0.5%	10	10.40 ± 0.96*	2.25 ± 0.09*	2.46 ± 0.21	0.53 ± 0.03	0.75 ± 0.04	0.16 ± 0.01	0.049 ± 0.009	0.011 ± 0.002
	2%	10	10.68 ± 0.82*	2.66 ± 0.09*	2.43 ± 0.24	0.61 ± 0.06	0.69 ± 0.06*	0.17 ± 0.01	0.047 ± 0.006	0.012 ± 0.002
	Female	Control	10	4.72 ± 0.36	2.11 ± 0.16	1.48 ± 0.07	0.66 ± 0.05	0.43 ± 0.04	0.19 ± 0.02	0.053 ± 0.010
0.03%		10	5.04 ± 0.26	2.10 ± 0.12	1.46 ± 0.10	0.61 ± 0.04*	0.44 ± 0.04	0.18 ± 0.02	0.055 ± 0.007	0.023 ± 0.003
0.125%		10	5.01 ± 0.51	2.10 ± 0.16	1.39 ± 0.10	0.58 ± 0.04*	0.42 ± 0.04	0.18 ± 0.01	0.049 ± 0.015	0.020 ± 0.006
0.5%		10	6.08 ± 0.77*	2.61 ± 0.15*	1.43 ± 0.13	0.61 ± 0.03*	0.42 ± 0.04	0.18 ± 0.01	0.047 ± 0.012	0.020 ± 0.005
2%		10	6.74 ± 0.49*	3.25 ± 0.21*	1.44 ± 0.06	0.70 ± 0.03	0.37 ± 0.04*	0.18 ± 0.02	0.054 ± 0.008	0.026 ± 0.004

* Significantly different from control group.

Table 7 (Continued)
Organ weights (1-year toxicity study)

Sex	Treatment	No. of animal	Heart		Brain		Adrenal		Testis	
			Absolute (g)	Relative (%)	Absolute (g)	Relative (%)	Absolute (g)	Relative (%)	Absolute (g)	Relative (%)
female	Control	10	1.10 ± 0.04	0.25 ± 0.01	2.10 ± 0.05	0.47 ± 0.02	0.043 ± 0.006	0.010 ± 0.001	3.38 ± 0.17	0.75 ± 0.04
	0.03%	10	1.18 ± 0.07*	0.25 ± 0.01	2.15 ± 0.08	0.45 ± 0.02	0.048 ± 0.004	0.010 ± 0.001	3.53 ± 0.46	0.74 ± 0.11
	0.125%	10	1.15 ± 0.07	0.25 ± 0.01	2.04 ± 0.06	0.44 ± 0.03	0.039 ± 0.004	0.008 ± 0.001	3.35 ± 0.36	0.73 ± 0.08
	0.5%	10	1.17 ± 0.08	0.25 ± 0.02	2.09 ± 0.04	0.46 ± 0.03	0.063 ± 0.067	0.014 ± 0.015	3.35 ± 0.25	0.73 ± 0.05
	2%	10	1.09 ± 0.09	0.27 ± 0.01*	2.04 ± 0.07	0.51 ± 0.02*	0.043 ± 0.006	0.011 ± 0.002	3.42 ± 0.18	0.85 ± 0.05*
	Control	10	0.70 ± 0.04	0.31 ± 0.01	1.88 ± 0.06	0.84 ± 0.04	0.049 ± 0.004	0.022 ± 0.002	---	---
	0.03%	10	0.71 ± 0.04	0.30 ± 0.02	1.86 ± 0.04	0.78 ± 0.03*	0.051 ± 0.007	0.021 ± 0.003	---	---
	0.125%	10	0.69 ± 0.05	0.29 ± 0.01*	1.88 ± 0.04	0.79 ± 0.05	0.054 ± 0.007	0.022 ± 0.003	---	---
	0.5%	10	0.73 ± 0.06	0.31 ± 0.03	1.83 ± 0.09	0.79 ± 0.08	0.049 ± 0.005	0.021 ± 0.003	---	---
	2%	10	0.65 ± 0.21	0.31 ± 0.10	1.66 ± 0.40	0.80 ± 0.21	0.044 ± 0.008	0.021 ± 0.003	---	---

Significantly different from control group.