行性腎症、甲状腺濾胞細胞の瀰漫性過形成が雌雄の 5000ppm 群で、脾臓の赤芽球系の髄外造血の軽微な亢進が雄の 5000pppm 群で観察された。なお、33 週で切迫解剖した動物では腎臓に腎芽腫が認められた。51 週で死亡した 5000ppm 群の雌では、副腎に褐色細胞腫が観察され、被膜外への浸潤及び肺への遠隔転移も認められることより悪性と判断された。

以上のことから、ジャマイカカッシア抽出物の無毒性量（NOAEL）は、雄では肝臓の重量及び病理組織学的変化を、雌では尿タンパク質の増加を指標に雌雄ともに 50ppm（雄で 2.1±0.6 mg/kg/day、雌で 2.5±0.6 mg/kg/day）と推定した。また、変異肝細胞巣の発現頻度（動物数）と大きさの増加が雄の 5000ppm 群で認められたことより、大量投与による肝臓への発がん促進作用の可能性が示唆された。

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F. 健康危機情報

比較的大量投与により肝臓、腎臓などへの影響が示唆された。また大量投与による肝臓への発がん促進作用の可能性が示唆された。

G. 研究発表

なし

H. 知的財産の出願・登録状況

なし

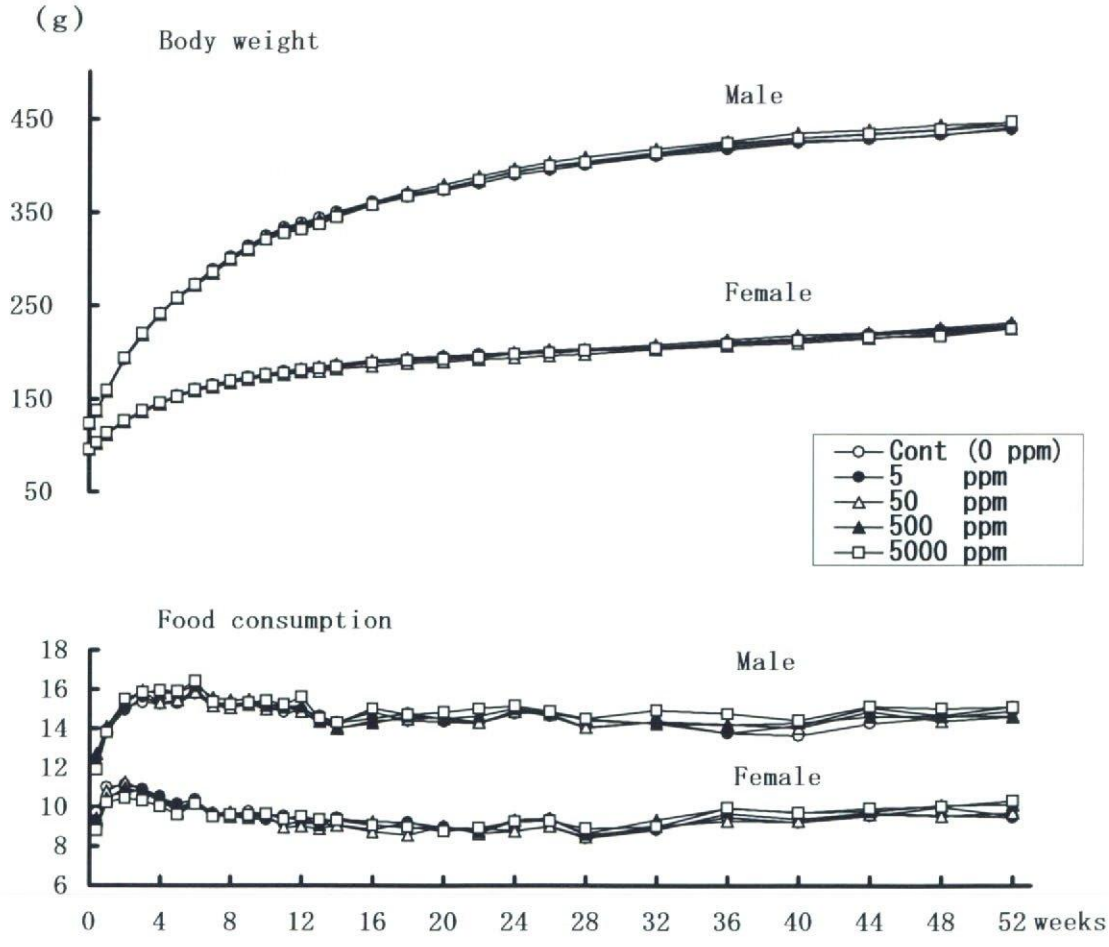


図１　体重及び摂餌量の推移（ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験）

表1　平均摂餌量及び平均被験物質摂取量(ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験)

Group	0 ppm	5 ppm	50 ppm	500 ppm	5000 ppm
Male					
Mean body weight (g)	368.6 ± 74.7	366.2 ± 74.8	369.2 ± 76.4	372.8 ± 77.7	369.1 ± 76.5
Mean food intake (g/rat/day)	14.5 ± 0.5	14.6 ± 0.5	14.6 ± 0.5	14.7 ± 0.5	15.0 ± 0.5
Mean jamaic quassia extract intake (mg/kg b.w. /day)	0 ±	0.21 ± 0.01	2.1 ± 0.6	20.6 ± 6.4	210.7 ± 60.2
Female					
Mean body weight (g)	192.7 ± 29.4	193.0 ± 28.8	189.6 ± 28.0	194.7 ± 29.9	187.9 ± 29.2
Mean food intake (g/rat/day)	9.4 ± 0.6	9.3 ± 0.6	9.3 ± 0.6	9.6 ± 0.5	9.5 ± 0.5
Mean jamaic quassia extract intake (mg/kg b.w. /day)	0 ±	0.25 ± 0.01	2.5 ± 0.6	25.0 ± 5.4	258.2 ± 57.8

Values are mean±SD.

表2　雄の血液学的検査値(ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験)

Group		Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	5000 ppm
No. of animals		20	20	20	20	20
RBC	$10^6/\mu l$	10.07 ± 0.37	10.04 ± 0.47	10.00 ± 0.99	10.22 ± 0.24	9.94 ± 0.35
Hb	g/dl	16.1 ± 0.7	16.0 ± 0.8	16.1 ± 1.0	16.2 ± 0.4	15.4 ± 0.4 *
Ht	%	53.1 ± 2.0	52.9 ± 2.3	53.1 ± 3.6	53.6 ± 1.4	51.5 ± 1.6 *
MCV	f l	52.7 ± 0.5	52.7 ± 0.5	53.3 ± 2.5	52.4 ± 0.6	51.8 ± 0.4 **
MCH	pg	16.0 ± 0.4	16.0 ± 0.4	16.2 ± 0.9	15.9 ± 0.4	15.6 ± 0.3 **
MCHC	g/dl	30.3 ± 0.6	30.3 ± 0.6	30.3 ± 0.7	30.2 ± 0.5	30.1 ± 0.6
Plt	$10^6/\mu l$	0.53 ± 0.10	0.57 ± 0.08	0.56 ± 0.07	0.53 ± 0.10	0.55 ± 1.20
WBC	$10^3/\mu l$	6.81 ± 0.55	6.95 ± 0.81	7.01 ± 1.16	7.75 ± 1.02 *	7.33 ± 0.81
Differential counts (%)						
Baso.		0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Eosino.		2.1 ± 1.7	1.6 ± 1.0	1.7 ± 0.8	1.7 ± 0.9	2.1 ± 1.1
Neut-B		0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Neut-S		34.1 ± 6.1	37.0 ± 4.4	35.7 ± 5.9	38.8 ± 4.6	35.5 ± 4.7
Lympho.		62.4 ± 6.3	60.3 ± 4.9	61.7 ± 5.9	58.1 ± 4.5	60.6 ± 4.9
Mono.		1.4 ± 1.0	1.1 ± 0.8	0.9 ± 0.7	1.4 ± 0.8	1.8 ± 1.0

Each value represents mean ±SD.
Significantly different from the control : * P<0.05. ** P<0.01.
RBC: red blood cell count, Hb: hemoglobin, Ht: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, Plt: platelet count, WBC: white blood cell count,
Baso: basophil, Eosino: eosinophil, Neut-B: band neutrophil, Neut-S: segmented neutrophil, Lympho: lymphocyte, Mono: monocyte.

表3　雌の血液学的検査値(ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験)

Group		Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	5000 ppm
No. of animals		20	20	20	20	18
RBC	$10^6/\mu l$	9.12 ± 0.70	9.01 ± 1.29	9.50 ± 1.94	9.01 ± 0.54	8.70 ± 0.94
Hb	g/dl	16.3 ± 1.4	16.0 ± 2.3	16.7 ± 3.5	15.9 ± 1.0	14.7 ± 1.6 **
Ht	%	51.8 ± 4.0	51.5 ± 7.4	53.8 ± 10.9	51.3 ± 3.1	47.8 ± 4.9 *
MCV	f l	56.8 ± 0.6	57.1 ± 0.5	56.7 ± 0.4	56.9 ± 0.6	54.9 ± 0.6 **
MCH	pg	17.8 ± 0.3	17.7 ± 0.3	17.6 ± 0.4	17.7 ± 0.4	16.9 ± 0.3 **
MCHC	g/dl	31.3 ± 0.6	31.0 ± 0.5	31.1 ± 0.7	31.1 ± 0.6	30.8 ± 0.5
Plt	$10^6/\mu l$	0.47 ± 0.10	0.44 ± 0.10	0.46 ± 0.17	0.46 ± 0.11	0.48 ± 0.13
WBC	$10^3/\mu l$	4.41 ± 1.56	4.48 ± 1.33	4.76 ± 1.38	4.93 ± 1.71	5.18 ± 1.72
Differential counts (%)						
Baso.		0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Eosino.		1.6 ± 0.9	1.3 ± 0.6	1.4 ± 1.1	1.4 ± 0.9	1.1 ± 0.9
Neut-B		0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Neut-S		29.3 ± 6.1	28.9 ± 5.9	27.1 ± 6.5	26.6 ± 7.4	27.1 ± 5.9
Lympho.		68.2 ± 6.7	68.5 ± 5.8	70.5 ± 6.9	71.0 ± 7.7	71.2 ± 5.6
Mono.		0.9 ± 0.8	1.3 ± 1.1	1.1 ± 0.8	1.0 ± 0.8	0.6 ± 0.4

Each value represents mean ±SD.
Significantly different from the control : * P<0.05. ** P<0.01.
RBC: red blood cell count, Hb: hemoglobin, Ht: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, Plt: platelet count, WBC: white blood cell count,
Baso: basophil, Eosino: eosinophil, Neut-B: band neutrophil, Neut-S: segmented neutrophil, Lympho: lymphocyte, Mono: monocyte.

表4　雄の血液生化学的検査値(ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験)

Group		Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	5000 ppm
No. of Animals		20	20	20	20	20
TP	g/dl	7.0 ± 0.2	7.0 ± 0.2	7.1 ± 0.2	7.2 ± 0.2 *	7.5 ± 0.2 **
Alb	g/dl	4.4 ± 0.1	4.4 ± 0.1	4.4 ± 0.1	4.5 ± 0.1 *	4.7 ± 0.2 **
A/G		1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.6 ± 0.1	1.7 ± 0.1
BUN	mg/dl	16.6 ± 1.3	16.9 ± 1.3	16.3 ± 1.3	16.9 ± 1.3	17.2 ± 1.3
CRN	mg/dl	0.36 ± 0.07	0.35 ± 0.05	0.36 ± 0.07	0.36 ± 0.06	0.34 ± 0.04
UA	mg/dl	0.43 ± 0.12	0.41 ± 0.12	0.44 ± 0.17	0.43 ± 0.12	0.40 ± 0.13
Glc	mg/dl	135 ± 7	138 ± 7	142 ± 15	137 ± 8	142 ± 12
NEFA	mEq/l	0.51 ± 0.06	0.53 ± 0.08	0.51 ± 0.09	0.50 ± 0.08	0.48 ± 0.08
PL	mg/dl	183 ± 19	188 ± 19	192 ± 23	197 ± 29	178 ± 17
TG	mg/dl	155 ± 24	176 ± 38	191 ± 48 *	184 ± 55	187 ± 37 *
T-Cho	mg/dl	124 ± 11	124 ± 10	127 ± 12	132 ± 18	115 ± 11
T-Bil	mg/dl	0.08 ± 0.03	0.08 ± 0.02	0.08 ± 0.03	0.08 ± 0.03	0.05 ± 0.02 **
ALP	mu/ml	516 ± 99	511 ± 79	505 ± 100	511 ± 115	371 ± 61 **
AlT	mu/ml	95 ± 20	99 ± 25	104 ± 29	94 ± 22	69 ± 11 **
AsT	mu/ml	96 ± 16	100 ± 18	108 ± 20	97 ± 19	67 ± 9 **
ChE	mu/ml	881 ± 76	889 ± 75	882 ± 69	887 ± 82	743 ± 91 **
γ-GTP	mu/ml	6.26 ± 4.69	5.98 ± 3.40	6.19 ± 3.75	7.19 ± 4.69	4.65 ± 2.80
LAP	mu/ml	54 ± 5	54 ± 3	54 ± 4	54 ± 4	52 ± 3
LDH	mu/ml	453 ± 338	382 ± 244	586 ± 568	524 ± 424	387 ± 211
Ca	mg/dl	10.6 ± 0.2	10.5 ± 0.2	10.7 ± 0.5	10.6 ± 0.2	10.7 ± 0.2
P	mg/dl	4.5 ± 0.4	4.4 ± 0.6	4.3 ± 0.4	4.3 ± 0.4	4.7 ± 0.5
Na	mEq/l	142 ± 2	143 ± 2	143 ± 3	142 ± 2	143 ± 2
K	mEq/l	4.2 ± 0.3	4.3 ± 0.3	4.3 ± 0.3	4.3 ± 0.4	4.3 ± 0.3
Cl	mEq/l	101 ± 2	102 ± 2	102 ± 3	101 ± 2	101 ± 2

Each value represents mean ±SD.
Significantly different from the control : * P<0.05. ** P<0.01.
TP: total protein, Alb: albumin, A/G: albumin-globulin ratio, BUN: blood urea nitrogen, CRN: creatinine, UA: uric acid, Glc: glucose,NEFA: non-esterified fatty acid, PL: phospholipid, TG: triglyceride, T-Cho: total cholesterol, T-Bil: total bilirubin, ALP: alkaline phosphatase, AlT: alanine aminotransferase, AsT: aspartate aminotransferase, ChE: cholinesterase, γ-GTP: γ-glutamyltranspeptidase, LAP: leucine aminopeptidase, LDH: lactate dehydrogenase, Ca: calcium, P: inorganic phosphorus, Na: sodium, K: potassium, Cl: chloride.

表5 雌の血液生化学的検査値(ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験)

Group		Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	5000 ppm	
No. of Animals		20	20	20	20	18	
TP	g/dl	7.4 ± 0.3	7.2 ± 0.3	7.4 ± 0.3	7.4 ± 0.3	8.0 ± 0.3	**
Alb	g/dl	4.9 ± 0.2	4.8 ± 0.3	4.9 ± 0.3	4.9 ± 0.2	5.2 ± 0.2	**
A/G		2.0 ± 0.2	19.4 ± 0.2	2.0 ± 0.1	2.0 ± 0.1	1.9 ± 0.1	
BUN	mg/dl	16.6 ± 2.3	16.9 ± 1.9	16.7 ± 1.8	17.0 ± 1.9	17.6 ± 3.0	
CRN	mg/dl	0.35 ± 0.08	0.37 ± 0.09	0.37 ± 0.07	0.35 ± 0.05	0.33 ± 0.08	
UA	mg/dl	0.48 ± 0.13	0.48 ± 0.16	0.58 ± 0.34	0.50 ± 0.16	0.57 ± 0.23	
Glc	mg/dl	116 ± 9	122 ± 13	121 ± 15	121 ± 8	129 ± 19	**
NEFA	mEq/l	0.73 ± 0.11	0.69 ± 0.11	0.75 ± 0.14	0.69 ± 0.10	0.64 ± 0.09	
PL	mg/dl	236 ± 25	263 ± 43	262 ± 26	263 ± 27	289 ± 25	*
TG	mg/dl	193 ± 71	211 ± 94	213 ± 77	220 ± 58	157 ± 63	
T-Cho	mg/dl	143 ± 17	144 ± 21	142 ± 14	145 ± 18	176 ± 10	**
T-Bil	mg/dl	0.10 ± 0.03	0.10 ± 0.04	0.10 ± 0.02	0.09 ± 0.05	0.04 ± 0.03	**
ALP	mu/ml	229 ± 79	236 ± 124	198 ± 29	195 ± 34	150 ± 23	**
AlT	mu/ml	43 ± 10	44 ± 12	44 ± 7	46 ± 13	40 ± 5	
AsT	mu/ml	70 ± 10	76 ± 25	74 ± 11	94 ± 81	64 ± 9	
ChE	mu/ml	3343 ± 134	3376 ± 342	3452 ± 148	3528 ± 263 **	3207 ± 207	
γ-GTP	mu/ml	3.02 ± 3.60	3.49 ± 4.56	1.56 ± 1.76	2.24 ± 2.41	6.02 ± 3.79	*
LAP	mu/ml	46 ± 4	47 ± 4	46 ± 4	44 ± 4	46 ± 8	
LDH	mu/ml	466 ± 193	457 ± 341	506 ± 285	451 ± 302	526 ± 350	
Ca	mg/dl	10.6 ± 0.2	10.4 ± 0.2	10.5 ± 0.3	10.5 ± 0.3	10.8 ± 0.3	
P	mg/dl	3.6 ± 0.7	3.5 ± 0.7	3.6 ± 0.7	3.4 ± 0.6	3.6 ± 0.5	
Na	mEq/l	143 ± 1	143 ± 1	143 ± 1	144 ± 2	146 ± 1	
K	mEq/l	4.1 ± 0.3	4.1 ± 0.3	4.2 ± 0.2	4.1 ± 0.3	4.1 ± 0.3	
Cl	mEq/l	102 ± 2	102 ± 2	102 ± 2	102 ± 2	101 ± 2	

Each value represents mean ±SD.
Significantly different from the control : * P<0.05. ** P<0.01.
TP: total protein, Alb: albumin, A/G: albumin-globulin ratio, BUN: blood urea nitrogen, CRN: creatinine, UA: uric acid, Glc: glucose,NEFA: non-esterified fatty acid, PL: phospholipid, TG: triglyceride, T-Cho: total cholesterol, T-Bil: total bilirubin, ALP: alkaline phosphatase, AlT: alanine aminotransferase, AsT: aspartate aminotransferase, ChE: cholinesterase, γ-GTP: γ-glutamyltranspeptidase, LAP: leucine aminopeptidase, LDH: lactate dehydrogenase, Ca: calcium, P: inorganic phosphorus, Na: sodium, K: potassium, Cl: chloride.

表6 雌雄の尿検査値(ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験)

Group	No.	pH					Protein[1]						Ketone body[2]			Glucose[3]		Occult blood					Billrubin		Urobilinogen[4]		
		6.0	6.5	7.0	7.5	8.0	−	±	+	++	+++	+4	−	±	+	−	+	−	±	+	++	+++	−	±	0.1	1	2
Male																											
Cont.(0 ppm)	20	1	11	7	1				4	15	1	0		5	14	1	20		19	0	1	0	0	20		20		
5 ppm	20	1	6	9	4				4	14	2	1		5	14	1	20		20	0	0	0	0	20		20		
50 ppm	20	2	7	5	5				3	15	2	0		4	12	4	20		20	0	0	0	1	20		20		
500 ppm	20	2	6	7	5				2	14	4	0		3	13	4	20		18	0	0	1	1	20		20		
5000 ppm	20	0	7	8	5				1	5	12	2	**	3	15	2	20		19	1	0	0	0	20		20		
Female																											
Cont.(0 ppm)	20	7	9	3	1	0		2	15	3	0			16	4		20		19	1				20		20		
5 ppm	20	3	14	2	0	1		0	16	4	0			14	6		20		20	0				20		20		
50 ppm	20	2	13	4	1	0		2	14	4	0			15	5		20		20	0				20		20		
500 ppm	20	4	13	1	0	2		0	12	8	0	*		13	7		20		20	0				20		20		
5000 ppm	19	3	9	6	1	0		0	2	13	4	**		14	5		19		19	0				19		19		

1) −: 陰性, +−:±, +: 30 mg/dL, ++: 100 mg/dL, +++: 300 mg/dL, +4: 1000 mg/dL
2) −: 陰性, +−: 5 mg/dL, +: 15 mg/dL
3) −: 陰性, +: 100 mg/dL
4) Ehrich unit /dL
Signifikantly different from the contrl: **P<0.01

表7 雄の臓器重量(ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験)

Group		Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	5000 ppm
No. of Animals		20	20	20	20	20
Body weight (g)		433.1 ± 21.2	432.0 ± 16.8	435.6 ± 26.0	439.3 ± 21.7	436.1 ± 22.4
Brain	(g)	2.05 ± 0.04	2.05 ± 0.05	2.03 ± 0.06	2.03 ± 0.08	2.02 ± 0.06
	(g/100g bw)	0.47 ± 0.03	0.47 ± 0.02	0.47 ± 0.02	0.46 ± 0.03	0.47 ± 0.02
Heart	(g)	1.13 ± 0.07	1.14 ± 0.07	1.15 ± 0.04	1.15 ± 0.05	1.17 ± 0.08
	(g/100g bw)	0.26 ± 0.02	0.26 ± 0.01	0.26 ± 0.01	0.26 ± 0.01	0.27 ± 0.01
Lung	(g)	1.13 ± 0.05	1.13 ± 0.05	1.14 ± 0.05	1.15 ± 0.05	1.15 ± 0.05
	(g/100g bw)	0.26 ± 0.01	0.26 ± 0.01	0.26 ± 0.01	0.26 ± 0.01	0.26 ± 0.01
Liver	(g)	10.46 ± 0.85	10.46 ± 0.79	10.65 ± 1.24	11.29 ± 1.31 *	12.88 ± 0.94 **
	(g/100g bw)	2.42 ± 0.16	2.42 ± 0.14	2.44 ± 0.19	2.57 ± 0.24 *	2.95 ± 0.14 **
Kidney	(g)	2.16 ± 0.11	2.16 ± 0.12	2.14 ± 0.14	2.22 ± 0.13	2.32 ± 0.14 **
	(g/100g bw)	0.50 ± 0.02	0.50 ± 0.02	0.49 ± 0.02	0.51 ± 0.03	0.53 ± 0.02 **
Spleen	(g)	0.74 ± 0.06	0.73 ± 0.04	0.74 ± 0.04	0.76 ± 0.06	0.76 ± 0.06
	(g/100g bw)	0.17 ± 0.01	0.17 ± 0.01	0.17 ± 0.01	0.17 ± 0.01	0.17 ± 0.01
Testis	(g)	3.37 ± 0.10	3.32 ± 0.18	3.29 ± 0.29	3.38 ± 0.25	3.33 ± 0.45
	(g/100g bw)	0.78 ± 0.04	0.77 ± 0.04	0.76 ± 0.07	0.77 ± 0.06	0.76 ± 0.11
Adrenal	(mg)	33.6 ± 3.0	34.1 ± 3.0	34.7 ± 3.0	35.5 ± 3.0	38.8 ± 4.1 **
	(mg/100g bw)	7.8 ± 0.7	7.9 ± 0.7	8.0 ± 0.9	8.1 ± 0.6	8.9 ± 0.9 **
Pituitary	(mg)	8.7 ± 2.2	9.6 ± 1.0	9.5 ± 0.6	9.5 ± 0.9	9.5 ± 1.1
	(mg/100g bw)	2.0 ± 0.5	2.2 ± 0.3	2.2 ± 0.2	2.2 ± 0.2	2.2 ± 0.3
Thyroid	(mg)	19.1 ± 2.2	20.9 ± 2.1	20.4 ± 1.9	21.1 ± 2.0	24.6 ± 1.9 **
	(mg/100g bw)	4.4 ± 0.5	4.8 ± 0.5	4.7 ± 0.4	4.8 ± 0.5	5.7 ± 0.5 **

Each value represents mean ±SD.
Significantly different from the control : * P<0.05. ** P<0.01.

表8 雌の臓器重量(ジャマイカカッシア抽出物のラットによる1年間反復投与毒性試験)

Group		Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	5000 ppm
No. of Animals		20	20	20	20	18
Body weight (g)		228.7 ± 19.2	227.7 ± 12.5	223.4 ± 14.6	230.5 ± 13.4	222.9 ± 11.4
Brain	(g)	1.87 ± 0.05	1.87 ± 0.04	1.86 ± 0.03	1.86 ± 0.06	1.86 ± 0.04
	(g/100g bw)	0.82 ± 0.07	0.82 ± 0.05	0.84 ± 0.06	0.81 ± 0.04	0.83 ± 0.05
Heart	(g)	0.73 ± 0.05	0.71 ± 0.04	0.72 ± 0.04	0.74 ± 0.04	0.77 ± 0.05 *
	(g/100g bw)	0.32 ± 0.02	0.31 ± 0.02	0.32 ± 0.02	0.32 ± 0.02	0.35 ± 0.02 **
Lung	(g)	0.80 ± 0.03	0.77 ± 0.08	0.78 ± 0.03	0.84 ± 0.18	0.82 ± 0.04
	(g/100g bw)	0.35 ± 0.03	0.34 ± 0.03	0.35 ± 0.02	0.36 ± 0.07	0.37 ± 0.02 *
Liver	(g)	5.23 ± 0.64	5.14 ± 0.58	5.05 ± 0.44	5.55 ± 0.96	7.54 ± 0.75 **
	(g/100g bw)	2.29 ± 0.20	2.25 ± 0.21	2.26 ± 0.17	2.41 ± 0.40	3.38 ± 0.23 **
Kidney	(g)	1.33 ± 0.11	1.35 ± 0.08	1.32 ± 0.07	1.35 ± 0.07	1.45 ± 0.09 **
	(g/100g bw)	0.58 ± 0.04	0.59 ± 0.03	0.59 ± 0.04	0.59 ± 0.02	0.65 ± 0.03 **
Spleen	(g)	0.45 ± 0.03	0.46 ± 0.06	0.45 ± 0.03	0.61 ± 0.60	0.49 ± 0.06
	(g/100g bw)	0.20 ± 0.02	0.20 ± 0.02	0.20 ± 0.01	0.26 ± 0.25	0.22 ± 0.02 *
Ovary	(mg)	48.0 ± 8.0	53.0 ± 27.0	54.0 ± 30.0	47.0 ± 10.0	52.0 ± 5.0
	(mg/100g bw)	21.0 ± 3.0	23.0 ± 12.0	24.0 ± 13.0	21.0 ± 4.0	23.0 ± 2.0
Adrenal	(mg)	41.0 ± 4.0	41.0 ± 4.0	41.0 ± 4.0	44.0 ± 4.0	49.0 ± 5.0 **
	(mg/100g bw)	18.0 ± 1.5	17.8 ± 1.5	18.5 ± 1.8	19.2 ± 1.9	21.9 ± 1.8 **
Pituitary	(mg)	15.1 ± 2.3	13.9 ± 2.3	14.3 ± 2.4	14.2 ± 2.0	14.6 ± 1.8
	(mg/100g bw)	6.7 ± 1.1	6.1 ± 0.9	6.4 ± 1.0	6.1 ± 0.8	6.6 ± 0.8
Thyroid	(mg)	14.8 ± 2.5	14.6 ± 1.6	14.1 ± 2.2	14.9 ± 1.8	17.2 ± 1.6 *
	(mg/100g bw)	6.5 ± 1.9	6.4 ± 0.8	6.3 ± 0.8	6.4 ± 0.7	7.7 ± 0.9 **

Each value represents mean ±SD.
Significantly different from the control : * $P<0.05$. ** $P<0.01$.

表9-1 病理組織学的検査(全動物)
腎臓、肝臓、脾臓、甲状腺:ジャマイカカッシヤ抽出物のラットによる1年間反復投与毒性試験

Tissue		Group	Male Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	5000 ppm	Female Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	5000 ppm
Observation		Animals examined	20	0	20	20	20	20	0	20	20	20
Kidney					NE					NE		
Chronic progressive nephropathy	±		20			20	3	12			12	17
	+		0			0	13	0			0	1
	++		0			0	4	0			0	0
	All (>±)		20			20	20 ##	12			12	18 #
Mineralization,papillary	±		8			7	7	3			2	2
Mineralization,corticomedull	±		0			0	0	0			1	1
Cell infiltration, pelvic	±		1			1	0	1			1	1
NEPHROBLASTOMA		Present	0			0	0	0			0	1
Liver												
Hypertrophy, hepatocytic, central	±		0		0	4	1	0		0	0	1
	+		0		0	0	18	0		0	0	17
	++		0		0	0	1	0		0	0	0
	All (>±)		0		0	4 #	20 ** ##	0		0	0	18 ** ##
Proliferation,bile ductular	±		0		0	0	20	14		17	14	13
	+		20		20	18	0	2		2	4	0
	++		0		0	2	0	0		0	1	0
	All (>±)		20		20	20	20 ##	16		19	19	13
Altered cell focus	±		10		10	12	11	19		20	19	18
	+		0		0	0	6	0		0	0	0
	++		0		0	0	1	0		0	0	0
	All (>±)		10		10	12	18 * ##	19		20	19	18
Hepatodiaphragmatic nodule	+		1		0	0	0	4		0	0	1
Vacuolation, hepatocyte,foca	±		4		2	5	1	1		1	2	3
Necrosis, focal	±		8		5	6	5	3		0	2	1
	+		1		1	1	1	0		0	1	0
	All (>±)		9		6	7	6	3		0	3	1
Necrosis, centrilobular	±		0		0	0	0	0		0	0	1
Microgranuloma	±		5		6	3	7	11		13	6	4
	+		0		0	0	0	0		1	2	0
	All (>±)		5		6	3	7	11		14	8	4
Tumor infiltration/metastasis	++		0		0	0	0	0		0	1	0
Spleen					NE					NE		
Hematopoiesis, extramedulla	±		5			4	17	8			7	7
	+		0			0	0	10			12	9
	++		0			0	0	0			0	1
	All (>±)		5			4	17 ** ##	18			19	17
Tumor infiltration/metastasis	++		0			0	0	0			1	0
HEMANGIOMA		Present	0			0	0	1			0	0
Thyroid					NE					NE		
Hyperplasia, follicular, diffu	±		1			0	7* #	0			0	6 * ##
Cyst, ultimobranchial	±		0			0	1	0			0	0
Cell infiltration,interstitial	±		0			0	0	2			0	0
Hyperplasia, C cell,diffuse	±		1			3	0	2			1	1
Hyperplasia, C cell, focal	±		2			3	2	0			2	0
ADENOMA, C CELL		Present	1			0	1	1			1	0

±;minimal, +;mild, ++;moderate
NE;not examined at the site
significantly different from control; *p<0.05, ** P<0.01(Fisher exact test). #P<0.05, ##<P(Mann-whiteny u test)

表9-2　病理組織学的検査(全動物)
副腎、骨、骨髄、精巣上体、眼球、造血系、ハーダー腺、心臓:ジャマイカカッシヤ抽出物のラットによる1年間反復投与毒性試験

Tissue		Group	Male					Female				
			Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	500 0	Cont. (0 ppm)	5 ppm	50 ppm	500 ppm	500 0
Observation		Animals examined	20	0	0	0	20	20	0	0	0	20
Adrenal												
Accessory adrenal	±		1				2	1				0
Hypertrophy,cortical cell, focal	±		2				1	1				1
Hyperplasia, cortical ,focal	±		0				0	1				0
Hyperplasia,medullary, focal	±		0				1	0				0
	+		3				0	0				0
	All (>±)		3				1	0				0
PHEOCHROMOCYTOMA,		Present	0				1	0				1
MALIGNANT		Present	0				0	0				1
	All		0				1	0				2
Bone+Bone marrow, femoral												
Hematopoiesis, increased	++		0				0	0				1
Microgranuloma, bone marrow	±		1				1	9				8
Bone+Bone marrow, sternal												
Degeneration,chondromucinous	±		7				5	8				4
Hematopoiesis, increased	++		0				0	0				1
Microgranuloma, bone marrow	±		4				2	9				5
	All (>±)		4				2	9				5
Epididymis								—				—
Cell infiltration, interstitial	±		0				1					
Hypospermia	+++		0				1					
Eye												
Atrophy,retinal	±		0				1	0				0
	+		0				0	0				1
	++		0				0	2				0
	All (>±)		0				1	2				1
Mineralization, corneal	±		0				0	0				1
Hemolymphoreticular(all sites)												
LEUKEMIA,												
LARGE GRANULAR LYMPHOCYTI		Present	0				0	0			1a)	0
Harderian gland												
Cell infiltration, interstitial	±		3				4	5				6
Pigmentation, intra-acinar	±		14				14	15				12
Heart												
Mineralization, myocardial	±		0				0	0				1
Cardiomyopathy	±		6				9	13				13
	+		14				11	0				0
	All (>±)		20				20	13				13
Lymph node,mesenteric												
Accumulation, macrophage	±		0				0	0				4
	+		20				19	20				15
	++		0				1	0				0
	All (>±)		20				20	20				19
Lung(bronchus)												
Mineralization, arterial wall	±		15				15	6				2
Accumulation, foamy cell	±		2				2	1				2
Hyperplasia, bronchiolo-alveolar	±		1				0	0				0
Metaplasia, osseous	±		1				2	0				0
Tumor infiltration/metastasis	±		0				0	0				1
ADENOMA,												
BRONCHIOLO-ALVEOLAR		Present	0				1	0				0

±; minimal, +;mild, ++;moderate
a) Animal No.573

表9-3 病理組織学的検査(全動物)

乳腺、卵巣、膵臓、下垂体、前立腺、胃、筋肉、精嚢、精巣、舌、子宮、膣::ジャマイカカッシヤ抽出物のラットによる1年間反復投与毒性試験

全動物

Tissue / Observation		Male Group	Male Cont. (0 ppm)	Male 5 ppm	Male 50 ppm	Male 500 ppm	Male 500 ppm	Female Group	Female Cont. (0 ppm)	Female 5 ppm	Female 50 ppm	Female 500 ppm	Female 500 ppm
		Animals examined	20	0	0	0	20		20	0	0	0	20
Mammary gland													
FIBROADENOMA		Present							1				
Ovary													
Cyst	±								1				0
Pancreas													
Atrophy, acinar, focal	±		4				7		6				5
	+		6				4		1				1
	All (≥±)		10				11		7				6
Cell infiltration, interstitial	±		12				11		6				8
Fibrosis,islet	±		1				3		0				0
	+		1				0		0				0
	All (≥±)		2				3		0				0
Pituitary													
Aberrant craniopharyngeal tissue	±		1				0		0				1
Cyst	±		1				5		1				0
	+		0				0		0				2
	All (≥±)		1				5		1				2
Hemorrhage, Rathke's pouch	±		0				0		2				1
	+		0				0		1				1
	All (≥±)		0				0		3				2
Cystlike structure	±		0				0		2				1
	+		0				0		3				3
	All (≥±)		0				0		5				4
Hyperplasia, anterior, focal	±		0				0		1				0
	+		1				1		1				0
	All (≥±)		1				1		2				0
ADENOMA,ANTERIOR		Present	0				0		1				0
Prostate													
Prostatitis	+		0				1						
Stomach													
Cyst,epidermal	±		1				0		0				0
Skeletal muscle, femoral													
Cell infiltration	±		1				0		0				0
Seminal vesicle									—				—
Diverticulum	±		1				0						
Cell infiltration, interstitial	±		1				0						
Testis									—				—
Atrophy, seminiferous tubular	±		6				3						
	++		1				3						
	All(>±)		7				6						
Arteritis	+		2				0						
Hyperplasia, Leydig cell, focal	±		19				18						
Tongue													
Cell infiltration, muscle layer	±		0				1		0				1
Uterus			—				—						
Hyperplasia,endometrial, cystic	±								0				1
	+								1				0
	All (≥±)								1				1
POLYP,ENDOMETRIAL STROMAL		Present							2				2
Vagina			—				—						
POLYP, VAGINAL STROMAL	Present												1

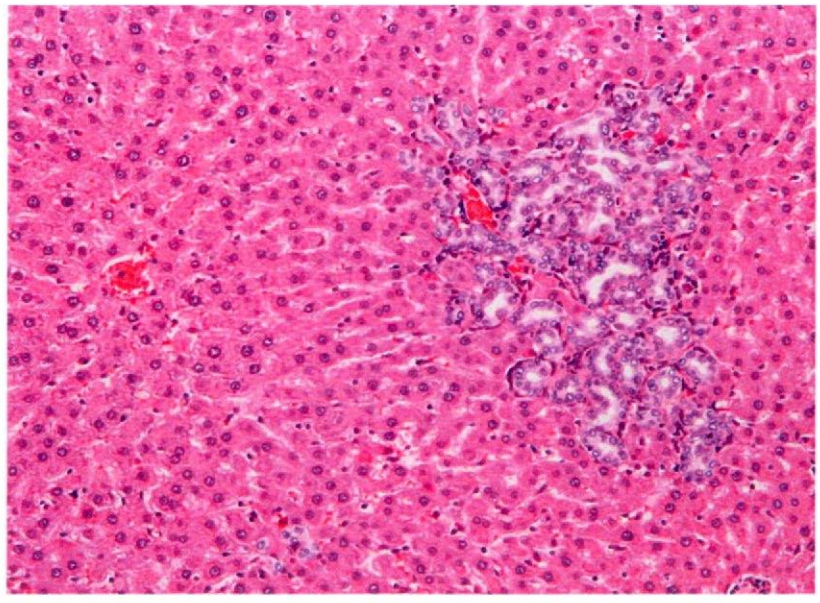
±;minimal, +;mild, ++;moderate

表10　病理組織学的検査（途中死亡動物）
ジャマイカカッシヤ抽出物のラットによる1年間反復投与毒性試験

Tissue		Group	Femal 5000 ppm
Observation		Animals examined	2
Kidney			
NEPHROBLASTOMA		Present	1
Liver			
Altered cell focus	±		2
Necrosis, focal	±		2
Necrosis, centrilobular	±		2
Spleen			
Hematopoiesis, extramedullary	++		1
Adrenal			
PHEOCHROMOCYTOMA, MALIGNANT		Present	1
Bone+Bone marrow, femoral			
Hematopoiesis, increased	++		1
Bone+Bone marrow, sternal			
Hematopoiesis, increased	++		1
Harderian gland			
Pigmentation, intra-acinar	±		1
Heart			
Mineralization, myocardial	±		1
Lymph node,mesenteric			
Accumulation, macrophage	±		1
Lung(bronchus)			
Accumulation, foamy cell	±		1
Tumor infiltration/metastasis	±		1
Uterus			
POLYP,ENDOMETRIAL STROMAL			1

±;minimal, +;mild, ++;moderate

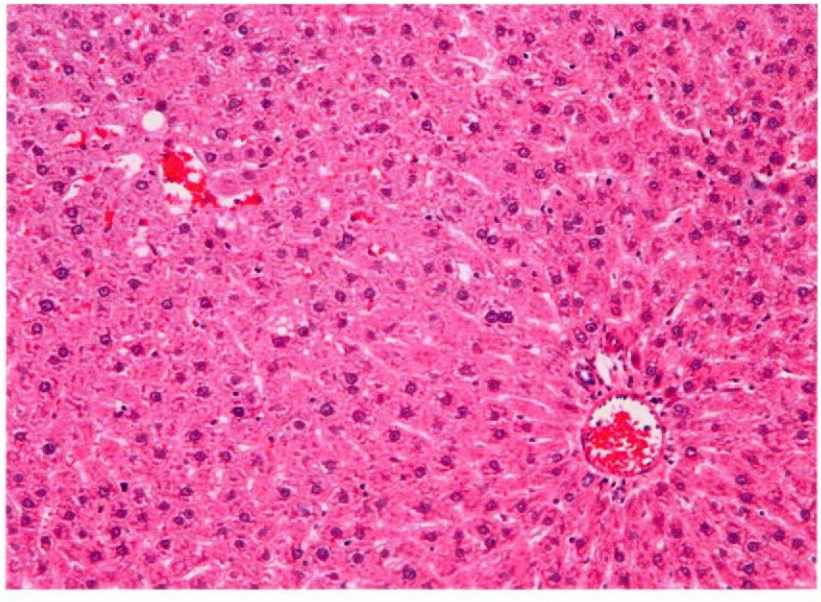
写真 1



Organ	:	Liver
Dose	:	0ppm
Animal No.	:	1
Sex	:	Male
Finding	:	Proliferation of bile ducts

HE Stain X100

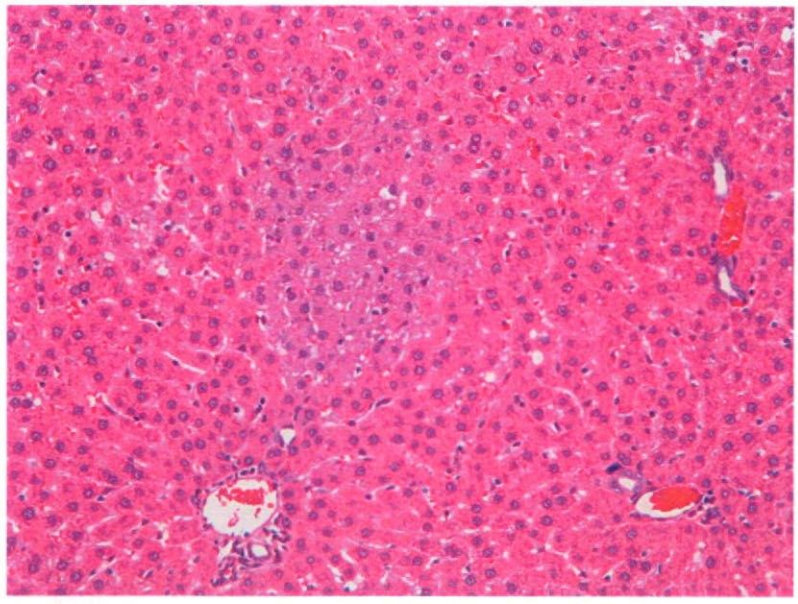
写真 2



Organ	:	Liver
Dose	:	5000ppm
Animal No.	:	94
Sex	:	Male
Finding	:	Central hypertrophy of hepatocytes

HE Stain X100

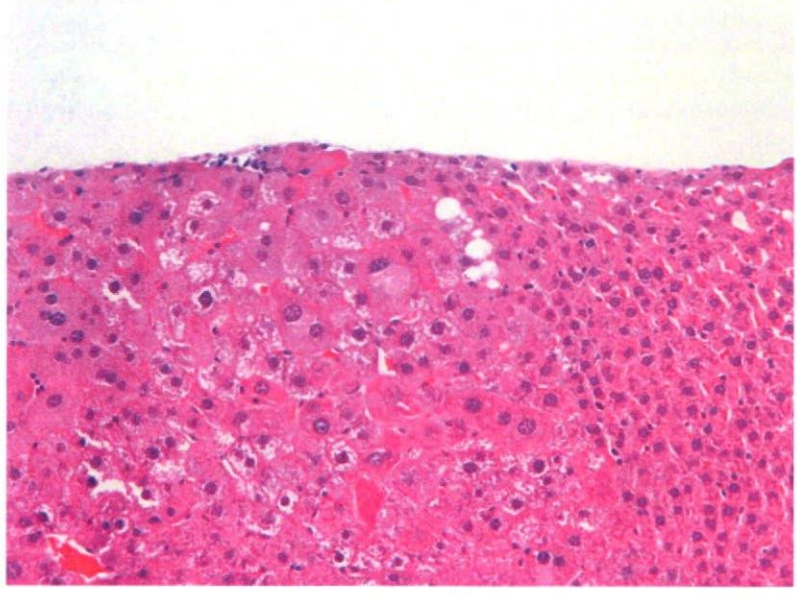
写真 3



Organ : Liver
Dose : 0ppm
Animal No. : 7
Sex : Male
Finding : Altered cell focus(minimal)

HE Stain X100

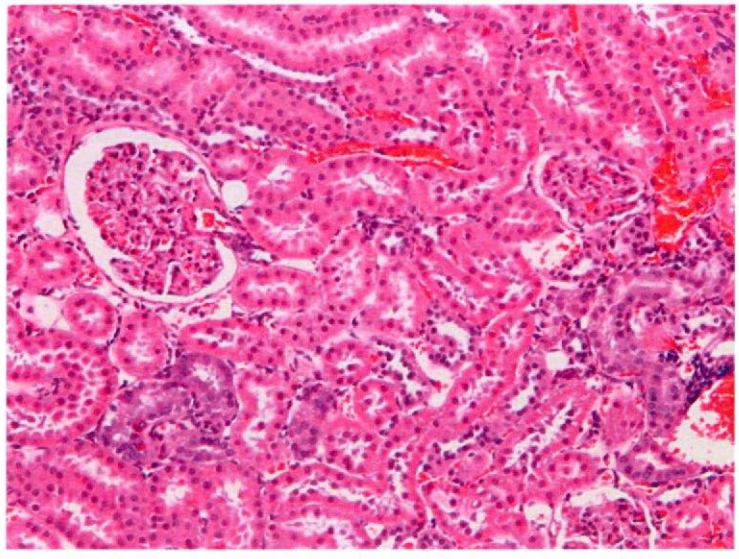
写真 4



Organ : Liver
Dose : 5000ppm
Animal No. : 92
Sex : Male
Finding : Altered cell focus(moderate)

HE Stain X100

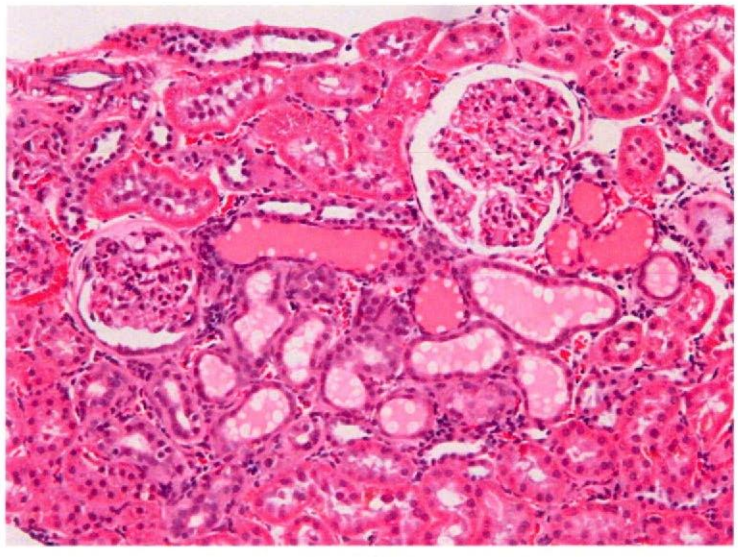
写真 5



Organ : Kidney
Dose : 0ppm
Animal No. : 1
Sex : Male
Finding : Chronic progressive nephropathy(minimal)

HE Stain X100

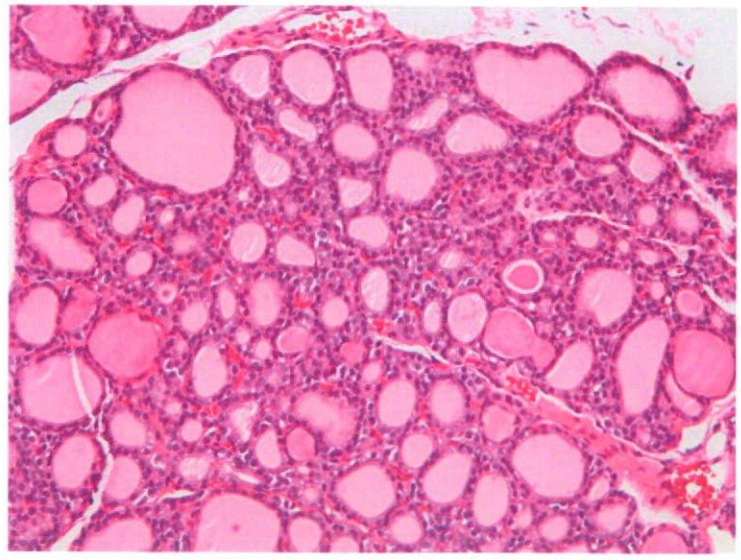
写真 6



Organ : Kidney
Dose : 5000ppm
Animal No. : 99
Sex : Male
Finding : Chronic progressive nephropathy(moderate)

HE Stain X100

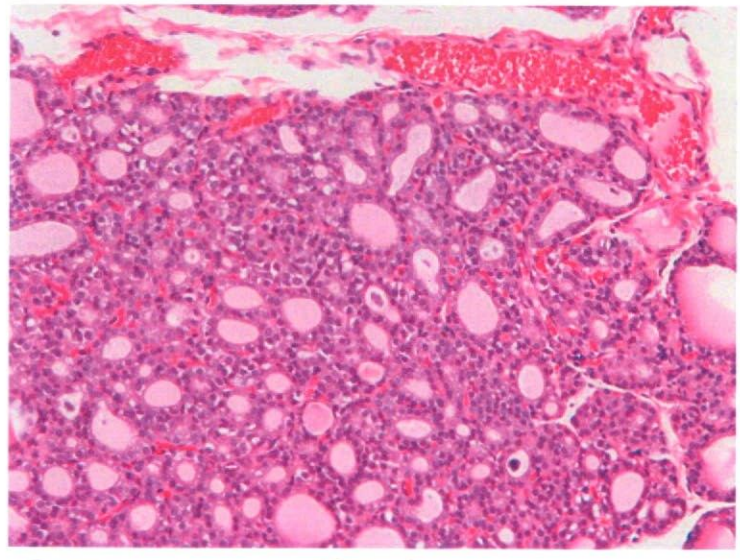
写真 7



Organ	:	Thyroid
Dose	:	0ppm
Animal No.	:	1
Sex	:	Male
Finding	:	No remarkable changes

HE Stain X100

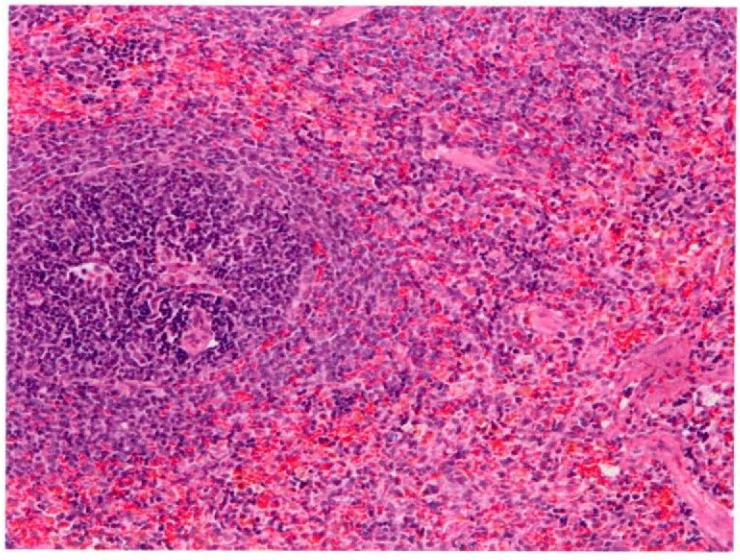
写真 8



Organ	:	Thyroid
Dose	:	5000ppm
Animal No.	:	87
Sex	:	Male
Finding	:	Diffuse follicular hyperplasia

HE Stain X100

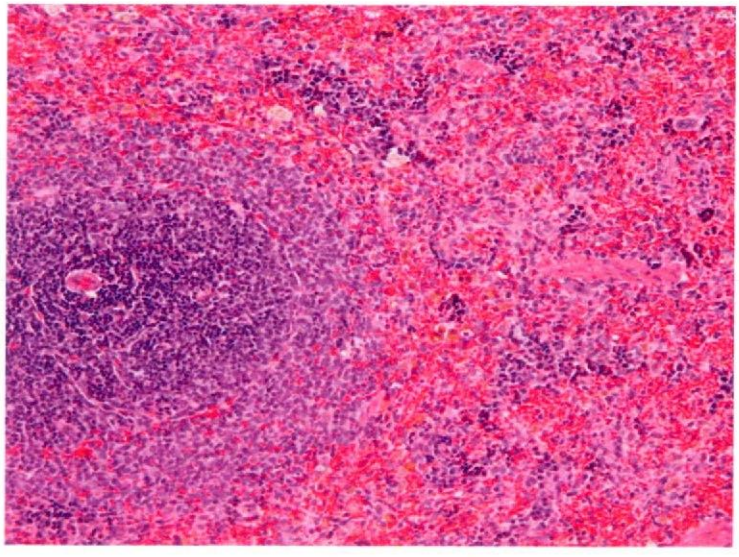
写真 9



Organ	:	Spleen
Dose	:	0ppm
Animal No.	:	2
Sex	:	Male
Finding	:	No remarkable changes

HE Stain X100

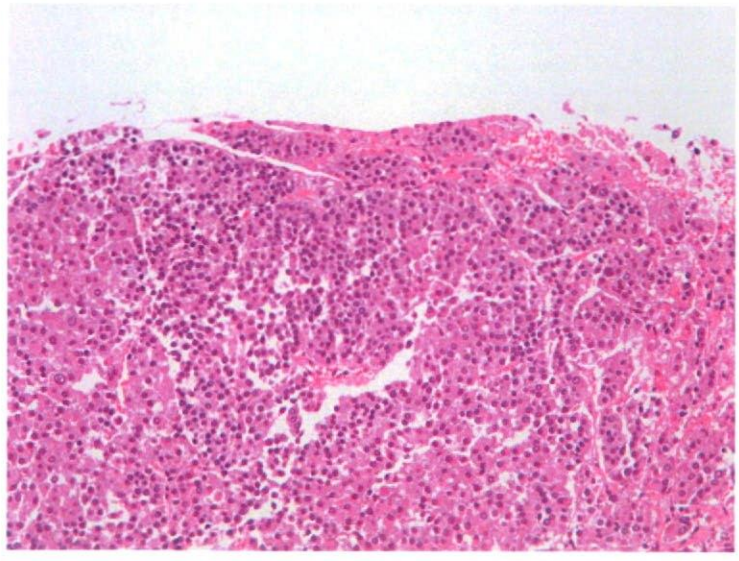
写真 10



Organ	:	Spleen
Dose	:	5000ppm
Animal No.	:	86
Sex	:	Male
Finding	:	Extramedullary hematopoiesis

HE Stain X100

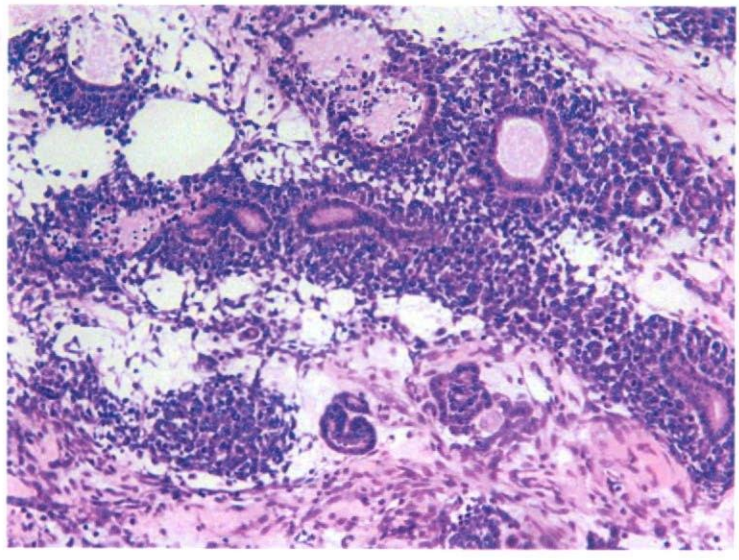
写真 11



Organ : Adrenal
Dose : 5000ppm
Animal No. : 590
Sex : Female
Finding : Malignant pheochromocytoma

HE Stain X100

写真 12



Organ : Kidney
Dose : 5000ppm
Animal No. : 593
Sex : Female
Finding : Nephroblastoma

HE Stain X100