

Table 12 Histopathological findings in rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks. (Continued)

ORGAN FINDING	SEX	FEMALE					
		TEST ARTICLE	CONTROL	0.04%	0.20%	1%	5%
		DOSE	GRADE	NO. OF ANIMALS	NO. OF ANIMALS	NO. OF ANIMALS	NO. OF ANIMALS
			- + + + + +	- + + + + +	- + + + + +	- + + + + +	- + + + + +
BRAIN			20	20	20	20	19
DILATATION' VENTRICLE			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
MINERALIZATION' VENTRICLE			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
SPINAL CORD			20	20	20	20	19
SWELLING' AXONAL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HEART			20	20	20	20	19
CARDIOMYOPATHY			20 0 0 0	19 1 0 0	20 0 0 0	20 0 0 0	18 1 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HEMORRHAGE' EPICARDIAL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
LUNG			20	20	20	20	19
CALCIFICATION' VESSEL			20 0 0 0	20 0 0 0	20 0 0 0	19 1 0 0	15 4 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
FOCAL FIBROSIS' ALVEOLAR WALL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
GRANULOMA			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HISTIOCYTOSIS' ALVEOLAR			20 0 0 0	17 3 0 0	19 1 0 0	20 0 0 0	18 1 0 0
TRACHEA			20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CELLULAR INFILTRATION' MONONUCLEAR CELL			19 1 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
DILATATION' GLAND' TRACHEAL			20 0 0 0	17 3 0 0	20 0 0 0	20 0 0 0	18 1 0 0

--:NOT REMARKABLE,+;SLIGHT,++;MODERATE,+++;MARKED

Table 12 Histopathological findings in rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks. (Continued)

ORGAN FINDING	SEX	TEST ARTICLE DOSE	FEMALE					
			CONTROL	0.04%	0.20%	1%	5%	
								GRADE
LIVER			20	20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CHOLANGITIS' EXTRAHEPATIC			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
DEPOSIT' PIGMENT' GLISSON'S SHEATH			20 0 0 0	19 0 1 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
DEPOSIT' PIGMENT' KUPFFER CELL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
FOCAL NECROSIS' HEPATOCELLULAR			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
FOCUS ALTERAD HEPATOCYTE' CLEAR CELL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
FOCUS ALTERAD HEPATOCYTE' VACUOLATED CELL			20 0 0 0	19 1 0 0	20 0 0 0	19 1 0 0	20 0 0 0	18 1 0 0
HEMATOPOIESIS' EXTRAMEDULLARY			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HYPERTROPHY' BILE DUCT			20 0 0 0	19 1 0 0	18 2 0 0	19 1 0 0	19 0 0 0	19 0 0 0
HYPERTROPHY' HEPATOCELLULAR			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
INCREASE' MITOTIC FIGURE' HEPATOCELLULAR			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
MICROGRANULOMA			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
NECROSIS' COAGULATIVE			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
SINGLE CELL NECROSIS' HEPATOCELLULAR			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
SPONGIOSIS HEPATIS			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
PANCREAS			20	20	20	20	20	19
ABSCESS			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
ATROPHY' ACINAR CELL' FOCAL			19 1 0 0	19 1 0 0	18 2 0 0	19 1 0 0	18 1 0 0	18 1 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL			20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
DEPOSIT' PIGMENT			20 0 0 0	20 0 0 0	19 1 0 0	20 0 0 0	20 0 0 0	19 0 0 0

--:NOT REMARKABLE,+;SLIGHT,++;MODERATE,+++;MARKED

Table 12 Histopathological findings in rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks. (Continued)

ORGAN FINDING	FEMALE					
	SEX TEST ARTICLE	GRADE				
	DOSE	CONTROL	0.04%	0.20%	1%	5%
GRADE	- + + + + +	- + + + + +	- + + + + +	- + + + + +	- + + + + +	- + + + + +
KIDNEY	NO.OF ANIMALS	20	20	20	20	19
CELL DEBRIS' INFLAMMATORY' PELVIS		17 3 0 0	18 2 0 0	19 1 0 0	17 3 0 0	17 2 0 0
CELLULAR INFILTRATION' INFLAMMATORY' PELVIS		20 0 0 0	19 1 0 0	19 1 0 0	19 1 0 0	19 0 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CHANGE' BASOPHILIC' RENAL TUBULE		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CHRONIC NEPHROPATHY		19 1 0 0	19 1 0 0	19 1 0 0	20 0 0 0	18 1 0 0
CYST		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
DEGENERATION' RENAL TUBULE' FOCAL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0
DILATATION' PELVIS		19 1 0 0	20 0 0 0	20 0 0 0	19 1 0 0	18 0 1 0
DILATATION' RENAL TUBULE		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
FOCUS' LYMPHOID CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HYALINE CAST		18 2 0 0	19 1 0 0	18 2 0 0	19 1 0 0	17 2 0 0
HYPERPLASIA' TRANSITIONAL CELL' PELVIS		19 1 0 0	19 1 0 0	19 1 0 0	15 5 0 0	18 1 0 0
MINERALIZATION' CORTICO-MEDULLARY JUNCTION		4 15 1 0	6 13 1 0	5 14 1 0	7 13 0 0	0 19 0 0
MINERALIZATION' PELVIS		9 11 0 0	12 7 1 0	14 5 1 0	11 8 1 0	11 6 2 0
NECROSIS' PAPILLARY		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
NECROSIS' RENAL TUBULE		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
PYKNOSIS' COLLECTING DUCT		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
URINARY BLADDER	NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' INFLAMMATORY		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
PROTEINACEOUS PLUG		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
THICKENING' MUCOSA		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
VACUOLIZATION' CYTOPLASMIC' MUCOSAL CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
SPLEEN	NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
DEPOSIT' HEMOSIDERIN		0 13 7 0	4 15 1 0**	1 16 3 0	1 16 3 0	2 12 5 0
HEMATOPOIESIS' EXTRAMEDULLARY		20 0 0 0	19 1 0 0	20 0 0 0	20 0 0 0	19 0 0 0
THYMUS	NO.OF ANIMALS	20	20	20	20	19
ATROPHY		5 13 2 0	13 7 0 0 *	15 5 0 0 **	14 6 0 0 *	10 9 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CYST		20 0 0 0	20 0 0 0	18 2 0 0	18 2 0 0	18 1 0 0
HEMORRHAGE		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
LYMPHOID HYPERPLASIA		20 0 0 0	20 0 0 0	20 0 0 0	19 1 0 0	19 0 0 0
NECROSIS		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0

--NOT REMARKABLE,+SLIGHT,++MODERATE,+++MARKED  
 \*: P<0.05, \*\*: P<0.01 (SIGNIFICANT DIFFERENCE FROM CONTROL)

Table 12 Histopathological findings in rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks. (Continued)

ORGAN FINDING	SEX TEST ARTICLE DOSE GRADE	FEMALE				
		CONTROL	0.04%	0.20%	1%	5%
		- + +++	- + +++	- + +++	- + +++	- + +++
MESENTERIC LN	NO.OF ANIMALS	20	20	20	20	19
ATROPHY' PARACORTEX		19 1 0 0	12 8 0 0 *	17 3 0 0	18 2 0 0	15 4 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CYST SINUSOIDAL		20 0 0 0	20 0 0 0	19 1 0 0	20 0 0 0	19 0 0 0
ERYTHROCYTES' SINUS		19 1 0 0	19 1 0 0	17 3 0 0	18 2 0 0	18 1 0 0
HYPERPLASIA' ENDOTHELIAL CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
SINUS HISTIOCYTOSIS		20 0 0 0	19 1 0 0	19 1 0 0	18 2 0 0	18 1 0 0
TONGUE	NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' INFLAMMATORY		20 0 0 0	19 1 0 0	20 0 0 0	20 0 0 0	19 0 0 0
PAROTID GLAND	NO.OF ANIMALS	20	20	20	S 20	19
CELLULAR INFILTRATION' MONONUCLEAR CELL		19 1 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
LACRIMAL GLAND	NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' INFLAMMATORY		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CELLULAR INFILTRATION' MONONUCLEAR CELL' PERIDUI		16 3 1 0	15 5 0 0	14 6 0 0	14 6 0 0	16 3 0 0
HARDERIAN ALTERATION		20 0 0 0	19 1 0 0	20 0 0 0	19 1 0 0	18 1 0 0
SUBMANDIBULAR LN	NO.OF ANIMALS	20	20	20	20	18
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 0 0 0
DEPOSIT' PIGMENT		16 4 0 0	18 2 0 0	12 8 0 0	15 5 0 0	15 3 0 0
ERYTHROCYTES' SINUS		19 1 0 0	20 0 0 0	19 1 0 0	20 0 0 0	17 1 0 0
HEMORRHAGE		19 1 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 0 0 0
HYPERPLASIA' LYMPHOCYTE		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 0 0 0
PLASMACYTOSIS		16 4 0 0	17 3 0 0	17 3 0 0	18 2 0 0	16 2 0 0
STOMACH	NO.OF ANIMALS	20	20	20	20	19
CYST' LAMINA PROPRIA		19 1 0 0	20 0 0 0	19 1 0 0	19 1 0 0	16 3 0 0
EDEMA' SUBMUCOSA'		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0
METAPLASIA' SQUAMOUS CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0
VACUOLIZATION' CYTOPLASMIC' SQUAMOUS CELL		18 2 0 0	19 1 0 0	19 1 0 0	19 1 0 0	18 1 0 0
DUODENUM	NO.OF ANIMALS	20	20	20	20	19
DILATATION' CYSTIC' CRYPT		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0

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LN:LYMPH NODE

\*: P<0.05 (SIGNIFICANT DIFFERENCE FROM CONTROL)

Table 12 Histopathological findings in rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks. (Continued)

ORGAN FINDING	SEX				
	TEST ARTICLE DOSE	FEMALE			
		CONTROL	0.04%	0.20%	1%
GRADE	- + +++	- + +++	- + +++	- + +++	- + +++
ILEUM					
CELLULAR INFILTRATION' LEUKEMIA CELL' SUBMUCOSA	20	20	20	20	19
	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CECUM					
NO.OF ANIMALS	20	20	20	20	19
CALCIFICATION' LAMINA PROPRIA	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
COLON					
NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
RECTUM					
NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
EDEMA' SUBMUCOSA	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
PITUITARY GLAND					
NO.OF ANIMALS	20	20	20	20	19
ADENOMA' PARS DISTALIS	20 0 0 0	19 1 0 0	19 1 0 0	18 2 0 0	17 2 0 0
CYST' PARS DISTALIS	19 1 0 0	20 0 0 0	17 3 0 0	20 0 0 0	19 0 0 0
CYST' PARS INTERMEDIA	20 0 0 0	19 1 0 0	17 3 0 0	19 1 0 0	19 0 0 0
HYPERPLASIA' PARS DISTALIS	17 3 0 0	19 1 0 0	17 3 0 0	18 2 0 0	15 4 0 0
THYROID GLAND					
NO.OF ANIMALS	20	20	20	20	19
ADENOMA' C-CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CELLULAR INFILTRATION' LEUKEMIA CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
DYSPLASIA	18 2 0 0	17 3 0 0	20 0 0 0	20 0 0 0	17 2 0 0
HYPERPLASIA' C-CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HYPERPLASIA' CYSTIC' FOLLICULAR CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HYPERPLASIA' FOCAL' FOLLICULAR CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HYPERTROPHY' FOLLICULAR CELL	20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
PARATHYROID GLAND					
NO.OF ANIMALS	19	20	20	20	19
ADENOMA	19 0 0 0	20 0 0 0	19 1 0 0	19 0 0 0	19 0 0 0
HYPERPLASIA' NODULAR	19 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0	19 0 0 0

-:NOT REMARKABLE;+:SLIGHT;+:MODERATE;+:MARKED

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ORGAN FINDING	SEX TEST ARTICLE DOSE GRADE	FEMALE				
		CONTROL	0.04%	0.20%	1%	5%
		- + + + + +	- + + + + +	- + + + + +	- + + + + +	- + + + + +
ADRENAL GLAND		20	20	20	20	19
APLASIA' MEDULLA' UNILATERAL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CYST'CORTEX		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0
GANGLIONEUROMA' BENIGN		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
HEMORRHAGE' CYSTIC' CORTICAL		20 0 0 0	19 1 0 0	20 0 0 0	18 2 0 0	19 0 0 0
HYPERPLASIA' NODULAR' CORTICAL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0
HYPERTROPHY' CORTICAL CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
VACUOLIZATION' CYTOPLASMIC' CORTICAL CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
OVARY		20	20	20	20	19
ATROPHY		20 0 0 0	20 0 0 0	20 0 0 0	19 1 0 0	19 0 0 0
CYST' CORPUS LUTEUM		20 0 0 0	19 1 0 0	19 1 0 0	19 1 0 0	19 0 0 0
CYST' FOLLICULAR		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0
DEPOSIT' PIGMENT		14 6 0 0	17 3 0 0	17 3 0 0	12 8 0 0	17 2 0 0
HEMORRHAGE		18 2 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
UTERUS		20	20	20	20	19
ATROPHY' ENDOMETRIUM		20 0 0 0	20 0 0 0	20 0 0 0	19 1 0 0	19 0 0 0
CELLULAR INFILTRATION' INFLAMMATORY' ENDOMETRIU		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0
DILATATION' ENDOMETRIAL GLAND		18 2 0 0	20 0 0 0	20 0 0 0	20 0 0 0	17 2 0 0
DILATATION' LUMEN		18 2 0 0	20 0 0 0	20 0 0 0	20 0 0 0	17 2 0 0
HYPERPLASIA' CYSTIC' ENDOMETRIUM		20 0 0 0	19 1 0 0	20 0 0 0	20 0 0 0	19 0 0 0
POLYP' ENDOMETRIAL STROMA		18 2 0 0	19 1 0 0	20 0 0 0	20 0 0 0	16 3 0 0
SKELETAL MUSCLE		20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
SUBCUTIS		20	20	20	20	19
HEMANGIOSARCOMA		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
SARCOMA' NOS		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
MAMMARY GLAND		19	20	20	20	16
CELLULAR INFILTRATION' INFLAMMATORY		19 0 0 0	19 1 0 0	20 0 0 0	20 0 0 0	16 0 0 0
DEGENERATION' ALVEOLAR/DUCTAL		19 0 0 0	18 2 0 0	20 0 0 0	20 0 0 0	16 0 0 0
DEPOSIT' PIGMENT		19 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	16 0 0 0
DILATATION' DUCT		19 0 0 0	18 2 0 0	20 0 0 0	20 0 0 0	16 0 0 0
MINERALIZATION		18 1 0 0	20 0 0 0	20 0 0 0	20 0 0 0	16 0 0 0

--NOT REMARKABLE, +SLIGHT, ++MODERATE, +++MARKED

Table 12 Histopathological findings in rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks. (Continued)

ORGAN FINDING	SEX		FEMALE			
	TEST ARTICLE DOSE	CONTROL	GRADE			
			0.04%	0.20%	1%	5%
			- + + + + + +	- + + + + + +	- + + + + + +	- + + + + + +
FEMUR BONE MARROW	NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
STERNUM BONE MARROW	NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
EYE	NO.OF ANIMALS	20	20	20	20	19
ATROPHY' RETINA' FOCAL		19 1 0 0	20 0 0 0	19 1 0 0	19 1 0 0	18 1 0 0
CATARACT		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	18 1 0 0
HARDERIAN GLAND	NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' MONONUCLEAR CELL		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
ADIPOSE TISSUE	NO.OF ANIMALS	20	20	20	20	19
LIPOMA' ABDOMINAL CAVITY		20 0 0 0	19 1 0 0	20 0 0 0	20 0 0 0	19 0 0 0
LIPOMA' PERIEPIDIDYMIS		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
CLITORAL GLAND	NO.OF ANIMALS	20	20	20	20	19
ABSCESS		20 0 0 0	20 0 0 0	18 2 0 0	20 0 0 0	19 0 0 0
CELLULAR INFILTRATION' INFLAMMATORY		15 5 0 0	17 3 0 0	16 4 0 0	16 4 0 0	16 3 0 0
DILATATION' DUCT		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	17 1 1 0
LYMPH NODE	NO.OF ANIMALS	20	20	20	20	19
CELLULAR INFILTRATION' LEUKEMIA CELL' ABDOMINAL LN		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0
PLASMACYTOSIS' POPLITEAL LN		20 0 0 0	20 0 0 0	20 0 0 0	20 0 0 0	19 0 0 0

-NOT REMARKABLE,+SLIGHT,++MODERATE,+++MARKED  
LN:LYMPH NODE

Table 13 Incidence of histopathological findings in renal pelvis of rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks.

SEX	ORGAN FINDING	TEST ARTICLE		CONTROL		0.04%		0.20%		1%		5%	
		DOSE	GRADE	-	+	-	+	-	+	-	+	-	+
MALE	KIDNEY			18	7/18	20	8/20	20	5/20	20	8/20	20	15/19*
	CELL DEBRIS 'INFLAMMATORY' PELVIS			11	6	15	5	17	3	13	7	8	10
	CELLULAR INFILTRATION 'INFLAMMATORY' PELVIS			15	2	20	0	17	2	18	2	14	5
	HYPERPLASIA 'TRANSITIONAL CELL' PELVIS			15	2	16	4	17	3	18	2	11	8
	MINERALIZATION 'PELVIS			17	0	15	5	17	3	16	4	6	12
	INCIDENCE OF ANIMALS WITH FINDINGS IN RENAL PELVIS			7/18		8/20		5/20		8/20		15/19*	
FEMALE	KIDNEY			20	20	20	20	20	20	20	20	20	19
	CELL DEBRIS 'INFLAMMATORY' PELVIS			17	3	18	2	19	1	17	3	17	2
	CELLULAR INFILTRATION 'INFLAMMATORY' PELVIS			20	0	19	1	19	1	19	1	19	0
	HYPERPLASIA 'TRANSITIONAL CELL' PELVIS			19	1	19	1	19	1	15	5	18	1
	MINERALIZATION 'PELVIS			9	11	12	7	14	5	11	8	11	6
	INCIDENCE OF ANIMALS WITH FINDINGS IN RENAL PELVIS			11/20		8/20		7/20		11/20		8/19	

\*: P<0.05 (SIGNIFICANT DIFFERENCE FROM CONTROL)



Appendix 1 Macroscopic findings of sacrificed rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks.

SEX	TEST ARTICLE AND DOSE	ANIMAL NO.	ORGAN	FINDING
MALE	CONTROL	1114	SUBCUTIS	MASS' LEFT CHEEK
		1115	SUBCUTIS	MASS' RIGHT ABDOMEN
	5%	1502	APPEARANCE FEMUR	STAINING' UROGENITAL REGION COLORED' YELLOWISH
FEMAL	5%	2517	APPEARANCE LIVER	STAINING' UROGENITAL REGION ENLARGEMENT FOCUS' RED
			PANCREAS ABDOMINAL CAVITY LYMPH NODE	DILATATION' EXTRAHEPATIC BILE DUCT ENLARGEMENT ENLARGED' PERIPANCREATIC

Appendix 2 Histopathological findings of sacrificed rats treated with the enzymatically-decomposed rutin by dietary administration for 52 weeks.

TEST ARTICLE AND DOSE	ANIMAL NO.	ORGAN	FINDING	GRADE		
CONTROL	1114	KIDNEY	CYST	+		
			MINERALIZATION' PELVIS	+		
			DEPOSIT' HEMOSIDERIN	+		
			ATROPHY	+		
			CELLULAR INFILTRATION' MONONUCLEAR CELL	+		
		PAROTID GLAND	HEMORRHAGE	+		
			HEMANGIOSARCOMA	+		
		SUBMANDIBULAR LN				
			SUBCUTIS			
		5%	1502	PANCREAS	DEPOSIT' PIGMENT	+
					HEMATOPOIESIS' EXTRAMEDULLARY	+
				SPLEEN	CYST' PARS INTERMEDIA	+
					VACUOLIZATION' CYTOPLASMIC' EPITHELIAL CELL	+
				PITUITARY GLAND	SARCOMA' NOS	+
					CELLULAR INFILTRATION' MONONUCLEAR CELL	+
EPIDIDYMIS						
	PREPUTIAL GLAND					
2517	HEART			LIVER	CARDIOMYOPATHY	+
					DILATATION' GLAND' TRACHEAL	+
		KIDNEY	CELLULAR INFILTRATION' LEUKEMIA CELL	+		
			MINERALIZATION' PELVIS	++		
		URINARY BLADDER	CELL DEBRIS' INFLAMMATORY' PELVIS	+		
			PROTEINACEOUS PLUG	+		
		SPLEEN	HEMATOPOIESIS' EXTRAMEDULLARY	+		
			CELLULAR INFILTRATION' LEUKEMIA CELL	+		
		THYMUS	ATROPHY	+		
			MESENTERIC LN	++		
		EPIDIDYMIS	VACUOLIZATION' CYTOPLASMIC' EPITHELIAL CELL	+		
			FEMUR BONE MARROW	++		
		STERNUM BONE MARROW	CELLULAR INFILTRATION' LEUKEMIA CELL	++		
			PREPUTIAL GLAND	CELLULAR INFILTRATION' MONONUCLEAR CELL	+	
		ABSCSS				
2517	HEART	LIVER	HEMORRHAGE' EPICARDIAL	+		
			NECROSIS' COAGULATIVE	+		
		PANCREAS	CHOLANGITIS' EXTRAHEPATIC	++		
			KIDNEY	HYPERTROPHIA' BILE DUCT	+	
		ABSCSS				
		PANCREAS	NECROSIS' RENAL TUBULE	+		
			KIDNEY	MINERALIZATION' CORTICO-MEDULLARY JUNCTION	+	
		THYMUS	NECROSIS	++		
			STOMACH	EDEMA' SUBMUCOSA'	++	
		ADRENAL GLAND	HYPERTROPHY' CORTICAL CELL	++		
			UTERUS	CELLULAR INFILTRATION' INFLAMMATORY' ENDOMETRIUM	+	

--NOT REMARKABLE +:SLIGHT. ++:MODERATE.+++MARKED LN:LYMPH NODE

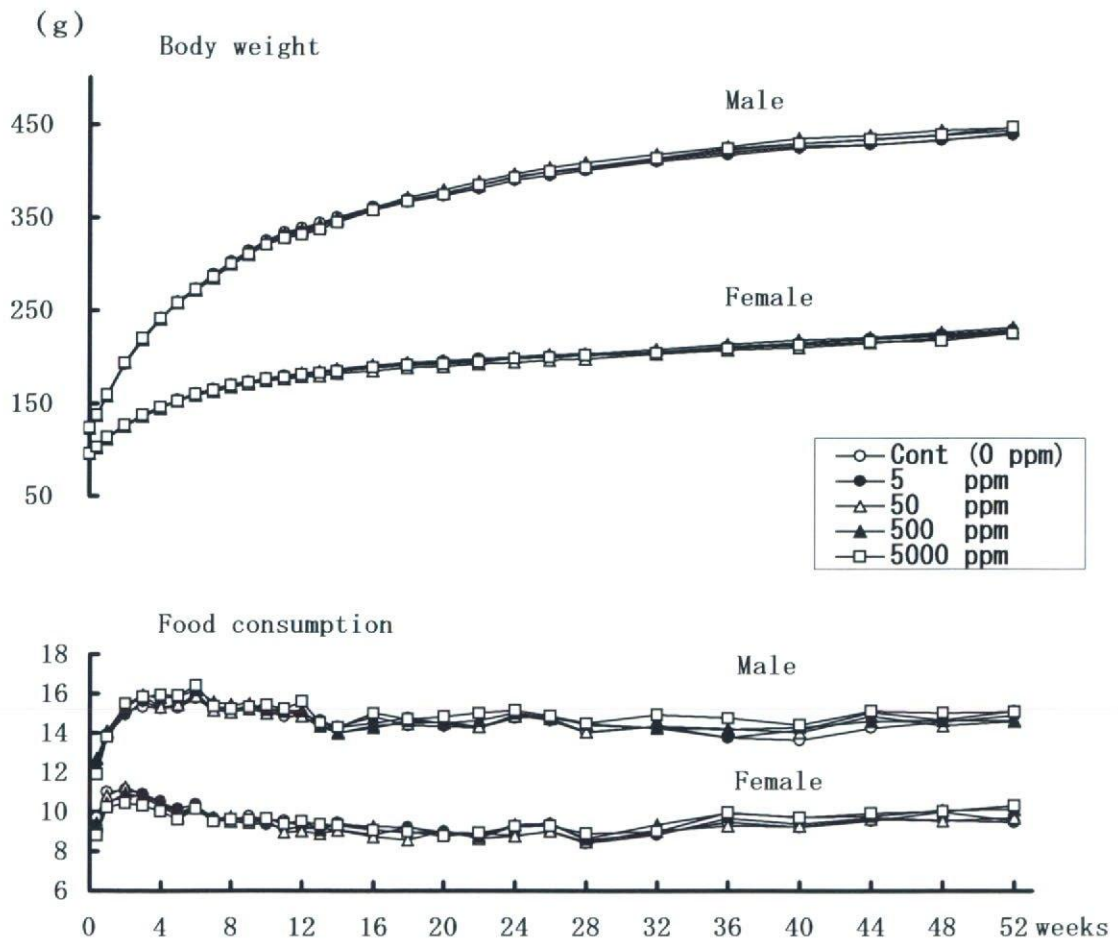


図1 体重及び摂餌量の推移 (ジャマイカカシヤ抽出物のラットによる1年間反復投与毒性試験)

表1 平均摂餌量及び平均被験物質摂取量(ジャマイカカussia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(ジャマイカカシヤ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 <sup>6</sup> /μl	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	fl	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 <sup>6</sup> /μl	0.53 ± 0.10	0.57 ± 0.08	0.56 ± 0.07	0.53 ± 0.10	0.55 ± 1.20
WBC	10 <sup>3</sup> /μl	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(ジャマイカカシヤ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 <sup>6</sup> /μl	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	fl	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 <sup>6</sup> /μl	0.47 ± 0.10	0.44 ± 0.10	0.46 ± 0.17	0.46 ± 0.11	0.48 ± 0.13
WBC	10 <sup>3</sup> /μl	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 **
AIT	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, AIT: 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	**
AIT	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, AIT: 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 <sup>1)</sup>						Ketone body <sup>2)</sup>			Glucose <sup>3)</sup>		Occult blood				Billrubin		Urobilinogen <sup>4)</sup>			
		6.0	6.5	7.0	7.5	8.0	-	±	+	++	+++	+4	-	±	+	-	+	-	±	+	++	+++	-	±	0.1	1	2
<b>Male</b>																											
Cont.(0 ppm)	20	1	11	7	1			4	15	1	0	5	14	1	20	19	0	1	0	0	0	20			20		20
5 ppm	20	1	6	9	4			4	14	2	1	5	14	1	20	20	0	0	0	0	0	20			20		20
50 ppm	20	2	7	5	5			3	15	2	0	4	12	4	20	20	0	0	0	1	1	20			20		20
500 ppm	20	2	6	7	5			2	14	4	0	3	13	4	20	18	0	0	1	1	1	20			20		20
5000 ppm	20	0	7	8	5			1	5	12	2	3	15	2	20	19	1	0	0	0	0	20			20		20
<b>Female</b>																											
Cont.(0 ppm)	20	7	9	3	1	0		2	15	3	0	16	4	20	19	1						20			20		20
5 ppm	20	3	14	2	0	1		0	16	4	0	14	6	20	20	0						20			20		20
50 ppm	20	2	13	4	1	0		2	14	4	0	15	5	20	20	0						20			20		20
500 ppm	20	4	13	1	0	2		0	12	8	0	13	7	20	20	0						20			20		20
5000 ppm	19	3	9	6	1	0		0	2	13	4	14	5	19	19	0						19			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) Ehrlich unit /dL

Significantly different from the contrl: \*\*P<0.01



表7 雄の臓器重量(ジャマイカカ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.	5	50	500	5000	Cont.	5	50	500	5000
		(0 ppm)	ppm	ppm	ppm	ppm	(0 ppm)	ppm	ppm	ppm	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 <sup>##</sup>	12		12	18 <sup>#</sup>		
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	1	
	+	0		0	0	18		0	0	17	
	++	0		0	0	1		0	0	0	
	All (>±)	0		0	4 <sup>#</sup>	20 <sup>**##</sup>		0	0	18 <sup>**##</sup>	
Proliferation, bile ductular	±	0		0	0	20		14	17	14	13
	+	20		20	18	0		2	2	4	0
	++	0		0	2	0		0	1	0	
	All (>±)	20		20	20	20 <sup>##</sup>		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 <sup>**##</sup>		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 <sup>**##</sup>	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 <sup>*#</sup>	0		0	6 <sup>**##</sup>		
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). <sup>#</sup>P<0.05, <sup>##</sup>P<0.01(Mann-whitney u test)

表9-2 病理組織学的検査(全動物)

副腎、骨、骨髓、精巢上体、眼球、造血系、ハーダー腺、心臓:ジャマイカカク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
<b>Adrenal</b>											
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, MALIGNANT	Present	0				1	0				1
	Present	0				0	0				1
	All	0				1	0				2
<b>Bone+Bone marrow, femoral</b>											
Hematopoiesis, increased	++	0				0	0				1
Microgranuloma, bone marrow	±	1				1	9				8
<b>Bone+Bone marrow, sternal</b>											
Degeneration, chondromucinous	±	7				5	8				4
Hematopoiesis, increased	++	0				0	0				1
Microgranuloma, bone marrow	±	4				2	9				5
	All (>±)	4				2	9				5
<b>Epididymis</b>											
Cell infiltration, interstitial	±	0				1					
Hypospermia	+++	0				1					
<b>Eye</b>											
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
<b>Hemolymphoreticular(all sites)</b>											
LEUKEMIA, LARGE GRANULAR LYMPHOCYTI	Present	0				0	0			1a)	0
<b>Harderian gland</b>											
Cell infiltration, interstitial	±	3				4	5				6
Pigmentation, intra-acinar	±	14				14	15				12
<b>Heart</b>											
Mineralization, myocardial	±	0				0	0				1
Cardiomyopathy	±	6				9	13				13
	+	14				11	0				0
	All (>±)	20				20	13				13
<b>Lymph node, mesenteric</b>											
Accumulation, macrophage	±	0				0	0				4
	+	20				19	20				15
	++	0				1	0				0
	All (>±)	20				20	20				19
<b>Lung(bronchus)</b>											
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