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H. 知的財産権の出願登録状況

1. 特許取得
該当なし。
2. 実用新案登録
該当なし。
3. その他
該当なし。

Table 1. Food consumption and intake of ferulic acid

Sex	Dose (%)	Food consumption	Mean intake of ferulic acid		Mean total intake of ferulic acid
		(g/rat/day)	(mg/rat/day)	(mg/kg/day)	(g/rat)
Male	0	13.9 ± 1.3 ^a	–	–	–
	0.5	12.2 ± 2.4 ^b	61.0	128.5	45.3
	1.0	12.4 ± 2.3 ^c	124.0	260.3	92.0
	2.0	14.5 ± 3.0	290.0	645.5	215.2
Female	0	9.3 ± 1.1	–	–	–
	0.5	7.7 ± 2.9 ^c	38.5	129.7	28.6
	1.0	7.3 ± 2.5 ^b	73.0	254.8	54.2
	2.0	9.2 ± 3.6	184.0	687.3	136.5

^a Means ± SD.

^{b,c} Significantly different from the “0%” group (^b P < 0.001 and ^c P < 0.005).

Table 2. Hematological data in F344 male rats fed with ferulic acid for 106 weeks

Item	Dose level of ferulic acid (%)			
	0	0.5	1.0	2.0
WBC	($\times 10^2/\mu\text{L}$) 35.6 \pm 12.6 ^a	53.5 \pm 23.1	62.3 \pm 26.6	50.0 \pm 7.6
RBC	($\times 10^4/\mu\text{L}$) 853.9 \pm 70.1	872.1 \pm 166.6	901.7 \pm 110.6	922.4 \pm 83.7
Hb	(g/dL) 14.2 \pm 1.0	14.5 \pm 1.3	15.4 \pm 1.7	15.2 \pm 1.5
Ht	(%) 45.3 \pm 3.0	44.6 \pm 6.9	48.0 \pm 4.4	47.1 \pm 3.8
MCV	(fL) 53.2 \pm 3.4	51.7 \pm 4.0	53.4 \pm 2.4	51.1 \pm 1.5
MCH	(pg) 16.6 \pm 0.9	17.0 \pm 2.6	17.1 \pm 0.7	19.4 \pm 9.2
MCHC	(g/dL) 34.2 \pm 9.4	32.9 \pm 3.9	31.9 \pm 0.6	32.2 \pm 0.7
PLT	($\times 10^4/\mu\text{L}$) 54.0 \pm 12.9	68.5 \pm 15.3	69.1 \pm 10.4	59.6 \pm 6.7
Differential cell counts (%)				
Neuro	65.6 \pm 4.8	64.5 \pm 8.9	73.9 \pm 9.4	68.1 \pm 3.3
Eosino	5.4 \pm 3.6	5.0 \pm 8.2	2.1 \pm 1.1	3.2 \pm 3.0
Baso	0.1 \pm 0.2	0.7 \pm 1.9	0.0 \pm 0.1	0.1 \pm 0.1
Lymph	22.0 \pm 6.8	24.8 \pm 7.6	18.8 \pm 8.3	21.7 \pm 4.1
Mono	7.0 \pm 4.7	5.0 \pm 3.0	5.1 \pm 4.5	7.0 \pm 3.6

^a Means \pm SD (10 rats from each group).

Table 3. Hematological data in F344 female rats fed with ferulic acid for 106 weeks

Item	Dose level of ferulic acid (%)			
	0	0.5	1.0	2.0
WBC	($\times 10^2/\mu\text{L}$) 39.3 \pm 18.3 ^a	40.3 \pm 20.0	39.9 \pm 17.1	29.4 \pm 74.0
RBC	($\times 10^4/\mu\text{L}$) 801.5 \pm 57.2	821.2 \pm 23.1	804.4 \pm 24.4	828.9 \pm 32.8
Hb	(g/dL) 14.2 \pm 1.3	14.8 \pm 0.4	14.6 \pm 0.3	14.9 \pm 0.3
Ht	(%) 44.4 \pm 4.3	46.0 \pm 1.5	45.2 \pm 1.0	46.4 \pm 1.1
MCV	(fL) 55.4 \pm 4.2	56.0 \pm 1.8	56.3 \pm 0.9	56.0 \pm 1.4
MCH	(pg) 17.8 \pm 1.2	18.1 \pm 0.5	18.1 \pm 0.3	18.0 \pm 0.5
MCHC	(g/dL) 32.1 \pm 0.5	32.3 \pm 0.4	32.2 \pm 0.3	32.2 \pm 0.5
PLT	($\times 10^4/\mu\text{L}$) 46.4 \pm 7.5	49.3 \pm 6.8	50.4 \pm 6.5	50.1 \pm 3.8
Differential cell counts (%)				
Neutro	72.9 \pm 6.6	77.2 \pm 4.9	70.0 \pm 7.0	68.6 \pm 4.4
Eosino	2.0 \pm 1.0	2.2 \pm 0.6	3.0 \pm 3.2	3.6 \pm 3.4
Baso	0.2 \pm 0.3	0.1 \pm 0.1	0.1 \pm 0.2	0.1 \pm 0.4
Lymph	21.0 \pm 6.7	18.2 \pm 5.0	23.9 \pm 5.4	25.4 \pm 4.8
Mono	4.0 \pm 3.3	2.4 \pm 1.9	3.0 \pm 2.8	2.2 \pm 1.6

^a Means \pm SD (10 rats from each group).

Table 4. Serum biochemical data in F344 male rats fed with ferulic acid for 106 weeks

Item	Dose level of ferulic acid (%)	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
TP (g/dL)		6.5 ± 0.3 ^a	6.2 ± 0.3	6.0 ± 0.3 ^b	6.1 ± 0.3 ^c
Alb (g/dL)		2.8 ± 0.1	2.7 ± 0.2	2.6 ± 0.1	2.7 ± 0.2
A/G		0.78 ± 0.04	0.75 ± 0.08	0.75 ± 0.05	0.80 ± 0.03
AST (IU/dL)		124.2 ± 29.4	110.6 ± 39.1	77.7 ± 15.8 ^e	80.8 ± 45.3 ^c
ALT (IU/dL)		63.8 ± 18.8	54.4 ± 13.6	41.3 ± 10.0 ^b	40.7 ± 6.4 ^b
ALP (IU/dL)		811.4 ± 116.0	770.4 ± 130.7	647.0 ± 189.2	563.8 ± 100.4 ^b
γ-GTP (IU/dL)		7.0 ± 2.9	12.6 ± 13.9	8.7 ± 7.5	8.5 ± 4.0
T.Bil (mg/dL)		0.10 ± 0.00	0.11 ± 0.03	0.10 ± 0.00	0.10 ± 0.00
T-Cho (mg/dL)		162.1 ± 34.2	171.4 ± 55.4	161.6 ± 42.8	144.7 ± 28.3
TG (mg/dL)		116.0 ± 37.6	135.1 ± 41.5	171.0 ± 55.7 ^e	158.4 ± 38.9
BUN (mg/dL)		16.2 ± 1.5	15.8 ± 1.9	15.2 ± 1.6	13.9 ± 2.3
CRE (mg/dL)		0.35 ± 0.04	0.33 ± 0.05	0.32 ± 0.03	0.34 ± 0.03
Glu (mg/dL)		123.3 ± 17.3	136.3 ± 11.6	129.6 ± 11.1	125.7 ± 11.5
Na ₂ (mEq/dL)		ND	ND	ND	ND
K (mEq/dL)		5.3 ± 0.8	5.7 ± 1.3	5.1 ± 0.3	4.7 ± 0.5
Cl (mEq/dL)		ND	ND	ND	ND
Ca (mEq/dL)		10.7 ± 0.4	10.9 ± 0.7	10.6 ± 0.2	10.6 ± 0.2

^a Means ± SD (10 rats from each group). ND = not determined.

^{b,c} Significantly different from the "0%" group (^b P < 0.01 and ^c P < 0.05).

Table 5. Serum biochemical data in F344 female rats fed with ferulic acid for 106 weeks

Item	Dose level of ferulic acid (%)			
	0	0.5	1.0	2.0
TP	(g/dL) 6.7 ± 0.6 ^a	6.6 ± 0.4	6.9 ± 0.4	6.7 ± 0.3
Alb	(g/dL) 3.1 ± 0.4	3.1 ± 0.2	3.3 ± 0.2	3.2 ± 0.2
A/G	0.85 ± 0.11	0.89 ± 0.06	0.91 ± 0.03	0.94 ± 0.04 ^b
AST	(IU/dL) 123.8 ± 26.3	101.2 ± 35.3	74.4 ± 15.3 ^c	69.8 ± 9.9 ^c
ALT	(IU/dL) 62.5 ± 7.2	49.5 ± 8.2 ^c	45.1 ± 3.8 ^c	44.3 ± 2.8 ^c
ALP	(IU/dL) 715.5 ± 193.2	538.9 ± 82.8 ^d	556.4 ± 61.8 ^b	419.9 ± 56.6 ^c
γ-GTP	(IU/dL) 2.1 ± 1.2	1.5 ± 0.5	1.2 ± 0.4	2.2 ± 0.8
T.Bil	(mg/dL) 0.11 ± 0.03	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00
T-Cho	(mg/dL) 136.7 ± 20.7	126.1 ± 14.9	132.2 ± 13.1	147.0 ± 13.0
TG	(mg/dL) 151.9 ± 123.2	178.3 ± 57.7	242.7 ± 109.6	106.7 ± 55.3
BUN	(mg/dL) 18.1 ± 1.6	17.5 ± 1.1	17.7 ± 1.3	15.9 ± 2.2 ^b
CRE	(mg/dL) 0.28 ± 0.02	0.28 ± 0.02	0.26 ± 0.02	0.26 ± 0.02
Glu	(mg/dL) 128.1 ± 19.1	121.4 ± 14.5	126.2 ± 14.3	128.0 ± 9.0
Na	(mEq/dL) ND	ND	ND	ND
K	(mEq/dL) 4.9 ± 0.8	4.8 ± 0.3	4.9 ± 0.4	4.9 ± 0.5
Cl	(mEq/dL) ND	ND	ND	ND
Ca	(mEq/dL) 10.9 ± 0.8	10.7 ± 0.3	10.9 ± 0.4	10.9 ± 0.4

^a Means ± SD (10 rats from each group). ND = not determined.

^{b,c,d} Significantly different from the "0%" group (^b P < 0.05, ^c P < 0.001, and ^d P < 0.01).

Table 6. Final body weight and organ weights data in F344 male rats fed with ferulic acid for 106 weeks

Item	Dose level of ferulic acid (%)			
	0	0.5	1.0	2.0
Body weight (g)	453.5 ± 39.5 ^a	474.6 ± 64.0	476.3 ± 29.0	449.2 ± 33.0
Absolute organ weight (g)				
Brain	2.39 ± 0.33	2.40 ± 0.14	2.46 ± 0.18	2.49 ± 0.19
Lungs	1.94 ± 0.26	2.08 ± 1.11	2.03 ± 0.32	2.16 ± 0.47
Heart	1.20 ± 0.10	1.24 ± 0.11	1.32 ± 0.15 ^b	1.25 ± 0.12
Spleen	1.19 ± 0.59	1.37 ± 0.70	1.35 ± 0.43	1.44 ± 1.35
Pancreas	0.77 ± 0.54	0.85 ± 0.45	0.65 ± 0.21	0.69 ± 0.12
Liver	15.71 ± 2.25	16.76 ± 2.11	17.55 ± 2.23 ^c	16.37 ± 1.79
Adrenals	0.085 ± 0.126	0.082 ± 0.064	0.077 ± 0.065	0.069 ± 0.037
Kidneys	2.94 ± 0.47	2.96 ± 0.29	3.07 ± 0.31	3.08 ± 0.39
Testes	4.59 ± 1.62	4.92 ± 1.16	5.53 ± 1.62 ^d	4.61 ± 1.18

^a Means ± SD.

^{b,c,d} Significantly different from the "0%" group (^b P < 0.001, ^c P < 0.01, and ^d P < 0.05).

Table 7. Relative organ weights data in F344 male rats fed with ferulic acid for 106 weeks

Item	Dose level of ferulic acid (%)			
	0	0.5	1.0	2.0
Relative organ weight (g/100g B.W.)				
Brain	0.53 ± 0.09 ^a	0.51 ± 0.06	0.52 ± 0.05	0.56 ± 0.05
Lungs	0.43 ± 0.08	0.45 ± 0.28	0.43 ± 0.06	0.48 ± 0.12
Heart	0.27 ± 0.02	0.27 ± 0.03	0.28 ± 0.03	0.28 ± 0.03
Spleen	0.26 ± 0.14	0.29 ± 0.16	0.28 ± 0.09	0.33 ± 0.34
Pancreas	0.17 ± 0.14	0.18 ± 0.10	0.14 ± 0.05	0.16 ± 0.03
Liver	3.46 ± 0.38	3.56 ± 0.47	3.68 ± 0.38	3.65 ± 0.33
Adrenals	0.019 ± 0.033	0.017 ± 0.013	0.016 ± 0.012	0.015 ± 0.007
Kidneys	0.65 ± 0.12	0.63 ± 0.08	0.65 ± 0.06	0.69 ± 0.09
Testes	1.02 ± 0.35	1.06 ± 0.30	1.16 ± 0.34	1.03 ± 0.26

^a Means ± SD.

Table 8. Final body weight and organ weights data in F344 female rats fed with ferulic acid for 106 weeks

Item	Dose level of ferulic acid (%)			
	0	0.5	1.0	2.0
Body weight (g)	278.1 ± 25.7 ^a	296.8 ± 28.4 ^b	286.5 ± 30.4	267.7 ± 24.9
Absolute organ weight (g)				
Brain	2.18 ± 0.13	2.21 ± 0.13	2.22 ± 0.13	2.19 ± 0.10
Lungs	1.63 ± 0.28	1.67 ± 0.32	1.59 ± 0.25	1.49 ± 0.20
Heart	0.840 ± 0.078	0.850 ± 0.065	0.829 ± 0.054	0.786 ± 0.052 ^c
Spleen	0.90 ± 1.43	1.10 ± 2.77	0.82 ± 0.68	0.50 ± 0.13
Pancreas	0.51 ± 0.11	0.47 ± 0.10	0.42 ± 0.12 ^d	0.43 ± 0.08 ^e
Liver	9.39 ± 1.50	9.83 ± 1.07	9.94 ± 1.72	8.89 ± 0.82
Adrenals	0.067 ± 0.010	0.067 ± 0.020	0.059 ± 0.008 ^e	0.045 ± 0.007 ^d
Kidneys	1.89 ± 0.24	1.98 ± 0.22	1.90 ± 0.19	1.81 ± 0.16
Ovaries	0.118 ± 0.028	0.122 ± 0.039	0.115 ± 0.045	0.147 ± 0.293
Uterus	1.43 ± 0.35	1.42 ± 0.49	1.59 ± 1.47	1.36 ± 0.32

^a Means ± SD.

^{b,c,d,e} Significantly different from the "0%" group (^b P < 0.05, ^c P < 0.01, ^d P < 0.001, and ^e P < 0.05).

Table 9. Relative organ weights data in F344 female rats fed with ferulic acid for 106 weeks

Item	Dose level of ferulic acid (%)			
	0	0.5	1.0	2.0
Relative organ weight (g/100g B.W.)				
Brain	0.79 ± 0.09 ^a	0.75 ± 0.10	0.78 ± 0.11	0.83 ± 0.09
Lungs	0.59 ± 0.14	0.57 ± 0.15	0.56 ± 0.12	0.56 ± 0.09
Heart	0.30 ± 0.04	0.29 ± 0.04	0.29 ± 0.04	0.30 ± 0.03
Spleen	0.33 ± 0.52	0.37 ± 0.93	0.30 ± 0.28	0.19 ± 0.05
Pancreas	0.18 ± 0.04	0.16 ± 0.04	0.15 ± 0.05 ^b	0.16 ± 0.04
Liver	3.38 ± 0.42	3.34 ± 0.45	3.50 ± 0.65	3.34 ± 0.37
Adrenals	0.024 ± 0.004	0.023 ± 0.011	0.021 ± 0.003	0.017 ± 0.003 ^c
Kidneys	0.68 ± 0.09	0.68 ± 0.13	0.67 ± 0.10	0.68 ± 0.08
Ovaries	0.043 ± 0.010	0.042 ± 0.020	0.041 ± 0.019	0.055 ± 0.106
Uterus	0.52 ± 0.14	0.48 ± 0.16	0.59 ± 0.65	0.51 ± 0.13

^a Means ± SD.

^{b,c} Significantly different from the "0%" group (^b P < 0.01 and ^c P < 0.001).

Table 10. Incidence of proliferative lesions in male rats fed with ferulic acid that were found dead during the study

Organs	Lesions	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
Lung	Alveolar cell hyperplasia	1 / 10 (10%)	1 / 18 (6%)	1 / 18 (6%)	0 / 10 (0%)
Forestomach	Hyperplasia	1 / 10 (10%)	1 / 18 (6%)	0 / 18 (0%)	0 / 10 (0%)
Liver	Intrahepatic bile duct proliferation	10 / 10 (100%)	18 / 18 (100%)	17 / 18 (94%)	9 / 10 (90%)
Prostate	Adenocarcinoma	0 / 10 (0%)	0 / 18 (0%)	1 / 18 (6%)	0 / 10 (0%)
Testis	Leydig cell tumor	7 / 10 (70%)	12 / 18 (67%)	16 / 18 (89%)	9 / 10 (70%)
Hematopoietic system	Leukemia	2 / 10 (20%)	2 / 18 (11%)	9 / 18 (50%)	2 / 10 (20%)
Pituitary gland	Adenoma	1 / 10 (10%)	0 / 18 (0%)	0 / 18 (0%)	0 / 10 (0%)
Thyroid	C-cell hyperplasia ^a	2 / 10 (20%)	3 / 18 (17%)	2 / 18 (11%)	0 / 10 (0%)
	C-cell adenoma	0 / 10 (0%)	2 / 18 (11%)	1 / 18 (6%)	2 / 10 (20%)
	C-cell adenocarcinoma	0 / 10 (0%)	0 / 18 (0%)	2 / 18 (11%)	1 / 10 (10%)
Parathyroid gland	Hyperplasia	1 / 10 (10%)	0 / 18 (0%)	0 / 18 (0%)	0 / 10 (0%)
Adrenal gland	Medullary hyperplasia	0 / 10 (0%)	1 / 18 (6%)	0 / 18 (0%)	0 / 10 (0%)
	Pheochromocytoma	0 / 10 (0%)	1 / 18 (6%)	0 / 18 (0%)	1 / 10 (10%)
Pancreas	Islet cell tumor	1 / 10 (10%)	1 / 18 (6%)	1 / 18 (6%)	0 / 10 (0%)
Bone	Osteosarcoma (肺転移)	0 / 10 (0%)	0 / 18 (0%)	0 / 18 (0%)	1 / 10 (10%)
Mesothelium	Mesothelioma	1 / 10 (10%)	1 / 18 (6%)	1 / 18 (6%)	1 / 10 (10%)
Skin	Fibroma	0 / 10 (0%)	4 / 18 (22%)	3 / 18 (17%)	4 / 10 (40%) ^a
	Schwannoma	0 / 10 (0%)	1 / 18 (6%)	0 / 18 (0%)	0 / 10 (0%)
	Lipoma	0 / 10 (0%)	1 / 18 (6%)	0 / 18 (0%)	0 / 10 (0%)
	Squamous cell carcinoma	0 / 10 (0%)	0 / 18 (0%)	2 / 18 (11%)	0 / 10 (0%)
	Sebaceous carcinoma	1 / 10 (10%)	0 / 18 (0%)	0 / 18 (0%)	0 / 10 (0%)

^a Significantly different from the "0%" group (P < 0.05).

Table 11. Incidence of proliferative lesions in female rats fed with ferulic acid that were found dead during the study

Organs	Lesions	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
Tongue	Hyperplasia	0 / 10 (0%)	0 / 10 (0%)	1 / 7 (14%)	0 / 13 (0%)
	Papilloma	0 / 10 (0%)	0 / 10 (0%)	0 / 7 (0%)	2 / 13 (15%)
Forestomach	Hyperplasia	0 / 10 (0%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
	Papilloma	0 / 10 (0%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
Small intestine	Adenocarcinoma	0 / 10 (0%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
Liver	Intrahepatic bile duct proliferation	5 / 10 (50%)	3 / 10 (30%)	0 / 7 (0%) ^a	1 / 13 (8%) ^a
	Cholangiofibroma	0 / 10 (0%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
Uterus	Stromal polyp	0 / 10 (0%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
	Adenocarcinoma	0 / 10 (0%)	0 / 10 (0%)	0 / 7 (0%)	0 / 13 (0%)
	Endometrial stromal sarcoma	0 / 10 (0%)	0 / 10 (0%)	0 / 7 (0%)	2 / 13 (51%)
Ovary	Luteoma	0 / 10 (0%)	0 / 10 (0%)	0 / 7 (0%)	0 / 13 (0%)
	Granulosa cell tumor	0 / 10 (0%)	0 / 10 (0%)	0 / 7 (0%)	0 / 13 (0%)
Hematopoietic system	Leukemia	0 / 10 (0%)	0 / 10 (0%)	2 / 7 (29%)	3 / 13 (23%)
Pituitary gland	Adenoma	1 / 10 (10%)	1 / 10 (10%)	0 / 7 (0%)	1 / 13 (8%)
Thyroid	C-cell hyperplasia	2 / 10 (20%)	2 / 10 (20%)	0 / 7 (0%)	1 / 13 (8%)
	C-cell adenoma	0 / 10 (0%)	0 / 10 (0%)	0 / 7 (0%)	0 / 13 (0%)
Adrenal gland	Pheochromocytoma	0 / 10 (0%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
	Malignant pheochromocytoma (肺、肝転移)	0 / 10 (0%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
Skin	Fibroma	0 / 10 (0%)	2 / 10 (20%)	3 / 7 (43%)	1 / 13 (8%)
	Malignant fibrous histiocytoma	1 / 10 (10%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
Mammary gland	Fibroadenoma	2 / 10 (20%)	0 / 10 (0%)	1 / 7 (14%)	3 / 13 (23%)
	Adenocarcinoma	1 / 10 (10%)	0 / 10 (0%)	0 / 7 (0%)	0 / 13 (0%)

^a Significantly different from the "0%" group (P < 0.05).

Table 12. Incidence of proliferative lesions in male rats fed with ferulic acid for 106 weeks

Organs	Lesions	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
Lung	Alveolar cell hyperplasia	0 / 42 (0%)	0 / 34 (0%)	2 / 34 (6%)	1 / 42 (2%)
	Adenoma	0 / 42 (0%)	1 / 34 (3%)	3 / 34 (9%)	2 / 42 (5%)
	Adenocarcinomas	0 / 42 (0%)	1 / 34 (3%)	0 / 34 (0%)	0 / 42 (0%)
Tongue	Hyperplasia	0 / 42 (0%)	0 / 34 (0%)	0 / 34 (0%)	1 / 42 (2%)
	Papilloma	1 / 42 (2%)	0 / 34 (0%)	1 / 34 (3%)	0 / 42 (0%)
Forestomach	Papilloma	3 / 42 (7%)	0 / 34 (0%)	0 / 34 (0%)	1 / 42 (2%)
Liver	Intrahepatic bile duct proliferation	42 / 42 (100%)	34 / 34 (100%)	33 / 34 (97%)	26 / 42 (62%) ^a
Prostate	Adenocarcinoma	0 / 42 (0%)	0 / 34 (0%)	0 / 34 (0%)	1 / 42 (2%)
Testis	Leydig cell tumor	40 / 42 (95%)	34 / 34 (100%)	33 / 34 (97%)	42 / 42 (100%)
Hematopoietic system	Leukemia	0 / 42 (0%)	0 / 34 (0%)	0 / 34 (0%)	2 / 42 (5%)
Thyroid	C-cell hyperplasia	6 / 42 (14%)	3 / 34 (9%)	1 / 34 (3%)	3 / 42 (7%)
	C-cell adenoma	11 / 42 (26%)	4 / 34 (12%)	10 / 34 (29%)	10 / 42 (24%)
Adrenal glands	Medullary hyperplasia	1 / 42 (2%)	1 / 34 (3%)	5 / 34 (15%)	2 / 42 (5%)
	Pheochromocytoma	0 / 42 (0%)	1 / 34 (3%)	1 / 34 (3%)	1 / 42 (2%)
Pancreas	Islet cell tumor	2 / 42 (5%)	4 / 34 (12%)	2 / 34 (6%)	1 / 42 (2%)
Mesothelium	Mesothelioma	0 / 42 (0%)	1 / 34 (3%)	1 / 34 (3%)	0 / 42 (0%)
Skin	Granular cell tumor	2 / 42 (5%)	0 / 34 (0%)	0 / 34 (0%)	0 / 42 (0%)
	Schwannoma	0 / 42 (0%)	1 / 34 (3%)	0 / 34 (0%)	0 / 42 (0%)
	Fibroma	2 / 42 (5%)	3 / 34 (9%)	3 / 34 (9%)	1 / 42 (2%)
	Lipoma	1 / 42 (2%)	0 / 34 (0%)	0 / 34 (0%)	0 / 42 (0%)
	Neurofibroma	2 / 42 (5%)	0 / 34 (0%)	0 / 34 (0%)	0 / 42 (0%)
	Fibrolipoma	1 / 42 (2%)	0 / 34 (0%)	0 / 34 (0%)	0 / 42 (0%)
	Angiofibroma	0 / 42 (0%)	1 / 34 (3%)	0 / 34 (0%)	0 / 42 (0%)
	Sebaceous adenoma	2 / 42 (5%)	0 / 34 (0%)	0 / 34 (0%)	0 / 42 (0%)
	Squamous cell carcinoma	1 / 42 (2%)	1 / 34 (3%)	0 / 34 (0%)	1 / 42 (2%)
	Malignant lymphoma	0 / 42 (0%)	1 / 34 (3%)	0 / 34 (0%)	0 / 42 (0%)
	Malignant fibrous histiocytoma	0 / 42 (0%)	4 / 34 (12%) ^b	5 / 34 (15%) ^b	2 / 42 (5%)
Mammary gland	Fibroadenoma	0 / 42 (0%)	0 / 34 (0%)	2 / 34 (6%)	0 / 42 (0%)

^{a,b} Significantly different from the "0%" group (^a P < 0.001 and ^b P < 0.05).

Table 13. Incidence of proliferative lesions in female rats fed with ferulic acid for 106 weeks

Organs	Lesions	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
Lung	Alveolar cell hyperplasia	0 / 42 (0%)	0 / 42 (0%)	1 / 45 (2%)	1 / 39 (3%)
	Aenoma	0 / 42 (0%)	1 / 42 (2%)	0 / 45 (0%)	0 / 39 (0%)
Tongue	Hyperplasia	0 / 42 (0%)	0 / 42 (0%)	1 / 45 (2%)	0 / 39 (0%)
	Papilloma	0 / 42 (0%)	0 / 42 (0%)	0 / 45 (0%)	1 / 39 (3%)
Forestomach	Hyperplasia	0 / 42 (0%)	0 / 42 (0%)	2 / 45 (4%)	1 / 39 (3%)
Liver	Intrahepatic bile duct proliferation	3 / 42 (7%)	7 / 42 (17%)	10 / 45 (22%)	11 / 39 (28%) ^a
Uterus	Stromal polyp	10 / 42 (24%)	6 / 42 (14%)	8 / 45 (18%)	4 / 39 (10%)
	Hemangioma	0 / 42 (0%)	0 / 42 (0%)	0 / 45 (0%)	2 / 39 (5%)
	Leiomyoma	0 / 42 (0%)	1 / 42 (2%)	0 / 45 (0%)	0 / 39 (0%)
	Adenocarcinoma	1 / 42 (2%)	1 / 42 (2%)	1 / 45 (2%)	1 / 39 (3%)
	Squamous cell carcinoma	0 / 42 (0%)	0 / 42 (0%)	0 / 45 (0%)	1 / 39 (3%)
	Endometrial stromaal sarcoma	4 / 42 (10%)	5 / 42 (12%)	3 / 45 (7%)	2 / 39 (5%)
Ovary	Luteoma	1 / 42 (2%)	0 / 42 (0%)	0 / 45 (0%)	0 / 39 (0%)
	Granulosa cell tumor	0 / 42 (0%)	1 / 42 (2%)	0 / 45 (0%)	0 / 39 (0%)
Meninges	Hemangioma	0 / 42 (0%)	0 / 42 (0%)	1 / 45 (2%)	0 / 39 (0%)
Hematopoietic sytem	Leukemia	1 / 42 (2%)	1 / 42 (2%)	2 / 45 (4%)	0 / 39 (0%)
Thyroid	C-cell hyperplasia	3 / 42 (7%)	8 / 42 (19%)	2 / 45 (4%)	0 / 39 (0%)
	C-cell adenoma	3 / 42 (7%)	4 / 42 (10%)	7 / 45 (16%)	6 / 39 (15%)
Adrenal gland	Medullary hyperplasia	0 / 42 (0%)	0 / 42 (0%)	0 / 45 (0%)	1 / 39 (3%)
Pancreas	Islet cell tumor	1 / 42 (2%)	0 / 42 (0%)	0 / 45 (0%)	2 / 39 (5%)
Skin	Sebaceous adenoma	0 / 42 (0%)	3 / 42 (7%)	0 / 45 (0%)	0 / 39 (0%)
	Malignant fibrous histiocyctoma	0 / 42 (0%)	0 / 42 (0%)	0 / 45 (0%)	1 / 39 (3%)
Mammary gland	Fibroadenoma	4 / 42 (10%)	4 / 42 (10%)	10 / 45 (22%)	1 / 39 (3%)

^a Significantly different from the "0%" group (P < 0.05).

Table 14. Incidence of proliferative lesions in male rats fed with ferulic acid that were found dead and killed at the end of the study

Organs	Lesions	Dose level of ferulic acid (%)				
		0	0.5	1.0	2.0	
Lung	Alveolar cell hyperplasia	0 / 52 (0%)	1 / 52 (2%)	2 / 52 (4%)	1 / 52 (2%)	
	Adenoma	0 / 52 (0%)	1 / 52 (2%)	3 / 52 (6%)	2 / 52 (4%)	
	Adenocarcinoma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	
Tongue	Hyperplasia	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	1 / 52 (2%)	
	Papilloma	1 / 52 (2%)	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	
Forestomach	Hyperplasia	3 / 52 (6%)	1 / 52 (2%)	0 / 52 (0%)	1 / 52 (2%)	
	Papilloma	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	
Liver	Intrahepatic bile duct proliferation	52 / 52 (100%)	52 / 52 (100%)	50 / 52 (96%)	35 / 52 (67%) ^a	
Prostate	Adenocarcinoma	0 / 52 (0%)	0 / 52 (0%)	1 / 52 (2%)	1 / 52 (2%)	
Testis	Leydig cell tumor	49 / 52 (94%)	46 / 52 (88%)	49 / 52 (94%)	51 / 52 (98%)	
Hematopoietic system	Leukemia	2 / 52 (4%)	2 / 52 (4%)	9 / 52 (17%) ^b	4 / 52 (8%)	
Pituitary gland	Adenoma	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	
Thyroid	C-cell hyperplasia	8 / 52 (15%)	6 / 52 (12%)	3 / 52 (6%)	3 / 52 (6%)	
	C-cell adenoma	11 / 52 (21%)	6 / 52 (12%)	11 / 52 (21%)	12 / 52 (23%)	
	C-cell adenocarcinoma	0 / 52 (%)	0 / 52 (0%)	2 / 52 (4%)	1 / 52 (2%)	
Parathyroid gland	Hyperplasia	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	
Adrenal gland	Medullary hyperplasia	1 / 52 (2%)	2 / 52 (4%)	5 / 52 (10%)	2 / 52 (4%)	
	Pheochromocytoma	0 / 52 (0%)	2 / 52 (4%)	1 / 52 (2%)	1 / 52 (2%)	
Pancreas	Islet cell tumor	3 / 52 (6%)	5 / 52 (10%)	3 / 52 (6%)	1 / 52 (2%)	
Bone	Osteosarcoma (肺転移)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	1 / 52 (2%)	
Mesothelium	Mesothelioma	1 / 52 (2%)	2 / 52 (4%)	2 / 52 (4%)	1 / 52 (2%)	
Skin	Granular cell tumor	2 / 52 (4%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	
	Neurofibroma	2 / 52 (4%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	
	Fibroma	2 / 52 (4%)	7 / 52 (13%)	6 / 52 (12%)	5 / 52 (10%)	
	Schwannoma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	
	Lipoma	1 / 52 (2%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	
	Angiofibroma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	
	Fibrolipoma	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	
	Sebaceous adenoma	2 / 52 (4%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	
	Sebaceous adenocarcinoma	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	
	Squamous cell carcinoma	1 / 52 (2%)	1 / 52 (2%)	2 / 52 (4%)	1 / 52 (2%)	
	Malignant lymphoma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	
	Malignant fibrous histiocytoma	0 / 52 (0%)	4 / 52 (8%)	5 / 52 (10%)	2 / 52 (4%)	
	Mammary gland	Fibroadenoma	0 / 52 (0%)	0 / 52 (0%)	2 / 52 (4%)	0 / 52 (0%)

^{a,b} Significantly different from the "0%" group (^a P < 0.001 and ^b P < 0.05).

Table 15. Incidence of proliferative lesions in female rats fed with ferulic acid that were found dead and killed at the end of the study

Organs	Lesions	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
Lung	Alveolar cell hyperplasia	0 / 52 (0%)	0 / 52 (0%)	1 / 52 (2%)	1 / 52 (2%)
	Adenoma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)
Tongue	Hyperplasia	0 / 52 (0%)	0 / 52 (0%)	2 / 52 (4%)	0 / 52 (0%)
	Papilloma	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	3 / 52 (6%)
Forestomach	Hyperplasia	0 / 52 (0%)	1 / 52 (2%)	2 / 52 (4%)	1 / 52 (2%)
	Papilloma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)
Small intestine	Adenocarcinoma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)
Liver	Intrahepatic bile duct proliferation	8 / 52 (15%)	10 / 52 (19%)	10 / 52 (19%)	12 / 52 (23%)
	Cholangiofibroma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)
Uterus	Stromal polyp	10 / 52 (19%)	7 / 52 (13%)	8 / 52 (15%)	4 / 52 (8%)
	Hemangioma	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	2 / 52 (4%)
	Leiomyoma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)
	Adenocarcinoma	1 / 52 (2%)	1 / 52 (2%)	1 / 52 (2%)	1 / 52 (2%)
	Squamous cell carcinoma	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	1 / 52 (2%)
	Endometrial stromal sarcoma	4 / 52 (8%)	5 / 52 (10%)	3 / 52 (6%)	4 / 52 (8%)
Ovary	Luteoma	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)
	Granulosa cell tumor	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)
Meninges	hemangioma	0 / 52 (0%)	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)
Hematopoietic system	Leukemia	1 / 52 (2%)	1 / 52 (2%)	4 / 52 (8%)	3 / 52 (6%)
Pituitary gland	Adenoma	1 / 52 (2%)	1 / 52 (2%)	0 / 52 (0%)	1 / 52 (2%)
Thyroid	C-cell hyperplasia	5 / 52 (10%)	10 / 52 (19%)	2 / 52 (4%)	1 / 52 (2%)
	C-cell adenoma	3 / 52 (6%)	4 / 52 (8%)	7 / 52 (13%)	6 / 52 (12%)
Adrenal gland	Medullary hyperplasiaH	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)	1 / 52 (2%)
	Pheochromocytoma	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)
	Malignant pheochromocytoma (肺、肝転移)	0 / 52 (0%)	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)
Pancreas	Islet cell tumor	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	2 / 52 (4%)
Skin	Fibroma	0 / 52 (0%)	2 / 52 (4%)	3 / 52 (6%)	1 / 52 (2%)
	Sevaceous adenoma	0 / 52 (0%)	3 / 52 (6%)	0 / 52 (0%)	0 / 52 (0%)
	Malignant fibrous histiocyoma	1 / 52 (2%)	1 / 52 (2%)	0 / 52 (0%)	1 / 52 (2%)
Mammary gland	Fibroadenoma	6 / 52 (12%)	4 / 52 (8%)	11 / 52 (21%)	4 / 52 (8%)
	Adenocarcinoma	1 / 52 (2%)	0 / 52 (0%)	0 / 52 (0%)	0 / 52 (0%)

Table 16. Incidence of non-proliferative lesions in rats fed with ferulic acid that were found dead during the study
<Males>

Organs	Lesions	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
Lung	Pneumonia	1 / 10 (10%)	1 / 18 (6%)	1 / 18 (6%)	1 / 10 (10%)
	Hemorrhage	0 / 10 (0%)	0 / 18 (0%)	2 / 18 (11%)	0 / 10 (0%)
Glandular stomach	Chronic gastritis	1 / 10 (10%)	0 / 18 (0%)	1 / 18 (6%)	1 / 10 (10%)
Liver	Fatty Liver	1 / 10 (10%)	0 / 18 (0%)	0 / 18 (100%)	0 / 10 (0%)
Pancreas	Chronic pancreatitis	1 / 10 (10%)	2 / 18 (11%)	3 / 18 (17%)	3 / 10 (30%)
Heart	Myocarditis	10 / 10 (100%)	18 / 18 (100%)	18 / 18 (100%)	10 / 10 (100%)
Kidney	Interstitial nephritis	10 / 10 (100%)	18 / 18 (100%)	18 / 18 (100%)	10 / 10 (100%)
Urinary bladder	Chronic cytitis	0 / 10 (0%)	1 / 18 (6%)	0 / 18 (0%)	0 / 10 (0%)

<Females>

Organs	Lesions	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
Lung	Pneumonia	0 / 10 (0%)	1 / 10 (10%)	0 / 7 (0%)	0 / 13 (0%)
	Hemorrhage	0 / 10 (0%)	2 / 10 (20%)	0 / 7 (0%)	0 / 13 (0%)
Liver	Fatty liver	3 / 10 (30%)	1 / 10 (10%)	1 / 7 (14%)	1 / 13 (8%)
	Chronic pericholangitis	1 / 10 (10%)	2 / 10 (20%)	1 / 7 (14%)	4 / 13 (31%)
Pnaceas	Chronic pancreatitis	0 / 10 (0%)	0 / 10 (0%)	1 / 7 (14%)	2 / 13 (15%)
Heart	Myocarditis	10 / 10 (100%)	10 / 10 (100%)	7 / 7 (100%)	13 / 13 (100%)
Kidney	Interstitial nephritis	10 / 10 (100%)	10 / 10 (100%)	7 / 7 (100%)	13 / 13 (100%)
	Hydronephrosis	0 / 10 (0%)	0 / 10 (0%)	0 / 7 (0%)	1 / 13 (8%)
Adrenal gland	Fatty degeneration	0 / 10 (0%)	0 / 10 (0%)	1 / 7 (14%)	0 / 13 (0%)

Table 17. Incidence of non-proliferative lesions in rats fed with ferulic acid for 106 weeks
<Males>

Organs	Lesions	Dose level of ferulic acid (%)			
		0	0.5	1.0	2.0
Glandular stomach	Chronic gastritis	0 / 42 (0%)	2 / 34 (6%)	1 / 34 (3%)	1 / 42 (2%)
Pancreas	Chronic pancreatitis	3 / 42 (7%)	2 / 34 (6%)	3 / 34 (9%)	5 / 42 (12%)
Heart	Myocarditis	42 / 42 (100%)	34 / 34 (100%)	34 / 34 (100%)	42 / 42 (100%)
Kidney	Interstitial nephritis	42 / 42 (100%)	34 / 34 (100%)	34 / 34 (100%)	42 / 42 (100%)
Skin	Dermoid cyst	1 / 42 (2%)	0 / 34 (0%)	0 / 34 (0%)	0 / 42 (0%)

<Females>

Organs	Lesions	Dose level (%)			
		0	0.5	1.0	2.0
Lung	Pneumonia	0 / 42 (0%)	1 / 42 (2%)	0 / 45 (0%)	0 / 39 (0%)
Glandular stomach	Chronic gastritis	0 / 42 (0%)	0 / 42 (0%)	3 / 45 (7%)	2 / 39 (5%)
Colon	Erosive colitis	0 / 42 (0%)	1 / 42 (2%)	0 / 45 (0%)	0 / 39 (0%)
Liver	Chronic pericholangitis	24 / 42 (100%)	18 / 42 (43%)	13 / 45 (29%)	9 / 39 (23%)
Pncreas	Chronic pancreatitis	6 / 42 (14%)	0 / 42 (0%)	7 / 45 (16%)	5 / 39 (13%)
Heart	Myocarditis	42 / 42 (100%)	42 / 42 (100%)	45 / 45 (100%)	39 / 39 (100%)
Kidney	Interstitial nephritis	42 / 42 (100%)	42 / 42 (100%)	45 / 45 (100%)	39 / 39 (100%)
Uterus	Adenomyosis	2 / 42 (5%)	1 / 42 (2%)	1 / 45 (2%)	0 / 39 (0%)
Adrenal gland	Fatty degeneration	0 / 42 (0%)	1 / 42 (2%)	1 / 45 (2%)	4 / 39 (10%)