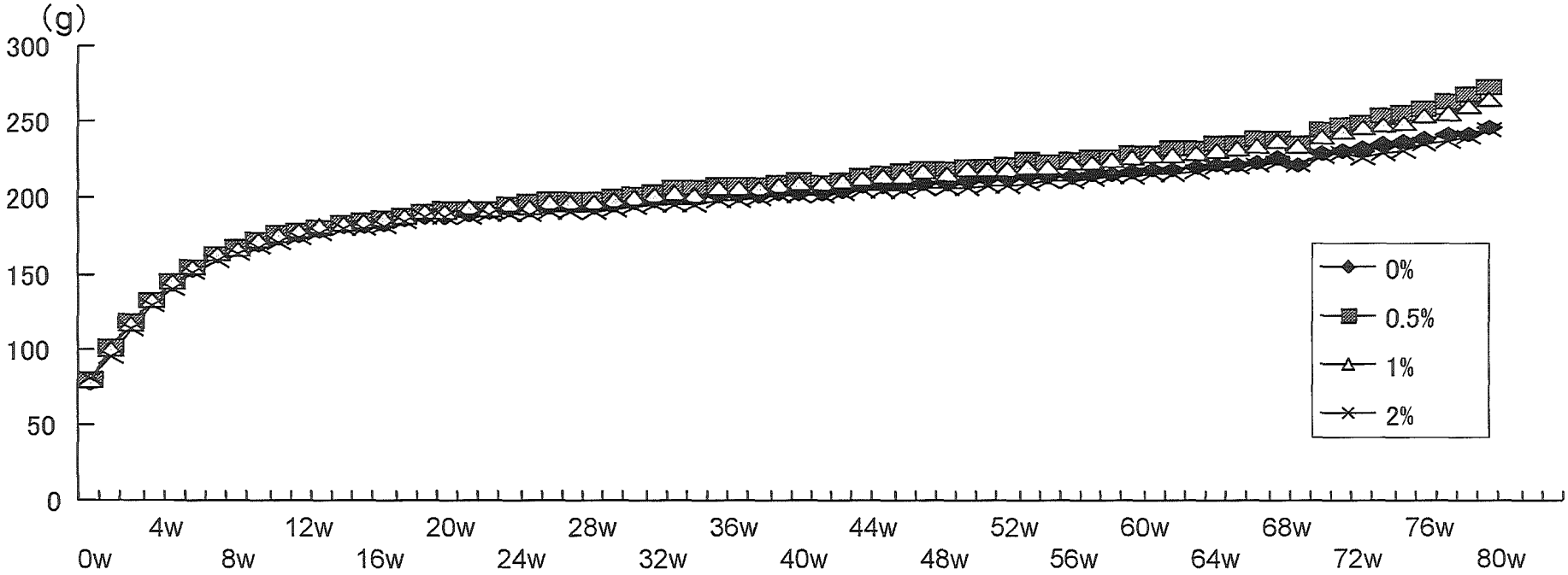

Fig. 4. Body weight curves for female F344 rats in a 2 year-bioassay of ferulic acid

Table 1. Food consumption and intake of ferulic acid

Sex	Dose	Food consumption	Intake of ferulic acid		Total intake of ferulic acid
		(g/rat/day)	(mg/rat/day)	(mg/kg/day)	(g/rat)
Male	0	14.2 ± 1.1 [a]	–	–	–
	0.5	11.9 ± 2.0	59.5 ± 10.1	120.1 ± 20.4	21.7 ± 3.7
	1.0	12.0 ± 2.4	119.8 ± 23.6	250.5 ± 49.3	43.6 ± 8.6
	2.0	12.8 ± 2.7	255.0 ± 53.8	557.6 ± 117.6	92.8 ± 19.6
Female	0	8.5 ± 1.2	–	–	–
	0.5	6.7 ± 1.9	33.7 ± 9.7	140.4 ± 40.4	11.3 ± 3.5
	1.0	7.0 ± 2.0	70.4 ± 20.3	294.1 ± 84.8	25.6 ± 7.4
	2.0	7.8 ± 2.4	155.4 ± 48.0	717.4 ± 221.6	56.6 ± 17.5

[a] Means ± SD.

Table 2. Hematological data in F344 male rats given ferulic acid for 52 weeks

Item		Dose level (%)			
		0	0.5	1.0	2.0
WBC	($\times 10^2/\mu L$)	44.3 ± 10.2 [a]	43.9 ± 13.8	41.4 ± 9.1	37.1 ± 6.7
RBC	($\times 10^4/\mu L$)	893.4 ± 37.0	896.2 ± 16.0	902.3 ± 17.3	899.1± 22.3
Hb	(g/dL)	14.6 ± 0.2	14.7 ± 0.3	14.8 ± 0.3	14.7 ± 0.6
Ht	(%)	44.7 ± 0.9	44.7 ± 0.9	45.2 ± 0.5	44.6 ± 1.1
MCV	(fL)	50.2 ± 1.5	49.9 ± 0.9	50.1 ± 0.7	49.6 ± 0.7
MCH	(pg)	16.4 ± 0.5	16.5 ± 0.2	16.4 ± 0.3	16.3 ± 0.4
MCHC	(g/dL)	32.7 ± 0.3	33.0 ± 0.6	32.7 ± 0.6	32.9 ± 1.0
PLT	($\times 10^4/\mu L$)	58.7 ± 5.5	54.6 ± 7.1	56.9 ± 7.1	53.5 ± 5.6
Differential cell counts	(%)				
Neutro		43.3 ± 18.5	35.8 ± 6.8	44.0 ± 9.4	38.6 ± 6.2
Eosino		1.1 ± 0.8	1.2 ± 0.8	0.5 ± 0.5	1.0 ± 1.3
Baso		0.2 ± 0.4	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.3
Lymph		53.0 ± 18.3	59.8 ± 7.1	51.4 ± 9.9	57.6 ± 6.6
Mono		2.4 ± 0.8	3.2 ± 1.2	4.1 ± 2.3	2.7 ± 1.1

[a] Means ± SD.

Table 3. Hematological data in F344 female rats given ferulic acid for 52 weeks

Item		Dose level (%)			
		0	0.5	1.0	2.0
WBC	($\times 10^2/\mu L$)	27.6 ± 7.0	20.4 ± 3.4 [b]	21.4 ± 5.0	21.1 ± 4.0 [b]
RBC	($\times 10^4/\mu L$)	779.0 ± 13.4	800.6 ± 24.8 [b]	811.2 ± 15.2 [c]	795.7 ± 12.0
Hb	(g/dL)	14.3 ± 0.3	14.6 ± 0.5	14.6 ± 0.2	14.2 ± 0.3
Ht	(%)	42.4 ± 1.2	44.8 ± 1.5	47.4 ± 5.3	43.6 ± 0.9
MCV	(fL)	54.4 ± 0.7	55.9 ± 0.7	56.0 ± 1.0	55.0 ± 0.8
MCH	(pg)	18.3 ± 0.3	18.2 ± 0.4	18.0 ± 0.3	17.9 ± 0.3
MCHC	(g/dL)	33.7 ± 0.6	32.5 ± 0.5	32.3 ± 0.4	32.5 ± 0.6
PLT	($\times 10^4/\mu L$)	55.5 ± 6.0	43.1 ± 7.9 [d]	43.0 ± 8.8 [d]	46.7 ± 7.5
Differential cell counts	(%)				
Neutro		36.6 ± 20.0	16.4 ± 9.7 [d]	22.4 ± 10.9	20.7 ± 8.3
Eosino		0.7 ± 0.7	1.1 ± 1.2	1.2 ± 0.5	1.3 ± 1.1
Baso		0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.4
Lymph		59.9 ± 19.7	80.7 ± 10.0 [d]	72.6 ± 11.0	75.4 ± 9.0
Mono		2.4 ± 1.1	1.7 ± 0.5	3.8 ± 0.5 [b]	2.4 ± 1.3

[a] Means ± SD.

Significantly different from control group by one-way ANOVA, Bonferroni multiple comparison test ([b] $P<0.05$, [c] $P<0.001$ and [d] $P<0.01$).

Table 4. Serum biochemical data in F344 male rats given ferulic acid for 52 weeks

Item		Dose level (%)			
		0	0.5	1.0	2.0
TP	(g/dL)	6.6 ± 0.1 [a]	6.6 ± 0.1	6.6 ± 0.2	6.6 ± 0.1
Alb	(g/dL)	2.7 ± 0.1	2.8 ± 0.1	2.8 ± 0.1	2.8 ± 0.1
A/G		0.71 ± 0.02	0.73 ± 0.02	0.71 ± 0.02	0.74 ± 0.03
AST	(IU/dL)	132.5 ± 12.5	134.3 ± 16.2	135.8 ± 18.8	109.9 ± 9.9 [b]
ALT	(IU/dL)	108.4 ± 12.6	100.1 ± 17.8	105.7 ± 15.7	85.0 ± 10.1 [b]
ALP	(IU/dL)	890.0 ± 88.7	940.4 ± 98.1	864.9 ± 106.9	802.1 ± 80.7
γ-GTP	(IU/dL)	5.1 ± 3.3	5.2 ± 3.0	4.4 ± 1.4	4.1 ± 1.6
T.Bil	(mg/dL)	0.02 ± 0.04	0.01 ± 0.03	0.00 ± 0.00	0.00 ± 0.00
CRE	(mg/dL)	0.31 ± 0.02	0.29 ± 0.01	0.28 ± 0.02 [b]	0.24 ± 0.02 [c]
BUN	(mg/dL)	19.6 ± 1.2	19.3 ± 1.0	18.4 ± 1.1	17.3 ± 0.8 [c]
T-Cho	(mg/dL)	121.0 ± 11.6	130.6 ± 17.9	122.7 ± 11.0	113.4 ± 10.2
Na	(mEq/dL)	141.9 ± 0.7	142.8 ± 1.5	143.5 ± 1.4	143.6 ± 0.7
K	(mEq/dL)	4.5 ± 0.2	4.5 ± 0.4	4.2 ± 0.3	4.2 ± 0.3
Cl	(mEq/dL)	101.4 ± 0.7	101.7 ± 0.5	102.9 ± 1.5	103.6 ± 1.4
Ca	(mEq/dL)	10.2 ± 0.1	10.4 ± 0.3	10.3 ± 0.2	10.4 ± 0.2
IP	(mEq/dL)	4.5 ± 0.3	4.3 ± 0.3	4.2 ± 0.4	4.7 ± 0.2

[a] Means ± SD.

Significantly different from control group by one-way ANOVA, Bonferroni multiple comparison test ([b] $P<0.01$ and [c] $P<0.001$).

Table 5. Serum biochemical data in F344 male rats given ferulic acid for 52 weeks

Item		Dose level (%)			
		0	0.5	1.0	2.0
TP	(g/dL)	7.2 ± 0.3	7.3 ± 0.3	7.2 ± 0.3	7.5 ± 0.4
Alb	(g/dL)	3.3 ± 0.2	3.4 ± 0.2	3.3 ± 0.2	3.5 ± 0.2
A/G		0.85 ± 0.06	0.88 ± 0.05	0.86 ± 0.04	0.87 ± 0.04
AST	(IU/dL)	79.8 ± 13.9	81.4 ± 13.3	85.0 ± 17.5	69.1 ± 6.2
ALT	(IU/dL)	50.1 ± 5.6	46.9 ± 6.3	50.0 ± 8.2	44.6 ± 5.6
ALP	(IU/dL)	478.7 ± 62.5	473.8 ± 64.8	513.6 ± 67.0	468.9 ± 51.0
γ-GTP	(IU/dL)	0.6 ± 0.5	0.3 ± 0.5	0.6 ± 0.7	0.6 ± 0.5
T.Bil	(mg/dL)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
CRE	(mg/dL)	0.27 ± 0.02	0.26 ± 0.02	0.27 ± 0.01	0.28 ± 0.03
BUN	(mg/dL)	19.0 ± 1.5	18.4 ± 2.3	18.9 ± 1.5	19.1 ± 2.2
T-Cho	(mg/dL)	125.5 ± 8.8	132.7 ± 10.6	128.5 ± 13.8	158.5 ± 18.4
Na	(mEq/dL)	142.8 ± 0.9	143.5 ± 1.0	142.9 ± 1.0	143.5 ± 1.1
K	(mEq/dL)	3.9 ± 0.3	3.8 ± 0.2	3.9 ± 0.2	3.9 ± 0.2
Cl	(mEq/dL)	103.5 ± 1.7	101.8 ± 1.3	101.6 ± 1.7	102.3 ± 1.1
Ca	(mEq/dL)	10.5 ± 0.4	10.6 ± 0.2	10.6 ± 0.3	10.7 ± 0.4
IP	(mEq/dL)	3.3 ± 0.4	3.6 ± 0.3	4.1 ± 0.6[b]	3.7 ± 0.4

[a] Means ± SD.

Significantly different from control group by one-way ANOVA, Bonferroni multiple comparison test ([b] $P<0.01$).

Table 6. Final body weight and organ weights data in F344 male rats given ferulic acid for 52 weeks

Item		Dose level (%)			
		0	0.5	1.0	2.0
Body weight	(g)	467.3 ± 17.2	495.3 ± 16.2 [b]	478.3 ± 14.3	457.3 ± 28.0
Absolute	(g)				
Brain		2.16 ± 0.13	2.31 ± 0.09 [c]	2.38 ± 0.09 [d]	2.35 ± 0.05 [d]
Lungs		1.85 ± 0.12	1.75 ± 0.14	2.06 ± 0.18	2.03 ± 0.22
Heart		1.21 ± 0.07	1.25 ± 0.05	1.23 ± 0.06	1.19 ± 0.09
Spleen		0.71 ± 0.03	0.71 ± 0.03	0.76 ± 0.05	0.75 ± 0.05
Pancreas		0.48 ± 0.06	0.48 ± 0.10	0.57 ± 0.17	0.62 ± 0.19
Liver		14.09 ± 0.87	15.05 ± 1.02	14.71 ± 0.79	14.57 ± 0.90
Adrenals		0.068 ± 0.081	0.045 ± 0.004	0.044 ± 0.004	0.042 ± 0.003
Kidneys		2.56 ± 0.18	2.70 ± 0.19	2.93 ± 0.15	2.81 ± 0.18
Testes		3.24 ± 0.39	3.26 ± 0.33	3.37 ± 0.27	3.26 ± 0.42

[a] Means ± SD.

Significantly different from control group by one-way ANOVA, Bonferroni multiple comparison test ([b] $P<0.05$, [c] $P<0.01$ and [d] $P<0.001$).

Table 7. Relative organ weights data in F344 male rats given ferulic acid for 52 weeks

Item		Dose level (%)			
		0	0.5	1.0	2.0
Relative	(g/100g B.W.)				
Brain		0.46 ± 0.03	0.47 ± 0.02	0.50 ± 0.02	0.51 ± 0.01
Lungs		0.40 ± 0.03	0.35 ± 0.03 [b]	0.43 ± 0.04	0.44 ± 0.05
Heart		0.26 ± 0.01	0.25 ± 0.01	0.26 ± 0.01	0.26 ± 0.02
Spleen		0.15 ± 0.01	0.14 ± 0.01	0.16 ± 0.01	0.16 ± 0.01
Pancreas		0.10 ± 0.01	0.10 ± 0.02	0.12 ± 0.04	0.14 ± 0.04 [b]
Liver		3.02 ± 0.19	3.03 ± 0.20	3.07 ± 0.17	3.19 ± 0.20
Adrenals		0.015 ± 0.017	0.009 ± 0.001	0.009 ± 0.001	0.009 ± 0.001
Kidneys		0.55 ± 0.04	0.55 ± 0.04	0.61 ± 0.03 [c]	0.61 ± 0.04 [c]
Testes		0.69 ± 0.08	0.66 ± 0.07	0.70 ± 0.06	0.71 ± 0.09

[a] Means ± SD.

Significantly different from control group by one-way ANOVA, Bonferroni multiple comparison test ([b] $P<0.05$ and [c] $P<0.01$).

Table 8. Final body weight and organ weights data in F344 female rats given ferulic acid for 52 weeks

Item		Dose level (%)			
		0	0.5	1.0	2.0
Body weight	(g)	226.5 ± 18.0	240.1 ± 11.4	239.4 ± 23.4	216.6 ±11.9
Absolute	(g)				
Brain		2.12 ± 0.04	2.15 ± 0.06	2.12 ± 0.06	2.11 ± 0.07
Lungs		1.47 ± 0.20	1.41 ± 0.12	1.40 ± 0.10	1.37 ± 0.15
Heart		0.709 ± 0.053	0.768 ± 0.069	0.748 ± 0.037	0.734 ± 0.070
Spleen		0.45 ± 0.04	0.47 ± 0.04	0.45 ± 0.04	0.43 ± 0.03
Pancreas		0.43 ± 0.13	0.43 ± 0.09	0.45 ± 0.07	0.42 ± 0.11
Liver		6.96 ± 0.62	7.37 ± 0.48	7.65 ± 0.59	7.68 ± 0.66
Adrenals		0.048 ± 0.003	0.053 ± 0.006	0.048 ± 0.004	0.040 ± 0.004 [b]
Kidneys		1.54 ± 0.16	1.64 ± 0.12	1.65 ± 0.10	1.51 ± 0.10
Ovaries		0.095 ± 0.015	0.100 ± 0.022	0.097 ± 0.008	0.084 ± 0.012
Uterus		1.43 ± 0.24	1.37 ± 0.21	1.22 ± 0.20	1.23 ± 0.20

[a] Means ± SD.

Significantly different from control group by one-way ANOVA, Bonferroni multiple comparison test ([b] $P<0.01$).

Table 9. Relative organ weights data in F344 female rats given ferulic acid for 52 weeks

Item		Dose level (%)			
		0	0.5	1.0	2.0
Relative	(g/100g B.W.)				
Brain		0.94 ± 0.02	0.90 ± 0.02 [b]	0.89 ± 0.03 [c]	0.97 ± 0.03
Lungs		0.65 ± 0.09	0.59 ± 0.05	0.58 ± 0.04	0.63 ± 0.07
Heart		0.31 ± 0.02	0.32 ± 0.03	0.31 ± 0.02	0.34 ± 0.03
Spleen		0.20 ± 0.02	0.20 ± 0.02	0.17 ± 0.02 [b]	0.20 ± 0.01
Pancreas		0.19 ± 0.06	0.18 ± 0.04	0.19 ± 0.03	0.19 ± 0.05
Liver		3.07 ± 0.27	3.07 ± 0.20	3.20 ± 0.25	3.55 ± 0.30 [b]
Adrenals		0.0212 ± 0.001	0.0221 ± 0.002	0.0201 ± 0.002	0.0185 ± 0.002 [d]
Kidneys		0.68 ± 0.07	0.68 ± 0.05	0.69 ± 0.04	0.70 ± 0.05
Ovaries		0.042 ± 0.007	0.042 ± 0.009	0.041 ± 0.003	0.039 ± 0.006
Uterus		0.63 ± 0.11	0.57 ± 0.09	0.51 ± 0.08	0.57 ± 0.09

[a] Means ± SD.

Significantly different from control group by one-way ANOVA, Bonferroni multiple comparison test ([b] $P<0.01$, [c] $P<0.001$ and [d] $P<0.05$).

Table 10. Mean food consumption in F344 rats at week 80 in two-years bioassay of ferulic acid

Sex	Dose	Food consumption (g/rat/day)
Male	0	13.8 ± 1.2 [a]
	0.5	11.9 ± 2.3
	1.0	12.2 ± 2.3
	2.0	14.3 ± 3.1
Female	0	9.0 ± 0.9
	0.5	7.1 ± 2.6
	1.0	6.8 ± 2.2
	2.0	8.5 ± 3.2

[a] Means ± SD.

研究成果の刊行に関する一覧表

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Kuroiwa Y, Nishikawa A, Imazawa T, Kanki K, Kitamura Y, Umemura T, Hirose M	Lack of subchronic toxicity of an aqueous extract of Agaricus blazei Murrill in F344 rats	Food Chem. Toxicol.	43	1047-1053	2005