Table1-1 Intra-run and inter-run analytical precision and accuracy of fisetin.

	precision				accuracy	
Conc. (μg/ml)	intra-day mean ±S.D.	(C.V.%)	inter-day mean ±S.D.	(C.V%)	intra-day relative error(%)	inter-day relative error(%)
100.00	100.85 ±1.38	7.72	100.66 ±0.97	5.05	+0.85	+0.66
50.00	47.72 ±0.38	4.48	48.64 ±0.60	6.43	-4.57	-2.72
25.00	26.17 ±0.17	3.65	25.03 ±0.17	3.63	+4.69	+0.11
6.25	6.19 ±0.07	6.05	6.14 ±0.11	8.95	-0.94	-1.82
3.13	3.32 ±0.04	6.22	3.08 ±0.03	5.17	+6.36	-1.57
1.56	1.67 ±0.01	2.68	1.71 ±0.01	2.53	+6.70	+9.38
0.78	0.80 ±0.01	3.90	0.77 ±0.02	8.57	+2.82	-1.03

Table 1-2 Recovery (%) of fisetin from rat serum (n=3)

Conc. (μg/ml)	1	2	3	Mean ±S.D.
50.00	84.27	84.06	80.28	82.87 ±2.24
12.50	100.29	89.95	97.04	95.76 ±5.29
3.13	95.45	95.25	97.64	96.11 ±1.32

Table 1-3 The serum concentrations (nmol/mL) of fisetin in six rats after intravenous administration of fisetin (10 mg/kg)

Time (min) \ Rats	1	2	3	4	5	6	Mean ±S.E.
5	64.76	106.59	25.46	32.65	23.32	36.33	48.18 ± 13.17
15	6.75	10.28	3.40	2.24	2.63	3.26	4.76 ± 1.28
30	1.43	3.75	1.10	1.45	1.31	2.63	1.94 ± 0.42
45	0.65	1.57	0.90	1.21	1.62	1.49	1.24 ± 0.16
90	0.40	0.91	ND	0.54	0.80	1.08	0.62 ± 0.16
240	0.72	ND	ND	ND	ND	ND	0.12 ± 0.12
480	ND	0.43	ND	ND	ND	0.58	0.17 ± 0.11
720	ND	ND	ND	ND	ND	ND	–

ND：not detectable

Table 1-4 The serum concentrations (nmol/mL) of fisetin sulfates in six rats after intravenous administration of fisetin (10 mg/kg)

Time (min) \ Rats	1	2	3	4	5	6	Mean ±S.E.
5	81.44	65.73	90.51	81.86	106.46	109.93	89.32 ± 6.82
15	64.26	59.80	73.72	69.12	79.27	86.40	72.10 ± 4.00
30	43.36	37.09	54.98	39.54	56.43	50.74	47.02 ± 3.33
45	34.36	28.24	45.27	36.98	44.90	50.67	40.07 ± 3.39
90	24.92	18.19	33.95	22.85	27.88	34.71	27.08 ± 2.63
240	13.49	11.67	19.13	15.23	14.39	19.88	15.63 ± 1.32
480	6.04	7.82	7.32	4.42	5.65	11.19	7.07 ± 0.96
720	5.17	6.91	4.35	3.26	4.26	5.46	4.90 ± 0.51

Table 1-5 The serum concentrations (nmol/mL) of fisetin glucuronides in six rats after intravenous administration of fisetin (10 mg/kg)

Time (min) \ Rats	1	2	3	4	5	6	Mean ±S.E.
5	29.28	66.49	29.66	30.64	26.85	46.07	38.17 ± 6.33
15	31.22	27.31	18.66	12.52	18.16	21.34	21.54 ± 2.76
30	18.45	14.28	12.45	7.30	10.42	13.98	12.81 ± 1.54
45	14.14	9.78	10.54	4.25	6.67	8.37	8.96 ± 1.39
90	9.31	5.30	6.93	3.56	3.89	6.99	6.00 ± 0.89
240	4.75	3.77	3.39	1.77	1.78	3.84	3.22 ± 0.49
480	2.04	2.67	0.71	ND	ND	0.50	0.99 ± 0.46
720	2.21	2.89	ND	ND	ND	0.56	0.94 ± 0.52

ND：not detectable

Table 1-6 The serum concentrations (nmol/mL) of fisetin in six rats after oral administration of fisetin (50 mg/kg)

Time (min) \ Rats	1	2	3	4	5	6	Mean ±S.E.
5	2.61	22.60	2.10	1.23	10.40	32.59	11.92 ± 5.30
15	1.49	4.10	0.61	0.56	0.63	1.64	1.51 ± 0.55
45	0.36	4.59	0.78	0.37	ND	1.26	1.23 ± 0.69
90	ND	0.91	1.04	0.39	ND	0.85	0.53 ± 0.19
180	ND	0.96	0.36	ND	ND	ND	0.22 ± 0.16
360	ND	0.34	ND	ND	ND	ND	0.06 ± 0.06
600	ND	0.31	ND	ND	ND	ND	0.05 ± 0.05
1440	ND	ND	ND	ND	ND	ND	–
2160	ND	ND	ND	ND	ND	ND	–
2880	ND	0.28	ND	ND	ND	ND	0.05 ± 0.05

ND：not detectable

Table 1-7 The serum concentrations (nmol/mL) of fisetin sulfates in six rats after oral administration of fisetin (50 mg/kg)

Time (min) \ Rats	1	2	3	4	5	6	Mean ±S.E.
5	12.02	59.65	18.15	24.96	59.87	148.45	53.85 ± 20.72
15	37.83	77.59	36.81	50.09	73.99	139.46	69.29 ± 15.74
45	21.72	85.16	18.82	31.89	45.32	107.30	51.70 ± 14.86
90	9.64	35.74	22.59	22.21	37.40	126.67	42.37 ± 17.36
180	8.25	30.62	13.92	10.64	20.06	38.66	20.36 ± 4.91
360	6.94	19.51	8.30	5.42	13.16	10.86	10.70 ± 2.09
600	4.92	14.82	4.40	3.17	6.80	30.86	10.83 ± 4.35
1440	4.93	18.66	6.18	13.58	2.75	10.16	9.38 ± 2.44
2160	12.76	11.92	20.70	1.66	1.54	1.62	8.37 ± 3.27
2880	1.41	2.34	4.12	0.85	6.22	1.02	2.66 ± 0.86

Table 1-8 The serum concentrations (nmol/mL) of fisetin glucuronides in six rats after oral administration of fisetin (50 mg/kg)

Time (min) \ Rats	1	2	3	4	5	6	Mean ±S.E.
5	6.77	19.94	7.68	11.70	16.11	34.29	16.08 ± 4.17
15	24.54	37.35	19.33	18.30	23.76	19.22	23.75 ± 2.92
45	11.97	43.43	7.40	8.61	8.36	9.10	14.81 ± 5.76
90	5.04	12.28	12.42	4.59	7.01	10.83	8.70 ± 1.46
180	4.72	10.00	7.31	2.92	3.42	1.21	4.93 ± 1.31
360	4.62	5.20	3.77	1.34	1.96	ND	2.81 ± 0.83
600	3.18	7.19	2.43	1.28	0.53	0.69	2.55 ± 1.02
1440	4.34	14.14	4.42	12.17	0.41	0.63	6.02 ± 2.38
2160	12.76	10.58	14.52	0.89	ND	0.35	6.51 ± 2.78
2880	1.16	2.30	2.26	ND	5.47	ND	1.86 ± 0.83

ND：not detectable

Table 1-9 Individual pharmacokinetic parameters of fisetin after intravenous administration of fisetin (10 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
AUC_{0-720} (nmol · min/mL)	1132.68	1799.19	422.36	787.07	532.26	1149.65	970.53 ± 205.85
Alpha	0.24	0.32	0.27	0.45	0.33	0.55	0.36 ± 0.05
Beta	0.00_4	0.04	0.03	0.02	0.01	0.02	0.02 ± 0.01
Alpha-HL (min)	2.89	2.16	2.56	1.54	2.12	1.27	2.09 ± 0.25
Beta-HL (min)	168.03	17.81	21.90	42.13	64.18	40.49	59.09 ± 22.81
A (min^{-1})	211.32	483.24	88.65	287.06	109.40	498.34	279.67 ± 72.91
B (min^{-1})	1.04	11.38	3.00	2.43	2.14	4.03	4.00 ± 1.53
Cl (mL/min)	8.33	5.53	21.51	13.32	19.69	8.66	12.84 ± 2.67
MRT_{0-720} (min)	56.98	6.79	9.97	13.21	36.37	13.43	22.79 ± 8.07
Vss (mL)	474.54	37.56	214.34	175.97	716.18	116.33	289.15 ± 104.61

Table 1-10 Individual pharmacokinetic parameters of fisetin sulfates after intravenous administration of fisetin (10 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
AUC_{0-720} (nmol · min/mL)	11324.59	15319.58	13903.43	10664.18	11854.80	16294.66	13226.87 ± 936.61
Alpha	0.04	0.03	0.04	0.04	0.04	0.05	$0.04 \pm 0.00_3$
Beta	0.00_3	0.00_1	0.00_4	0.00_3	0.00_4	0.00_3	$0.00_3 \pm 0.000_4$
Alpha-HL (min)	15.91	23.03	15.63	16.16	16.04	12.89	16.61 ± 1.38
Beta-HL (min)	232.70	635.70	196.43	216.81	184.54	230.05	282.70 ± 71.02
A (min^{-1})	66.35	62.78	59.21	68.51	86.46	88.69	72.00 ± 5.10
B (min^{-1})	29.20	14.43	44.35	28.99	37.01	44.13	33.02 ± 4.63
Cl (mL/min)	0.83	0.65	0.65	0.98	0.88	0.61	0.77 ± 0.06
MRT_{0-720} (min)	293.67	796.76	258.34	269.43	225.21	300.18	357.26 ± 88.58
Vss (mL)	244.60	517.84	168.77	264.79	199.11	183.42	263.09 ± 53.10

Table 1-11 Individual pharmacokinetic parameters of fisetin glucuronides after intravenous administration of fisetin (10 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
AUC_{0-720} (nmol · min/mL)	4871.22	4301.27	2454.95	1386.37	1571.04	2762.67	2891.25 ± 580.89
Alpha	0.02	0.11	0.09	0.13	0.05	0.11	0.08 ± 0.02
Beta	0.00_2	0.00_3	0.01	0.01	0.01	0.01	$0.00_5 \pm 0.00_1$
Alpha-HL (min)	29.08	6.48	7.91	5.53	13.08	6.15	11.37 ± 3.71
Beta-HL (min)	403.72	257.04	118.71	110.53	128.52	131.09	191.60 ± 47.89
A (min^{-1})	28.79	97.74	27.06	45.61	28.04	60.61	47.97 ± 11.32
B (min^{-1})	6.29	9.14	12.53	6.41	5.62	11.77	8.63 ± 1.22
Cl (mL/min)	1.94	2.31	3.70	7.56	6.67	3.60	4.30 ± 0.94
MRT_{0-720} (min)	448.46	294.05	151.16	119.67	129.35	154.06	216.13 ± 53.22
Vss (mL)	868.40	680.68	559.28	904.69	862.90	555.24	738.53 ± 65.58

Table 1-12 Individual pharmacokinetic parameters of fisetin after oral administration of fisetin (50 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
T_{max} (min)	5.00	5.00	5.00	5.00	ND	5.00	5.00
C_{max} (nmol/mL)	2.61	22.60	2.10	1.23	ND	32.59	12.23 ± 6.47
AUC_{0-2880} (nmol · min/mL)	54.78	954.25	143.60	43.08	ND	343.60	307.86 ± 170.33
$AUMC_{0-2880}$ (nmol· min^2 /mL)	787.88	455127.38	10812.00	1628.25	ND	5561.63	94783.43 ± 90103.42
MRT_{0-2880} (min)	14.38	476.95	75.29	37.80	ND	16.19	124.12 ± 88.89

ND：not detectable

Table 1-13 Individual pharmacokinetic parameters of fisetin sulfates after oral administration of fisetin (50 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
T_{max} (min)	15.00	45.00	15.00	15.00	15.00	5.00	18.33 ± 5.58
C_{max} (nmol/mL)	37.83	85.16	36.81	50.09	73.99	148.45	72.06 ± 17.23
AUC_{0-2880} (nmol · min/mL)	2.11E5	4.78E5	3.03E5	2.02E5	2.07E5	5.01E5	3.17(± 0.57) E5
$AUMC_{0-2880}$ (nmol· min^2 /mL)	2.93E7	4.93E7	4.60E7	2.06E7	1.59E7	2.77E7	3.15(± 0.55) E7
MRT_{0-2880} (min)	1388.51	1031.61	1516.98	1017.37	767.04	553.82	1045.89 ± 148.35

Table 1-14 Individual pharmacokinetic parameters of fisetin glucuronides after oral administration of fisetin (50 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
T_{max} (min)	15.00	45.00	15.00	15.00	15.00	5.00	18.33 ± 5.58
C_{max} (nmol/mL)	24.54	43.43	19.33	18.30	23.76	34.29	27.28 ± 3.97
AUC_{0-2880} (nmol · min/mL)	1.76E5	2.92E5	1.94E5	1.23E5	0.48E5	0.29E5	1.44(± 0.40) E5
$AUMC_{0-2880}$ (nmol· min^2 /mL)	2.75E7	3.78E7	3.12E7	1.50E7	0.66E7	0.13E7	1.99(± 0.59) E7
MRT_{0-2880} (min)	1557.05	1298.17	1612.75	1222.60	1365.96	460.71	1252.87 ± 169.84

Table 1-15 Comparison of pharmacokinetic parameters of fisetin sulfates and glucuronides after intravenous administration of fisetin (10 mg/kg) to six rats.

Conjugates / Parameters	Sulfates Mean±S.E	Glucuronides Mean±S.E	Difference	P
AUC_{0-720} (nmol·min·mL^{-1})	13226.9 ± 936.6	2891.3 ± 580.9	4.57	0.000***
Cl (mL/min)	0.8 ± 0.1	4.3 ± 0.9	0.18	0.31
MRT_{0-720} (min)	357.3 ± 88.6	216.1 ± 53.2	1.65	0.25
Vss (mL)	263.1 ± 53.1	738.5 ± 65.6	0.36	0.002**
K10-HL (min)	90.0 ± 10.2	40.7 ± 11.6	2.21	0.003**

**p<0.01 ***p<0.001

Table 1-16 Comparison of pharmacokinetic parameters of fisetin sulfates and glucuronides after oral administration of fisetin (50 mg/kg) to six rats.

Conjugates / Parameters	Sulfates Mean±S.E	Glucuronides Mean±S.E	Difference	P
T_{max} (min)	18.33 ± 5.58	18.33 ± 5.58	1.00	1.000
C_{max} (nmol/mL)	72.06 ± 17.23	27.28 ± 3.97	2.64	0.031*
AUC_{0-720} (nmol·min·mL^{-1})	3.17(±0.57)E5	1.44(±0.40)E5	2.21	0.026*
AUMC (nmol·min^2·mL^{-1})	3.15(± 0.55)E7	1.99(± 0.59)E7	1.58	0.242
MRT (min)	1045.89 ± 148.35	1252.87 ± 169.84	0.83	0.569

*p<0.05

Table 1-17 Individual pharmacokinetic parameters of fisetin after intravenous administration of fisetin (10 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
T_{max} (min)	5.00	5.00	5.00	5.00	5.00	5.00	5.00
C_{max} (nmol/mL)	64.76	106.59	25.46	32.65	23.32	36.33	48.19 ± 13.17
AUC_{0-720} (nmol · min/mL)	704.03	1171.60	256.70	343.08	294.03	572.28	556.95 ± 141.97
$AUMC_{0-720}$ (nmol· min^2 /mL)	2.17E4	4.25E4	0.24E4	0.50E4	0.58E4	4.81E4	2.09(± 0.82)E4
MRT_{0-720} (min)	30.80	36.26	9.31	14.64	19.60	83.97	32.43 ± 11.09

Table 1-18 Individual pharmacokinetic parameters of fisetin sulfates after intravenous administration of fisetin (10 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
T_{max} (min)	5.00	5.00	5.00	5.00	5.00	5.00	5.00 0.00
C_{max} (nmol/mL)	81.44	65.73	90.51	81.86	106.46	109.93	89.32 ± 6.82
AUC_{0-720} (nmol · min/mL)	10225.50	9399.20	13102.40	9830.18	11374.33	14787.30	11453.15 ± 860.28
$AUMC_{0-720}$ (nmol· min^2 /mL)	2.07E6	2.27E6	2.52E6	1.79E6	2.04E6	3.11E6	2.30(± 0.19) E6
MRT_{0-720} (min)	202.78	241.74	191.98	181.88	179.52	210.14	201.34 ± 9.41

Table 1-19 Individual pharmacokinetic parameters of fisetin glucuronides after intravenous administration of fisetin (10 mg/kg) to six rats.

Parameters	1	2	3	4	5	6	Mean ± S.E.
T_{max} (min)	15.00	5.00	5.00	5.00	5.00	5.00	6.67 ± 1.67
C_{max} (nmol/mL)	31.22	66.49	29.66	30.64	26.85	46.07	38.49 ± 6.24
AUC_{0-720} (nmol · min/mL)	3899.58	3587.15	2380.58	1103.15	1297.55	2690.60	2493.10 ± 468.62
$AUMC_{0-720}$ (nmol· min^2 /mL)	7.64E5	8.07E5	2.85E5	0.76E5	0.84E5	3.70E5	3.98(± 1.31) E5
MRT_{0-720} (min)	195.99	225.10	119.64	68.55	64.95	137.65	135.31 ± 26.71

Table 2-1 Cyclosporine blood concentrations (ng/mL) of six rats after oral administration of cyclosporine (2.5 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	Mean ±S.E.
20	105.34	134.03	104.31	78.70	86.00	34.34	90.45 ± 13.69
40	78.16	112.08	71.16	71.85	92.28	110.57	89.35 ± 7.61
60	94.25	131.70	134.36	104.29	89.70	44.49	99.80 ± 13.45
180	64.25	176.99	61.40	44.23	69.66	46.06	77.10 ± 20.40
300	34.29	107.91	35.91	32.16	58.59	23.50	48.73 ± 12.76
540	21.82	50.58	18.32	18.90	44.43	15.98	28.34 ± 6.16

Table 2-2 Cyclosporine blood concentrations (ng/mL) of six rats after oral administrations of cyclosporine (2.5 mg/kg) and 5-hydroxyflavone (20 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	Mean ±S.E.
20	155.89	106.97	241.25	70.56	119.47	61.48	125.94 ± 13.69
40	254.61	154.32	304.56	83.28	177.46	148.6	187.14 ± 7.61
60	160.56	169.62	266.79	159.33	171.36	309.38	206.17 ± 13.45
180	197.82	261.83	218.41	225.96	223.87	267.07	232.49 ± 20.40
300	205.79	227.33	158.14	141.16	329.40	361.25	237.18 ± 12.76
540	119.96	127.63	104.10	70.43	150.92	147.32	120.06 ± 6.16

Table 2-3 Cyclosporine blood concentrations (ng/mL) of seven rats after oral administrations of cyclosporine (2.5 mg/kg) and 5-hydroxyflavone (40 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	G	Mean ±S.E.
20	5.52	13.91	18.3	9.75	ND	23.45	21.43	13.19 ± 3.25
40	25.17	25.87	34.2	56.06	19.22	33.62	33.54	32.53 ± 4.46
60	24.64	31.71	49.81	52.91	22.13	26.82	34.55	34.65 ± 4.60
180	7.45	17.25	39.67	42.11	5.66	13.67	18.23	20.58 ± 5.54
300	ND	ND	52.6	25.02	ND	ND	ND	11.09 ± 7.76
540	ND	ND	ND	ND	ND	ND	ND	–

ND：not detectable

Table 2-4 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with 5-hydroxyflavone (20 mg/kg) (treatment).

Parameters \ Rats	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	284.29 ± 17.58	136	0.000***
T_{max} (min)	66.67 ± 23.48	173.33 ± 47.52	160	0.148
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	10.26 (± 0.74) E4	221	0.000***
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	26.18 (± 2.57) E6	293	0.000***
MRT (min)	203.22 ± 9.19	252.89 ±8.22	24	0.020*

*p<0.05 ***p<0.001

Table 2-5 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with 5-hydroxyflavone (40 mg/kg) (treatment).

Rats Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	36.55 ± 4.91	-70	0.001***
T_{max} (min)	66.67 ± 23.48	85.71 ± 35.91	29	0.935
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	0.59 (± 0.16) E4	-81	0.011*
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	0.73 (± 0.29) E6	-89	0.061
MRT (min)	203.22 ± 9.19	99.77 ±13.98	-51	0.000***

*p<0.05 ***p<0.001

Table 2-6 Cyclosporine blood concentrations (ng/mL) of six rats after oral administrations of cyclosporine (2.5 mg/kg) and flavone (20 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	Mean ±S.E.
20	173.04	54.70	44.07	64.28	159.29	75.26	95.11 ± 22.93
40	214.55	44.32	20.97	56.44	208.01	93.76	106.34 ± 34.56
60	204.08	40.48	40.54	60.80	175.55	111.13	105.43 ± 28.93
180	168.43	72.11	34.46	58.79	151.08	118.85	100.62 ± 21.92
300	125.71	32.20	34.60	62.90	128.52	92.02	79.32 ± 17.53
540	91.81	18.34	20.91	54.48	89.36	72.66	57.93 ± 13.29

Table 2-7 Cyclosporine blood concentrations (ng/mL) of six rats after oral administrations of cyclosporine (2.5 mg/kg) and flavone (40 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	Mean ±S.E.
20	ND	ND	ND	ND	ND	4.64	0.77 ± 0.77
40	9.72	18.86	20.31	16.94	14.90	26.96	17.95 ± 2.35
60	11.89	14.41	12.57	11.34	17.52	16.75	14.08 ± 1.06
180	ND	ND	4.78	ND	17.24	5.66	4.61 ± 2.73
300	ND	ND	ND	ND	ND	ND	–
540	ND	ND	ND	ND	ND	ND	–

ND：not detectable

Table 2-8 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with flavone (20 mg/kg) (treatment).

Rats / Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	120.31 ± 30.47	0	1.000
T_{max} (min)	66.67 ± 23.48	80.00 ± 31.83	20	0.912
$AUC_{0\text{-}540}$ (ng ·min·mL^{-1})	3.20 (± 0.62) E4	4.47 (± 1.03) E4	40	0.422
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	10.78 (± 2.40) E6	62	0.212
MRT (min)	203.22 ± 9.19	242.41 ± 7.24	19	0.018*

*$p<0.05$

Table 2-9 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with flavone (40 mg/kg) (treatment).

Rats Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	18.75 ± 2.01	-84	0.005**
T_{max} (min)	66.67 ± 23.48	46.67 ± 4.22	-30	0.814
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	0.13 (± 0.04) E4	-96	0.018*
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	0.10 (± 0.04) E6	-98	0.032*
MRT (min)	203.22 ± 9.19	65.55 ± 9.94	-68	0.000***

*p<0.05 **p<0.01 ***p<0.001

Table 2-10 Cyclosporine blood concentrations (ng/mL) of six rats after oral administrations of cyclosporine (2.5 mg/kg) and fisetin (20 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	Mean ±S.E.
20	31.48	26.69	6.52	70.50	65.26	38.50	39.83 ± 9.90
40	59.38	11.32	50.82	61.56	110.17	23.76	52.84 ±14.12
60	55.79	111.77	83.67	42.90	91.61	17.46	67.20 ±14.20
180	26.73	82.92	118.99	138.49	75.07	43.49	80.95 ±17.45
300	4.63	49.73	64.65	42.24	55.47	55.00	45.29 ±8.67
540	ND	7.11	28.73	4.02	44.20	19.99	17.34 ±6.93

ND：not detectable

Table 2-11 Cyclosporine blood concentrations (ng/mL) of seven rats after oral administrations of cyclosporine (2.5 mg/kg) and fisetin (40 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	G	Mean ±S.E.
20	37.97	20.10	ND	13.09	27.30	29.86	ND	18.33 ± 5.57
40	46.19	32.72	18.72	25.91	62.84	39.72	24.48	35.80 ± 5.74
60	37.88	33.38	49.51	15.63	21.43	36.08	20.54	30.64 ± 4.52
180	30.99	16.82	11.02	ND	26.94	21.02	8.46	16.46 ± 4.10
300	14.79	ND	ND	ND	17.54	ND	ND	4.62 ± 3.00
540	ND	ND	ND	ND	ND	ND	ND	–

ND：not detectable

Table 2-12 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with fisetin (20 mg/kg) (treatment).

Rats / Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	98.97 ± 13.85	-18	0.369
T_{max} (min)	66.67 ± 23.48	133.33 ± 42.79	100	0.228
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	2.64 (± 0.42) E4	-17	0.626
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	5.63 (± 1.08) E6	-15	0.770
MRT (min)	203.22 ± 9.19	202.29 ± 22.84	0	0.999

Table 2-13 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with fisetin (40 mg/kg) (treatment).

Rats Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	39.31 ± 6.03	-67	0.000_3***
T_{max} (min)	66.67 ± 23.48	46.67 ± 4.22	-30	0.856
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	0.42 (± 0.09) E4	-87	0.001***
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	0.40 (± 0.14) E6	-94	0.002**
MRT (min)	203.22 ± 9.19	82.56 ± 13.11	-59	0.000***

**p<0.01 ***p<0.001

Table 2-14 Cyclosporine blood concentrations (ng/mL) of five rats after oral administrations of cyclosporine (2.5 mg/kg) and quercetin (20 mg/kg).

Rats / Time (min)	A	B	C	D	E	Mean ±S.E.
20	11.88	22.12	18.35	28.44	13.2	18.80 ± 3.03
40	7.63	33.47	20.82	40.61	19.66	24.44 ± 5.75
60	18.25	32.41	14.57	35.99	12.17	22.68 ± 4.84
180	18.27	24.13	27.77	36.76	20.51	25.49 ± 3.25
300	17.57	25.26	21.72	40.33	15.93	24.16 ± 4.36
540	12.31	21.13	41.31	26.49	4.89	21.23 ± 6.23

Table 2-15 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with quercetin (20 mg/kg) (treatment).

Rats Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	30.83 ± 4.88	-74	0.000_2***
T_{max} (min)	66.67 ± 23.48	196.00 ± 91.52	194	0.169
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	1.24 (± 0.21) E4	-61	0.022*
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	3.35 (± 0.62) E6	-50	0.095
MRT (min)	203.22 ± 9.19	266.18 ± 15.70	31	0.006**

*p<0.05 **p<0.01 ***p<0.001

Table 2-16 Cyclosporine blood concentrations (ng/mL) of six rats after oral administrations of cyclosporine (2.5 mg/kg) and morin (20 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	Mean ±S.E.
20	77.63	198.34	114.95	66.52	112.44	89.09	109.83 ± 19.33
40	258.05	300.41	199.81	160.15	319.96	184.36	237.12 ± 26.71
60	255.33	281.76	308.56	156.61	334.16	163.28	249.95 ± 30.44
180	178.50	166.60	312.53	146.87	245.52	120.83	195.14 ± 29.02
300	101.24	133.16	199.83	140.24	175.16	79.36	138.17 ± 18.28
540	34.02	87.61	89.21	42.11	81.30	19.01	58.88 ± 12.57

Table 2-17 Cyclosporine blood concentrations (ng/mL) of seven rats after oral administrations of cyclosporine (2.5 mg/kg) and morin (37.5 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	G	Mean ±S.E.
20	84.45	115.71	98.52	22.80	108.63	55.08	145.32	90.07 ± 15.36
40	133.87	201.59	135.96	51.97	177.75	57.00	124.71	126.12 ± 21.15
60	140.62	227.22	149.21	60.59	178.13	59.81	118.21	133.40 ± 22.91
180	93.58	218.73	125.58	85.22	127.52	162.70	231.92	149.32 ± 21.86
300	55.66	163.74	82.79	69.69	87.54	76.09	142.90	96.92 ± 15.23
540	19.77	75.20	34.91	24.64	36.08	52.58	55.88	42.72 ± 7.37

Table 2-18 Cyclosporine blood concentrations (ng/mL) of six rats after oral administrations of cyclosporine (2.5 mg/kg) and morin (50 mg/kg).

Time (min) \ Rats	A	B	C	D	E	F	Mean ±S.E.
20	27.31	13.63	41.75	14.73	31.54	29.43	26.40 ± 4.36
40	55.48	19.89	101.51	35.83	76.70	71.56	60.16 ± 12.04
60	52.02	129.74	42.58	21.24	37.95	28.18	51.95 ± 16.17
180	42.56	19.26	11.84	5.91	10.56	7.84	16.33 ± 5.57
300	28.76	ND	ND	ND	ND	ND	4.79 ± 4.79
540	ND	ND	ND	ND	ND	ND	–

ND：not detectable

Table 2-19 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with morin (20 mg/kg) (treatment).

Rats Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	258.28 ± 29.19	114	0.001***
T_{max} (min)	66.67 ± 23.48	66.67± 22.90	0	1.000
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	7.98 (± 1.00) E4	149	0.001***
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	16.77 (± 2.40) E6	152	0.002**
MRT (min)	203.22 ± 9.19	207.87 ± 6.69	2	0.986

**p<0.01 ***p<0.001

Table 2-20 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with morin (37.5 mg/kg) (treatment).

Rats Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	167.86 ± 19.32	39	0.422
T_{max} (min)	66.67 ± 23.48	111.43 ± 24.24	67	0.512
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	5.42 (± 0.75) E4	69	0.200
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	11.92 (± 1.78) E6	79	0.205
MRT (min)	203.22 ± 9.19	219.26 ± 8.28	8	0.688

Table 2-21 Comparison of pharmacokinetic parameters of cyclosporine between rats receiving cyclosporine (2.5 mg/kg) (control) and cyclosporine with morin (50 mg/kg) (treatment).

Rats Parameters	Control Mean±S.E	Treatment Mean±S.E	Difference (%)	P
C_{max} (ng/mL)	120.64 ± 12.61	78.47 ± 13.61	-35	0.470
T_{max} (min)	66.67 ± 23.48	43.33 ± 3.33	-35	0.865
AUC_{0-540} (ng ·min·mL^{-1})	3.20 (± 0.62) E4	0.71 (± 0.15) E4	-78	0.099
AUMC (ng ·min^2·mL^{-1})	6.66 (± 1.52) E6	0.62 (± 0.23) E6	-91	0.094
MRT (min)	203.22 ± 9.19	77.36 ± 12.82	-62	0.000***

***p<0.001

Table 3-1 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted jejunum of rats (n=3, control).

Time (min) \ Rats	1	2	3	Mean ± S.E.
20	119	79	102	100.00 ± 11.59
40	137	337	318	264.00 ± 63.74
60	243	498	742	494.33 ± 144.06
80	717	639	896	750.67 ± 76.08
100	1229	900	1499	1209.33 ± 173.20

Table 3-2 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted jejunum of rats (n=3) in the presence of 5-hydroxyflavone at concentration of 420 μM.

Time (min) \ Rats	1	2	3	Mean ± S.E.
20	45	97	77	73.00 ± 15.14
40	230	375	311	305.33 ± 41.95
60	402	747	633	594.00 ± 101.48
80	662	1078	946	895.33 ± 122.73
100	1062	1276	1407	1248.33 ± 100.55

Table 3-3 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted jejunum of rats (n=3) in the presence of 5-hydroxyflavone at concentration of 840 μM.

Time (min) \ Rats	1	2	3	Mean ± S.E.
20	28	35	66	43.00 ± 11.68
40	179	231	285	231.67 ± 30.60
60	287	496	575	452.67 ± 85.92
80	514	903	909	775.33 ± 130.68
100	795	1017	1511	1107.67 ± 211.60

Table 3-4 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted jejunum of rats (n=3) in the presence of flavone at concentration of 900 μM.

Time (min) \ Rats	1	2	3	Mean ± S.E.
20	20	31	56	35.67 ± 10.65
40	80	136	166	127.33 ± 25.20
60	134	503	341	326.00 ± 106.78
80	255	621	508	461.33 ± 108.20
100	316	715	840	623.67 ± 158.01

Table 3-5 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted jejunum of rats (n=3) in the presence of morin at concentration of 830 μM.

Time (min) \ Rats	1	2	3	Mean ± S.E.
20	39	15	4	19.33 ± 10.33
40	48	29	15	30.67 ± 9.56
60	57	30	25	37.33 ± 9.94
80	76	63	34	57.67 ± 12.41
100	84	87	58	76.33 ± 9.21

Table 3-6 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted ileum of rats (n=3, control).

Time (min) \ Rats	1	2	3	Mean ± S.E.
20	ND	32	26	29.00 ± 3.00
40	12	176	144	160.00 ± 16.00
60	103	356	292	324.00 ± 32.00
80	179	537	466	501.50 ± 35.50
100	350	636	905	770.50 ± 134.50

ND：not detectable

Table 3-7 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted ileum of rats (n=3) in the presence of 5-hydroxyflavone at concentration of 420 μM.

Rats / Time (min)	1	2	3	Mean ± S.E.
20	10	26	17	17.67 ± 4.63
40	52	140	94	95.33 ± 25.41
60	152	311	230	231.00 ± 45.90
80	266	544	370	393.33 ± 81.10
100	478	676	561	571.67 ± 57.41

Table 3-8 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted ileum of rats (n=3) in the presence of 5-hydroxyflavone at concentration of 840 μM.

Rats / Time (min)	1	2	3	Mean ± S.E.
20	21	13	65	33.00 ± 16.17
40	100	113	232	148.33 ± 42.00
60	219	256	417	297.33 ± 60.78
80	307	529	612	482.67 ± 91.04
100	565	639	945	716.33 ± 116.31

Table 3-9 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted ileum of rats (n=3) in the presence of flavone at concentration of 900 μM.

Rats / Time (min)	1	2	3	Mean ± S.E.
20	18	21	10	16.33 ± 3.28
40	40	64	20	41.33 ± 12.72
60	71	147	53	90.33 ± 28.81
80	169	192	119	160.00 ± 21.55
100	267	358	171	265.33 ± 53.99

Table 3-10 Transport of rhodamine 123 (ng/mL) from serosal to mucosal side across the everted ileum of rats (n=3) in the presence of morin at concentration of 820 μM.

Time (min) \ Rats	1	2	3	Mean ± S.E.
20	ND	5	10	5.00 ± 2.89
40	9	26	39	24.67 ± 8.69
60	16	46	64	42.00 ± 14.00
80	28	67	98	64.33 ± 20.25
100	44	104	185	111.00 ± 40.85

ND：not detectable