Table 4-1 MTX serum concentration (μmol/L) of eight rats after oral administration of MTX (5.0 mg/kg) alone.

Time (min) \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
15	0.13	0.26	0.18	0.14	0.24	0.22	0.32	0.16	0.21 ± 0.02
30	0.24	0.18	0.12	0.12	0.18	0.16	0.18	0.17	0.17 ± 0.01
60	0.31	0.13	0.12	0.08	0.14	0.18	0.14	0.14	0.16 ± 0.02
120	0.12	0.08	0.10	0.04	0.08	0.12	0.10	0.12	0.10 ± 0.01
240	0.03	0.06	0.07	0.02	0.07	0.10	0.16	0.06	0.07 ± 0.02
480	0.03	0.07	0.05	0.04	0.02	ND	0.01	ND	0.03 ± 0.01
720	0.02	0.05	0.04	0.03	0.02	ND	ND	ND	0.02 ± 0.01
1440	0.02	ND	ND	ND	0.01	ND	ND	ND	—
1980	0.01	ND	ND	ND	ND	ND	ND	ND	—
2880	ND	ND	ND	ND	ND	ND	ND	ND	—

ND: not detectable

Table 4-2 MTX serum concentration (μmol/L) of eight rats after oral coadministration of MTX (5.0 mg/kg) with Rhei Rhizoma decoction (2.0 g/kg).

Time (min) \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
15	0.03	0.03	0.03	0.02	0.18	ND	0.01	0.01	0.04 ± 0.02
30	0.02	0.07	0.01	0.02	0.23	0.01	0.01	0.02	0.05 ± 0.03
60	0.04	0.07	0.01	0.03	0.33	0.02	0.02	0.03	0.07 ± 0.04
120	0.04	0.07	0.05	0.05	0.27	0.03	0.07	0.02	0.08 ± 0.03
240	0.16	0.02	0.07	0.08	0.18	0.09	0.03	0.01	0.08 ± 0.02
480	0.15	0.04	0.08	0.09	0.10	0.15	0.05	0.04	0.09 ± 0.02
720	0.11	0.08	0.10	0.10	0.03	0.14	0.09	0.09	0.09 ± 0.01
1440	0.12	0.09	0.09	0.10	0.12	0.21	0.09	0.10	0.12 ± 0.01
1980	0.14	0.04	0.08	0.10	0.02	0.04	0.01	0.01	0.06 ± 0.02
2880	0.11	0.02	0.03	0.08	0.02	0.03	ND	ND	0.04 ± 0.01

ND: not detectable

Table 4-3 MTX serum concentration (μmol/L) of eight rats after oral coadministration of MTX (5.0 mg/kg) and Rhei Rhizoma decoction (1.0 g/kg).

Rat / Time (min)	1	2	3	4	5	6	7	8	Mean ± S.E.
15	0.20	0.08	0.11	0.15	0.37	0.10	0.14	0.16	0.16 ± 0.03
30	0.11	0.14	0.15	0.15	0.38	0.10	0.16	0.18	0.17 ± 0.03
60	0.14	0.17	0.18	0.12	0.28	0.11	0.14	0.17	0.16 ± 0.02
120	0.18	0.11	0.17	0.07	0.14	0.11	0.11	0.09	0.12 ± 0.01
240	0.10	0.09	0.15	0.03	0.03	0.07	0.09	0.09	0.08 ± 0.01
480	0.10	0.18	0.06	0.12	0.10	0.14	0.04	0.14	0.11 ± 0.02
720	0.08	0.09	0.06	0.11	0.10	0.05	0.10	0.22	0.10 ± 0.02
1440	0.18	0.07	0.12	0.10	0.15	0.17	0.13	0.20	0.14 ± 0.02
1980	0.11	0.01	0.08	0.19	0.01	0.07	0.12	0.04	0.08 ± 0.02
2880	ND	0.01	0.00	0.05	0.06	0.07	0.08	0.06	0.04 ± 0.01

ND: not detectable

Table 4-4 Pharmacokinetic parameters of MTX after oral administration of 5.0 mg/kg MTX alone.

Rat / Parameter	1	2	3	4	5	6	7	8	Mean ± S.E.
AUC_{0-120}	58.17	48.22	40.64	22.19	44.28	27.54	46.92	20.44	38.55 ± 4.82
AUC_{0-2880}	69.60	54.60	49.20	28.80	51.75	31.80	54.15	26.93	45.85 ± 5.35
$AUC_{0-\infty}$	74.10	72.60	63.60	39.60	54.45	43.80	55.35	34.13	54.70 ± 5.26
C_{max}	0.31	0.26	0.18	0.14	0.24	0.22	0.32	0.17	0.23 ± 0.02
T_{max}	60.00	15.00	15.00	15.00	15.00	15.00	15.00	30.00	22.50 ± 5.67
MRT	538.48	299.84	279.79	306.41	364.09	106.27	168.78	99.86	270.44 ± 51.62

AUC (μmol · min/L)

Cmax (μmol/L)

Tmax (min)

MRT (min)

Table 4-5 Pharmacokinetic parameters of MTX after oral coadministration of 5.0 mg/kg MTX with Rhei Rhizoma decoction (2.0 g/kg).

Parameter \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
AUC_{0-120}	21.30	23.20	19.50	24.22	20.34	28.01	21.08	19.44	22.10 ± 1.20
AUC_{0-2880}	254.40	157.58	185.93	215.70	216.83	288.83	90.98	90.98	181.54 ± 27.54
$AUC_{0-\infty}$	254.40	157.58	185.93	215.70	216.83	288.83	95.48	95.48	188.78 ± 24.72
C_{max}	0.16	0.09	0.10	0.10	0.33	0.21	0.09	0.09	0.15 ± 0.03
T_{max}	240.00	1440.00	720.00	720.00	60.00	1440.00	240.00	240.00	570.00 ± 178.87
MRT	1117.86	1261.06	1149.08	1236.68	908.40	1144.06	713.57	713.57	977.56 ± 81.92

AUC (μmol · min/L)

Cmax (μmol/L)

Tmax (min)

MRT (min)

Table 4-6 Pharmacokinetic parameters of MTX after oral coadministration of 5.0 mg/kg MTX with Rhei Rhizoma decoction (1.0 g/kg).

Parameter \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
AUC_{0-120}	26.30	19.20	56.76	38.22	25.34	58.01	23.98	17.28	35.40 ± 5.73
AUC_{0-2880}	251.48	180.30	195.83	326.63	245.40	277.80	243.20	307.45	222.93 ± 18.01
$AUC_{0-\infty}$	300.98	180.30	231.83	326.63	245.40	277.80	300.00	359.40	266.13 ± 20.15
C_{max}	0.20	0.18	0.18	0.19	0.38	0.17	0.20	0.20	0.21 ± 0.03
T_{max}	15.00	480.00	60.00	1980.00	30.00	1440.00	30.00	720.00	576.43 ± 246.65
MRT	1065.84	822.01	961.10	1471.83	1133.17	1377.76	1458.20	1151.50	1184.27 ± 83.85

AUC (μmol · min/L)

Cmax (μmol/L)

Tmax (min)

MRT (min)

Table 4-7 Comparison of pharmacokinetic parameters of MTX in rats between oral administration of MTX (5.0 mg/kg) alone and coadministration with decoction of Rhei Rhizoma (RR, 1.0 g/kg and 2.0 g/kg).

Parameter	MTX alone	MTX + RR (1 g/kg)	Difference (%)	MTX + RR (2 g/kg)	Difference (%)
AUC_{0-120}	38.55 ± 4.82	35.40 ± 5.73	-8.2	22.10 ± 1.20	-42.7*
AUC_{0-2880}	45.85 ± 5.35	222.93 ± 18.01	386.2***	181.54 ± 27.54	295.9***
$AUC_{0-\infty}$	54.70 ± 5.26	266.13 ± 20.15	386.5***	188.78 ± 24.72	245.1***
C_{max}	0.23 ± 0.02	0.21 ± 0.03	-9.3	0.15 ± 0.03	-33.3*
T_{max}	22.50 ± 5.67	576.43 ± 264.65	2461.9*	570.00 ± 178.87	2433.3*
MRT	270.44 ± 51.62	1184.27 ± 83.85	337.9***	977.56 ± 81.92	261.5***

*P＜0.05, **P＜0.01, ***P＜0.001

Data expressed as Mean ± S.E.

AUC (μmol · min/L)

Cmax (μmol/L)

Tmax (min)

MRT (min)

Table 4-8 MTX serum concentration (μmol/L) of eight rats after intravenous administration of MTX alone (1.0 mg/kg).

Time (min) \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
5	5.20	4.24	6.40	7.84	4.96	6.16	6.80	6.00	5.95 ± 0.40
15	2.52	1.72	2.88	3.60	2.88	2.24	2.56	2.55	2.62 ± 0.19
30	1.20	1.00	1.40	2.00	2.24	1.16	1.24	1.40	1.46 ± 0.15
45	0.76	0.60	1.08	1.12	1.44	0.72	0.80	1.00	0.94 ± 0.10
60	0.48	0.46	0.82	0.84	1.08	0.54	0.64	0.66	0.69 ± 0.07
90	0.28	0.30	0.58	0.38	0.56	0.30	0.38	0.47	0.41 ± 0.04
120	0.20	0.19	0.25	0.20	0.41	0.17	0.23	0.23	0.24 ± 0.03
180	0.11	0.09	0.43	0.07	0.17	0.05	0.08	0.09	0.14 ± 0.04
240	0.09	0.07	0.16	0.03	0.09	0.06	0.04	0.05	0.07 ± 0.01
300	0.06	0.02	0.09	ND	0.04	0.02	0.02	0.03	0.04 ± 0.01

ND: not detectable

Table 4-9 MTX serum concentration (μmol/L) of six rats after intravenous administration of MTX (1.0 mg/kg) and coadministration with Rhei Rhizoma decoction (2.0 g/kg).

Time (min) \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
5	7.04	9.12	7.68	7.76	9.12	6.56	7.00	6.80	7.64 ± 0.35
15	3.72	3.44	2.48	3.12	3.20	2.88	3.26	3.01	3.14 ± 0.13
30	2.12	1.96	1.32	1.80	1.60	1.92	1.99	2.01	1.84 ± 0.09
45	1.36	1.28	0.92	0.96	1.04	1.08	1.00	1.17	1.10 ± 0.06
60	1.16	0.96	0.72	0.68	0.72	0.92	0.91	0.89	0.87 ± 0.06
90	0.97	0.68	0.52	0.38	0.44	0.82	0.86	0.96	0.70 ± 0.08
120	0.51	0.32	0.52	0.19	0.21	0.59	0.59	0.59	0.44 ± 0.06
180	0.22	0.13	0.10	0.12	0.10	0.24	0.25	0.20	0.17 ± 0.02
240	0.18	0.05	0.05	0.05	0.07	0.16	0.16	0.09	0.10 ± 0.02
300	0.03	0.04	0.04	0.05	0.04	0.20	0.10	0.07	0.07 ± 0.02

Table 4-10 Pharmacokinetic parameters of MTX after intravenous administration of MTX (1.0 mg/kg) to eight rats.

Parameter \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
AUC_{0-300}	160.57	132.04	230.25	223.92	221.02	163.94	185.26	184.48	187.69 ± 12.43
$t_{1/2}$	83.86	42.08	39.18	29.84	41.03	34.55	46.00	61.71	47.28 ± 6.19
V	0.67	0.68	0.24	0.23	0.30	0.36	0.40	174.52	37.03 ± 21.76
Cl	4.80	8.40	3.10	3.60	3.70	5.20	4.60	1.60	4.45 ± 0.66
MRT	38.02	38.09	53.46	23.53	44.50	37.77	28.55	39.32	36.65 ± 3.46

AUC (μmol · min/L)

$t_{1/2}$ (min)

V (L)

Cl (mL/min)

MRT (min)

Table 4-11 Pharmacokinetic parameters of MTX between rats after intravenous administration of MTX (1.0 mg/kg) and oral coadministration with Rhei Rhizoma decoction (2.0 g/kg).

Parameter \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
AUC_{0-300}	254.55	228.40	187.60	185.55	198.25	232.05	264.17	256.75	225.92 ± 11.29
$t_{1/2}$	47.41	46.17	50.35	57.89	78.01	79.84	90.78	55.15	63.20 ± 6.06
V	0.26	0.29	0.41	0.44	0.61	0.55	146.42	94.03	30.38 ± 20.22
Cl	3.80	4.30	5.70	5.20	5.40	4.70	1.12	1.18	3.91 ± 0.64
MRT	58.97	44.12	49.64	41.88	40.89	67.73	57.10	52.89	51.65 ± 3.32

AUC (μmol · min/L)

$t_{1/2}$ (min)

V (L)

Cl (mL/min)

MRT (min)

Table 4-12 Comparison of pharmacokinetic parameters of MTX in rats between intravenous administration of MTX (1.0 mg/kg) alone and oral coadministration with Rhei Rhizoma decoction (RR, 2.0 g/kg).

Parameter	MTX alone	MTX + RR	Difference (%)
AUC_{0-300}	187.69 ± 12.43	225.92 ± 11.29	20.4
$t_{1/2}$	47.28 ± 6.19	63.20 ± 6.06	33.7*
V	0.37 ± 0.22	0.30 ± 0.20	-17.9
Cl	4.45 ± 0.66	3.91 ± 0.64	-12.1
MRT	36.65 ± 3.46	51.65 ± 3.32	40.9*

Data expressed as Mean ± S.E.

* $P < 0.05$

AUC (μmol · min/L)

$t_{1/2}$ (min)

V (L)

Cl (mL/min)

MRT (min)

Table 4-13 MTX serum concentration (μmol/L) of eight rats after oral coadministration of MTX (5.0 mg/kg) and Scutellariae Radix decoction (2.0 g/kg).

Time (min) \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
15	0.08	0.07	0.08	0.10	0.07	0.25	0.03	0.10	0.10 ± 0.02
30	0.26	0.07	0.08	0.14	0.22	0.24	0.06	0.12	0.14 ± 0.02
60	0.20	0.05	0.06	0.12	0.23	0.15	0.11	0.13	0.14 ± 0.02
120	0.10	0.06	0.07	0.07	0.15	0.10	0.09	0.06	0.09 ± 0.01
240	0.03	0.08	0.07	0.12	0.19	0.05	0.08	0.06	0.09 ± 0.01
480	0.07	0.06	0.12	0.12	0.10	0.04	0.02	0.08	0.08 ± 0.01
720	0.07	0.03	0.09	0.05	0.10	0.07	0.03	0.07	0.06 ± 0.01
1440	0.08	0.05	0.09	0.01	0.06	0.09	0.08	0.04	0.07 ± 0.01
1980	0.04	0.02	0.01	0.14	0.01	0.06	0.06	0.03	0.05 ± 0.01
2880	ND	0.03	0.06	0.02	ND	ND	0.05	ND	0.02 ± 0.01

ND: not detectable

Table 4-14 MTX serum concentration (μmol/L) of eight rats after oral coadministration of MTX (5.0 mg/kg) and Scutellariae Radix decoction (1.0 g/kg).

Time (min) \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
15	0.45	0.23	0.30	0.27	0.26	0.44	0.30	0.21	0.31 ± 0.03
30	0.29	0.20	0.21	0.27	0.24	0.21	0.26	0.25	0.24 ± 0.01
60	0.21	0.21	0.22	0.22	0.21	0.14	0.21	0.20	0.20 ± 0.01
120	0.12	0.39	0.10	0.18	0.12	0.11	0.16	0.11	0.16 ± 0.03
240	0.15	0.05	0.11	0.10	0.08	0.06	0.08	0.09	0.09 ± 0.01
480	0.21	0.02	0.14	0.13	0.10	0.12	0.11	0.15	0.12 ± 0.02
720	0.15	0.01	0.06	0.09	0.13	0.14	0.11	0.06	0.09 ± 0.02
1440	0.09	0.09	0.16	0.13	0.13	0.05	0.09	0.07	0.10 ± 0.01
1980	0.02	0.12	0.16	0.09	0.10	ND	0.07	0.08	0.08 ± 0.02
2880	0.04	0.12	0.03	0.06	0.10	0.02	0.07	0.09	0.07 ± 0.01

ND: not detectable

Table 4-15 Pharmacokinetic parameters of MTX after oral coadministration of MTX (5.0 mg/kg) with Scutellariae Radix decoction (2.0 g/kg).

Parameter \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
AUC_{0-120}	44.22	33.22	49.61	44.28	27.53	23.06	48.17	22.44	36.57 ± 4.00
AUC_{0-2880}	142.05	112.88	187.50	206.85	176.55	150.00	164.55	112.35	156.59 ± 12.00
$AUC_{0-\infty}$	160.05	112.88	187.50	206.85	181.05	177.00	164.55	156.84	168.34 ± 9.80
C_{max}	0.26	0.08	0.12	0.14	0.23	0.25	0.11	0.13	0.17 ± 0.02
T_{max}	30.00	240.00	480.00	30.00	60.00	15.00	60.00	60.00	121.88 ± 57.01
MRT	910.42	1190.11	1187.23	1315.26	659.71	975.92	1460.69	795.98	1061.91 ± 96.19

AUC (μmol · min/L)

Cmax (μmol/L)

Tmax (min)

MRT (min)

Table 4 -16 Pharmacokinetic parameters of MTX after oral coadministration of MTX (5.0 mg/kg) with Scutellariae Radix decoction (1.0 g/kg).

Parameter \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
AUC_{0-120}	40.59	60.60	38.70	49.20	47.50	44.84	56.25	44.02	47.71 ± 2.66
AUC_{0-2880}	272.03	268.20	339.83	302.33	329.25	174.83	261.13	245.64	272.03 ± 18.59
C_{max}	0.45	0.39	0.30	0.27	0.26	0.44	266.40	250.88	275.47 ± 18.24
T_{max}	15.00	120.00	15.00	15.00	15.00	15.00	0.30	0.25	0.33 ± 0.03
MRT	906.80	1570.19	1340.77	1247.60	1373.07	788.71	1234.39	1347.44	1226.12 ± 90.80

AUC (μmol · min/L)

Cmax (μmol/L)

Tmax (min)

MRT (min)

Table 4-17 Comparison of pharmacokinetic parameters of MTX in rats between oral administration of MTX (5.0 mg/kg) alone and coadministration with decoction of Scutellariae Radix (SR, 2.0 g/kg and 1.0 g/kg).

Parameter	MTX alone	MTX + SR (1 g/kg)	Difference (%)	MTX + SR (2 g/kg)	Difference (%)
AUC_{0-120}	38.55 ± 4.82	47.71 ± 2.66	23.8	36.57 ± 4.00	-5.2
AUC_{0-2880}	45.85 ± 5.35	272.03 ± 18.59	493.3***	159.20 ± 8.91	247.2***
$AUC_{0-\infty}$	54.70 ± 5.26	275.47 ± 18.24	403.6***	176.40 ± 9.98	222.5***
C_{max}	0.23 ± 0.02	0.33 ± 0.03	44.6*	0.17 ± 0.02	-27.0*
T_{max}	22.50 ± 5.67	30.00 ± 13.00	33.3	102.30 ± 41.98	354.7
MRT	270.44 ± 51.62	1226.12 ± 90.80	353.4***	1072.20 ± 81.11	296.5***

Data expressed as Mean ± S.E.

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

AUC (μmol · min/L)

Cmax (μmol/L)

Tmax (min)

MRT (min)

Table 4-18 MTX blood concentration (μmol/L) of eight rats after intravenous administration of MTX (1.0 mg/kg) and oral coadministration with Scutellariae Radix (2.0 g/kg).

Time (min) \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
5	7.92	6.48	9.12	7.60	9.12	6.00	6.60	7.10	7.49 ± 0.42
15	3.84	2.68	3.28	3.48	3.28	1.84	4.10	2.60	3.14 ± 0.26
30	2.12	1.32	1.68	1.84	1.72	1.80	1.73	1.66	1.73 ± 0.08
45	1.20	0.72	0.96	1.08	1.12	1.80	1.06	1.02	1.12 ± 0.11
60	0.84	0.76	0.64	0.80	0.88	1.40	0.96	0.81	0.89 ± 0.08
90	0.44	0.30	0.40	0.48	0.44	0.90	0.58	0.59	0.52 ± 0.06
120	0.27	0.17	0.22	0.26	0.25	0.82	0.28	0.25	0.32 ± 0.07
180	0.13	0.10	0.11	0.13	0.12	0.68	0.11	0.20	0.20 ± 0.07
240	0.06	0.06	0.05	0.06	0.05	0.42	0.07	0.12	0.11 ± 0.04
300	0.04	0.04	0.03	0.05	0.03	0.23	0.04	0.08	0.07 ± 0.02

Table 4-19 Pharmacokinetic parameters of MTX between rats after intravenous administration of MTX (1.0 mg/kg) and oral coadministration with decoction of Scutellariae Radix (2.0 g/kg).

Parameter \ Rat	1	2	3	4	5	6	7	8	Mean ± S.E.
AUC_{0-300}	214.05	157.25	195.80	201.30	207.35	290.30	227.13	224.06	214.66 ± 13.26
$t_{1/2}$	59.93	85.72	61.47	55.43	54.06	76.73	82.22	90.78	70.79 ± 5.19
V	0.40	0.70	0.44	0.39	0.40	0.34	153.47	178.69	41.85 ± 27.21
Cl	5.00	6.00	5.00	5.00	5.00	3.00	1.29	1.36	3.96 ± 0.64
MRT	42.93	43.77	39.18	44.67	40.99	92.34	41.56	48.35	49.22 ± 6.23

AUC (μmol · min/L)

$t_{1/2}$ (min)

V (L)

Cl (mL/min)

MRT (min)

Table 4-20 Comparison of pharmacokinetic parameters of MTX in rats between receiving MTX (1.0 mg/kg) alone and oral coadministration with decoction of Scutellariae Radix (SR, 2.0 g/kg).

Parameter	MTX alone	MTX + SR	Difference (%)
AUC_{0-300}	187.69 ± 12.43	214.66 ± 13.26	14.4
$t_{1/2}$	47.28 ± 6.19	70.79 ± 5.19	49.7*
V	0.37 ± 0.22	0.42 ± 0.27	13.1
Cl	4.45 ± 0.66	3.96 ± 0.64	-11.1
MRT	36.65 ± 3.46	49.22 ± 6.23	34.3

Data expressed as Mean ± S.E.

* $P < 0.05$

AUC (μmol · min/L)

$t_{1/2}$ (min)

V (L)

Cl (mL/min)

MRT (min)