

Table 1-1 Intraday and interday analytical precision and accuracy of hesperetin in serum.

Conc ($\mu\text{g/mL}$)	Intraday			Interday		
	Mean \pm S.D.	(C.V.%)	Accuracy (%)	Mean \pm S.D.	(C.V.%)	Accuracy (%)
100.0	97.1 \pm 2.1	(2.1)	-2.9	96.1 \pm 2.8	(2.9)	-3.9
50.0	47.7 \pm 1.6	(3.4)	-4.6	48.9 \pm 0.8	(1.6)	-2.2
25.0	25.6 \pm 0.4	(1.7)	2.4	24.4 \pm 0.4	(1.7)	-2.4
12.5	13.7 \pm 0.8	(6.2)	9.6	11.8 \pm 0.5	(4.2)	-5.6
6.3	5.8 \pm 0.3	(5.0)	-6.6	5.9 \pm 0.3	(4.7)	-6.2
3.1	3.5 \pm 0.2	(7.2)	11.3	2.8 \pm 0.2	(6.6)	-8.6
1.6	1.7 \pm 0.1	(5.1)	7.7	1.5 \pm 0.1	(5.2)	-6.9
0.8	0.7 \pm 0.0	(7.0)	-9.0	0.9 \pm 0.1	(7.3)	11.5
0.4	0.5 \pm 0.0	(9.4)	15.4	0.3 \pm 0.0	(9.7)	-17.4

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

Conc. Spiked ($\mu\text{g/mL}$)				Mean \pm S.D.
	a	b	c	
100.0	93.8	98.6	98.9	97.0 \pm 3.0
12.5	98.5	98.2	102.8	99.9 \pm 2.6
0.4	101.6	104.8	106.9	104.4 \pm 2.7

Table 1-3 Concentrations of hesperetin (nmol/mL) in serum after intravenous administration of hesperetin (10.0 mg/kg) to six rats.

Time (min)	Rat						Mean \pm S.E.
	1	2	3	4	5	6	
3	6.6	21.8	9.5	16.1	7.2	19.4	13.4 \pm 2.7
15	5.9	5.7	2.9	3.7	5.2	8.2	5.3 \pm 0.8
30	4.0	2.4	2.3	3.0	3.5	0.3	2.6 \pm 0.5
60	2.3	2.4	2.3	2.3	2.3	ND	2.3 \pm 0.4
120	ND	ND	ND	ND	ND	ND	-
180	ND	ND	ND	ND	ND	ND	-
240	ND	ND	ND	ND	ND	ND	-
480	ND	ND	ND	ND	ND	ND	-

ND: not detectable

Table 1-4 Concentrations of hesperetin sulfates (nmol/mL) in serum after intravenous administration of hesperetin (10.0 mg/kg) to six rats.

Time (min)	Rat						Mean \pm S.E.
	1	2	3	4	5	6	
3	6.5	33.9	21.9	15.5	4.3	20.9	17.2 \pm 4.5
15	6.1	18.1	5.9	7.4	4.1	22.0	10.6 \pm 3.1
30	4.9	8.3	3.2	6.2	3.4	9.3	5.9 \pm 1.0
60	4.6	5.2	3.1	3.4	3.1	5.4	4.1 \pm 0.4
120	3.7	3.3	3.0	3.0	2.8	4.2	3.3 \pm 0.2
180	3.1	2.6	2.9	3.0	2.5	3.8	3.0 \pm 0.2
240	2.8	2.6	1.2	2.0	2.2	4.0	2.5 \pm 0.4
480	2.0	ND	ND	ND	ND	ND	0.3 \pm 0.8

ND: not detectable

Table 1-5 Concentrations of hesperetin glucuronides (nmol/mL) in serum after intravenous administration of hesperetin (10.0 mg/kg) to six rats.

Time (min)	Rat						Mean \pm S.E.
	1	2	3	4	5	6	
3	3.6	15.3	27.5	9.9	3.1	5.4	10.8 \pm 3.8
15	3.0	12.3	10.9	4.3	2.5	3.9	6.2 \pm 1.8
30	3.0	3.7	5.2	2.8	2.5	3.0	3.4 \pm 0.4
60	2.8	3.7	3.5	2.8	2.4	2.9	3.0 \pm 0.2
120	2.5	3.0	2.7	2.6	1.1	2.7	2.4 \pm 0.3
180	1.6	2.7	2.5	2.1	ND	2.5	2.3 \pm 0.4
240	1.2	0.8	2.4	0.7	ND	2.4	1.5 \pm 0.4
480	ND	ND	ND	ND	ND	ND	-

ND: not detectable

Table 1-6 Pharmacokinetic parameters of hesperetin after intravenous administration of hesperetin to six rats.

Parameters	1	2	3	4	5	6	Mean \pm S.E.
AUC ₀₋₄₈₀ (nmol . min . mL ⁻¹)	263.8	376.2	215.8	307.6	249.2	294.5	284.5 \pm 20.7
AUC ₀₋ (nmol . min . mL ⁻¹)	332.8	448.2	284.8	376.6	318.2	299.0	343.3 \pm 22.5
t _{1/2} (min)	36.1	19.9	34.2	24.4	35.1	4.4	25.7 \pm 4.6
V (L)	2.2	1.3	2.5	1.3	1.8	0.4	1.6 \pm 0.3
Cl (mL/min)	43.1	44.6	50.2	36.6	36.2	60.3	45.2 \pm 3.4
MRT ₀₋₄₈₀ (min)	23.2	14.4	20.5	16.9	22.7	7.3	17.5 \pm 2.2

Table 1-7 Pharmacokinetic parameters of hesperetin sulfates after intravenous administration of hesperetin to six rats.

Parameters	1	2	3	4	5	6	Mean \pm S.E.
AUC ₀₋₄₈₀ (nmol . min . mL ⁻¹)	1526.3	1449.8	869.2	947.6	694.1	1538.8	1171.0 \pm 140.2
AUC ₀₋ (nmol . min . mL ⁻¹)	1526.3	1761.8	1229.2	1307.6	958.1	1994.8	1463.0 \pm 140.4
t _{1/2} (min)	289.2	82.4	172.0	142.9	264.2	97.4	174.7 \pm 31.9
V (L)	2.5	0.9	2.7	2.2	4.1	1.3	2.5 \pm 0.4
Cl (mL/min)	6.0	7.5	11.1	10.6	10.8	9.6	9.3 \pm 0.8
MRT ₀₋₄₈₀ (min)	192.1	75.1	96.7	96.4	107.5	82.1	108.3 \pm 15.9

Table 1-8 Pharmacokinetic parameters of hesperetin glucuronides after intravenous administration of hesperetin to six rats.

Parameters	1	2	3	4	5	6	Mean \pm S.E.
AUC ₀₋₄₈₀ (nmol . min . mL ⁻¹)	548.7	898.3	1075.9	637.3	259.2	683.9	683.9 \pm 105.5
AUC ₀₋ (nmol . min . mL ⁻¹)	692.7	1258.3	1363.9	973.3	292.2	971.9	925.4 \pm 145.6
t _{1/2} (min)	162.9	148.8	91.1	399.5	85.5	275.6	193.9 \pm 45.4
V (L)	4.0	1.8	1.7	4.2	5.2	4.8	3.4 \pm 0.6
Cl (mL/min)	17.1	8.6	12.8	7.3	41.9	12.1	17.6 \pm 4.8
MRT ₀₋₄₈₀ (min)	98.8	94.5	77.2	115.4	49.0	108.9	90.6 \pm 9.0

Table 1-9 Concentration of hesperetin sulfates (nmol/mL) in serum after oral administration of hesperetin (50.0 mg/kg) to six rats.

Time (min)	Rat						Mean \pm S.E.
	1	2	3	4	5	6	
5	4.0	8.0	5.0	5.2	5.0	12.2	6.5 \pm 1.3
15	3.5	5.6	4.6	18.0	4.0	19.4	9.2 \pm 3.0
30	3.2	5.3	4.1	17.2	3.5	8.4	7.0 \pm 2.2
60	3.1	3.3	3.7	6.2	3.1	5.4	4.1 \pm 0.6
90	3.3	3.3	4.5	5.8	3.2	4.4	4.1 \pm 0.4
120	3.5	3.3	3.7	6.7	4.8	4.9	4.5 \pm 0.5
180	6.3	3.3	3.9	7.9	5.2	3.1	4.9 \pm 0.8
240	8.1	3.5	4.2	8.5	3.3	4.0	5.3 \pm 1.0
360	3.6	3.2	3.4	2.5	3.2	3.0	3.1 \pm 0.2
480	3.1	3.9	3.8	3.9	3.1	2.5	3.4 \pm 0.2
720	ND	ND	2.5	2.8	ND	2.4	1.3 \pm 0.6

ND: not detectable

Table 1-10 Concentration of hesperetin glucuronides (nmol/mL) in serum after oral administration of hesperetin (50.0 mg/kg) to six rats.

Time (min)	Rat						Mean \pm S.E.
	1	2	3	4	5	6	
5	2.8	4.6	3.2	3.2	3.5	3.4	3.4 \pm 0.3
15	2.8	3.6	3.3	12.0	3.0	3.8	4.7 \pm 1.5
30	2.7	3.5	3.2	7.8	3.0	3.1	3.9 \pm 0.8
60	2.7	3.0	3.0	3.5	2.5	2.9	2.9 \pm 0.1
90	2.8	2.7	2.8	3.6	2.8	2.9	2.9 \pm 0.1
120	3.1	2.6	3.0	3.6	3.7	2.9	3.1 \pm 0.2
180	4.2	2.6	3.3	5.4	3.8	2.6	3.7 \pm 0.4
240	5.4	2.9	2.9	4.7	2.9	2.6	3.6 \pm 0.5
360	2.6	2.6	2.8	2.8	2.7	2.3	2.6 \pm 0.1
480	ND	3.0	3.0	2.9	2.7	2.4	2.7 \pm 0.1
720	ND	ND	ND	ND	ND	2.4	0.4 \pm 0.4

ND: not detectable

Table 1-11 Pharmacokinetic parameters of hesperetin sulfates after oral administration of hesperetin to six rats.

Parameters	1	2	3	4	5	6	Mean \pm S.E.
AUC ₀₋₇₂₀ ($\mu\text{mol} \cdot \text{min} \cdot \text{mL}^{-1}$)	2.9	2.5	2.6	3.9	2.4	2.7	2.8 \pm 0.2
T _{max} (min)	240.0	5.0	5.0	15.0	180.0	15.0	76.7 \pm 42.9
C _{max} (nmol \cdot mL ⁻¹)	8.1	8.0	5.0	18.0	5.2	19.4	10.6 \pm 2.6
t _{1/2} (min)	557.0	699.3	704.0	305.3	719.1	580.7	594.2 \pm 64.2
V/F (L)	11.3	13.9	17.6	7.7	17.9	14.8	13.9 \pm 1.6
Cl/F (mL/min)	14.0	13.8	17.4	17.4	17.3	17.6	16.3 \pm 0.7
MRT(min)	314.3	333.0	332.8	265.8	323.4	272.5	307.0 \pm 12.3

Table 1-12 Pharmacokinetic parameters of hesperetin glucuronides after oral administration of hesperetin to six rats.

Parameters	1	2	3	4	5	6	Mean \pm S.E.
AUC ₀₋₇₂₀ ($\mu\text{mol} \cdot \text{min} \cdot \text{mL}^{-1}$)	2.2	2.0	2.1	2.6	2.0	1.8	2.1 \pm 0.1
T _{max} (min)	240.0	5.0	15.0	15.0	180.0	15.0	78.3 \pm 42.4
C _{max} (nmol \cdot mL ⁻¹)	5.4	4.6	3.3	12.0	3.8	3.8	5.5 \pm 1.3
t _{1/2} (min)	477.4	1278.1	1291.8	450.7	1498.1	1794.7	1131.8 \pm 224.5
V/F (L)	12.2	19.6	26.2	14.2	25.5	26.6	20.7 \pm 2.6
Cl/F (mL/min)	17.7	10.6	14.1	21.8	11.8	10.3	22.5 \pm 1.9
MRT(min)	325.4	347.0	344.7	296.7	338.2	343.6	333.4 \pm 7.8