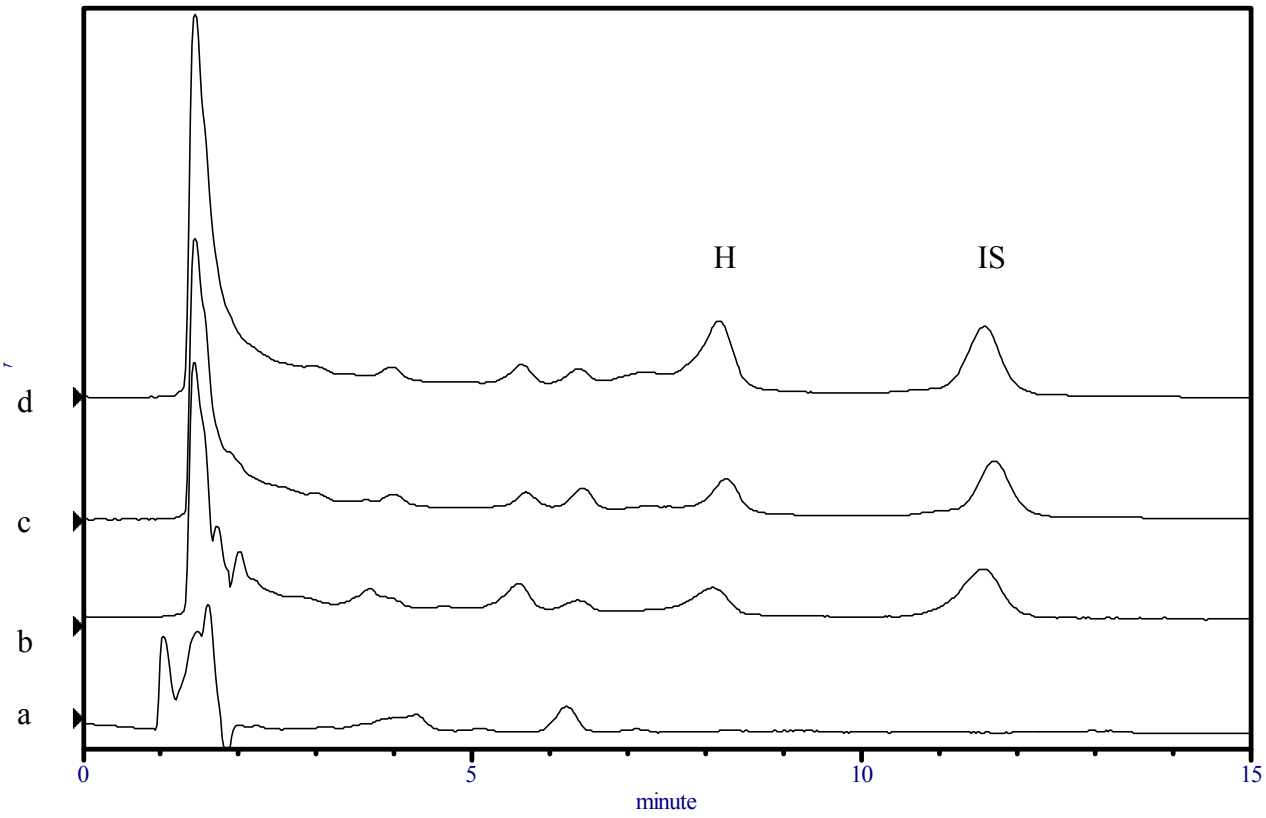


Fig.1-1 Chromatograms of hesperetin and the internal standard (5,7- dimethoxycoumarin) in rat serum.

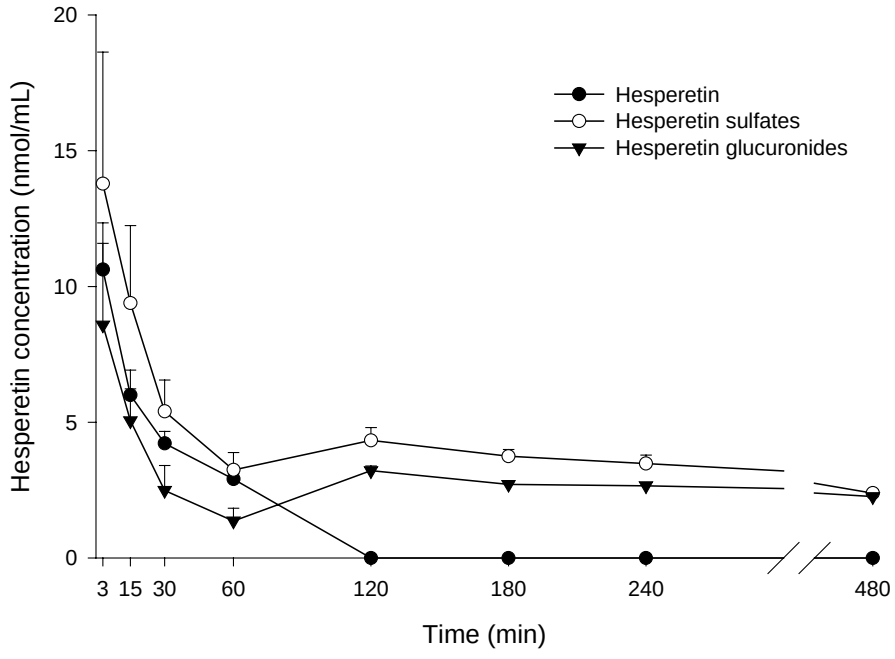
(a): blank serum,

(b): serum spiked with hesperetin (3.2 μg/mL) and the internal standard,

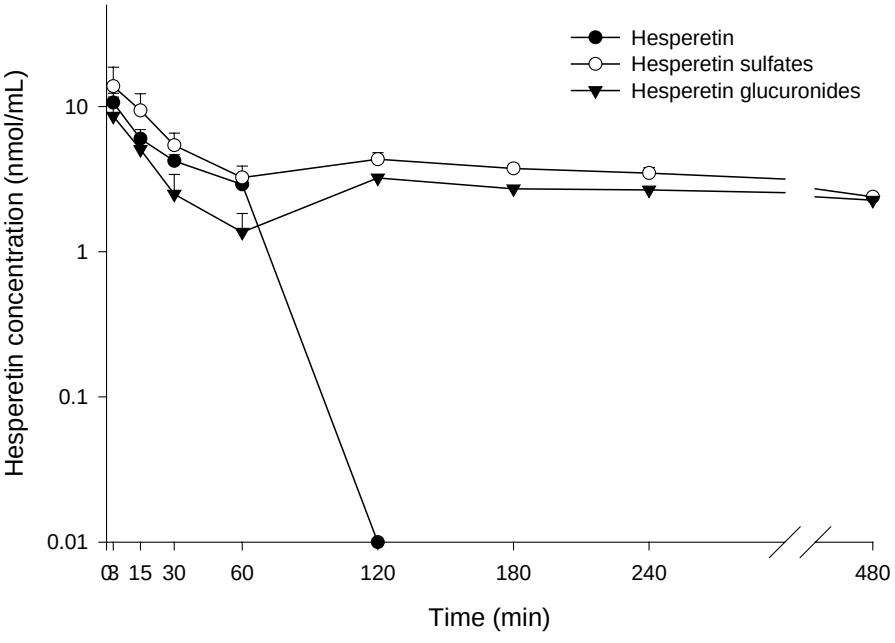
(c): a serum sample hydrolyzed with glucuronidase,

(d): a serum sample hydrolyzed with sulfatase.

H: hesperetin, IS: 5,7- dimethoxycoumarin.



(a)



(b)

Fig. 1-2 (a): Mean (± S.E.) serum concentration-time profiles of hesperetin (●), hesperetin sulfates (○) and hesperetin glucuronides (▼) after intravenous administration of hesperetin (10.0 mg/kg) to six rats.

(b): the semi-log diagram of (a).

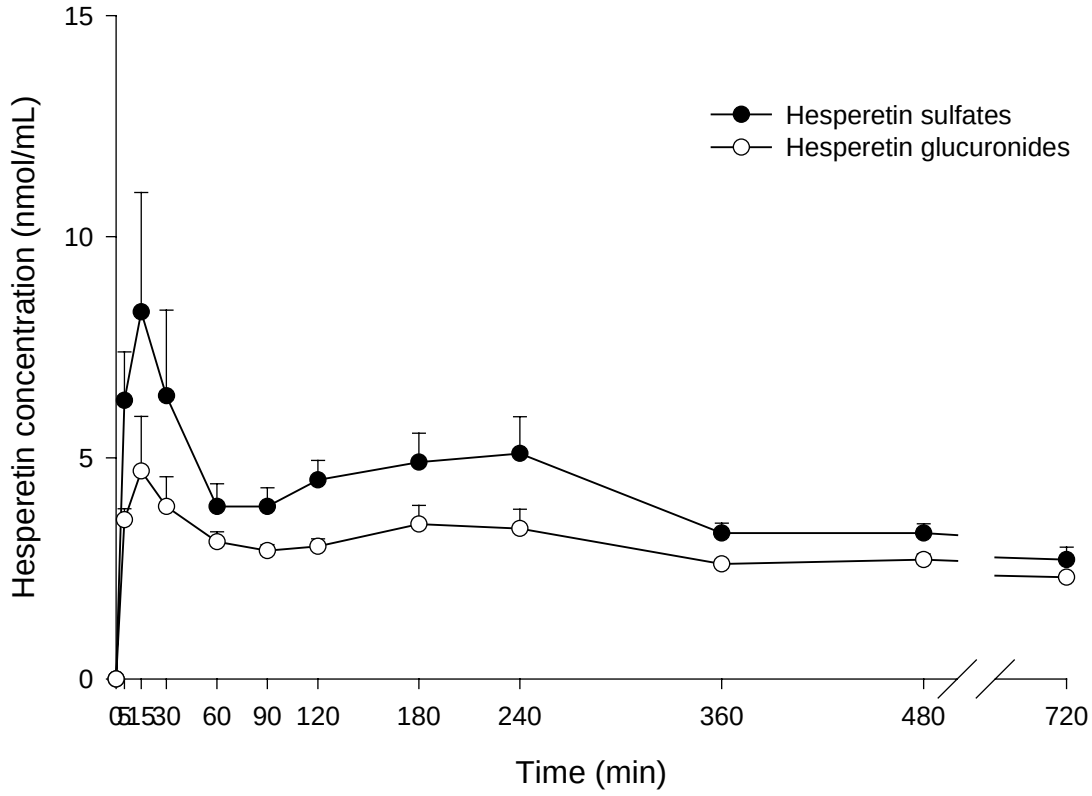


Fig. 1-3: Mean (± S.E.) serum concentration-time profiles of hesperetin sulfates (●) and hesperetin glucuronides (○) after oral administration of hesperetin (50.0 mg/kg) to six rats.

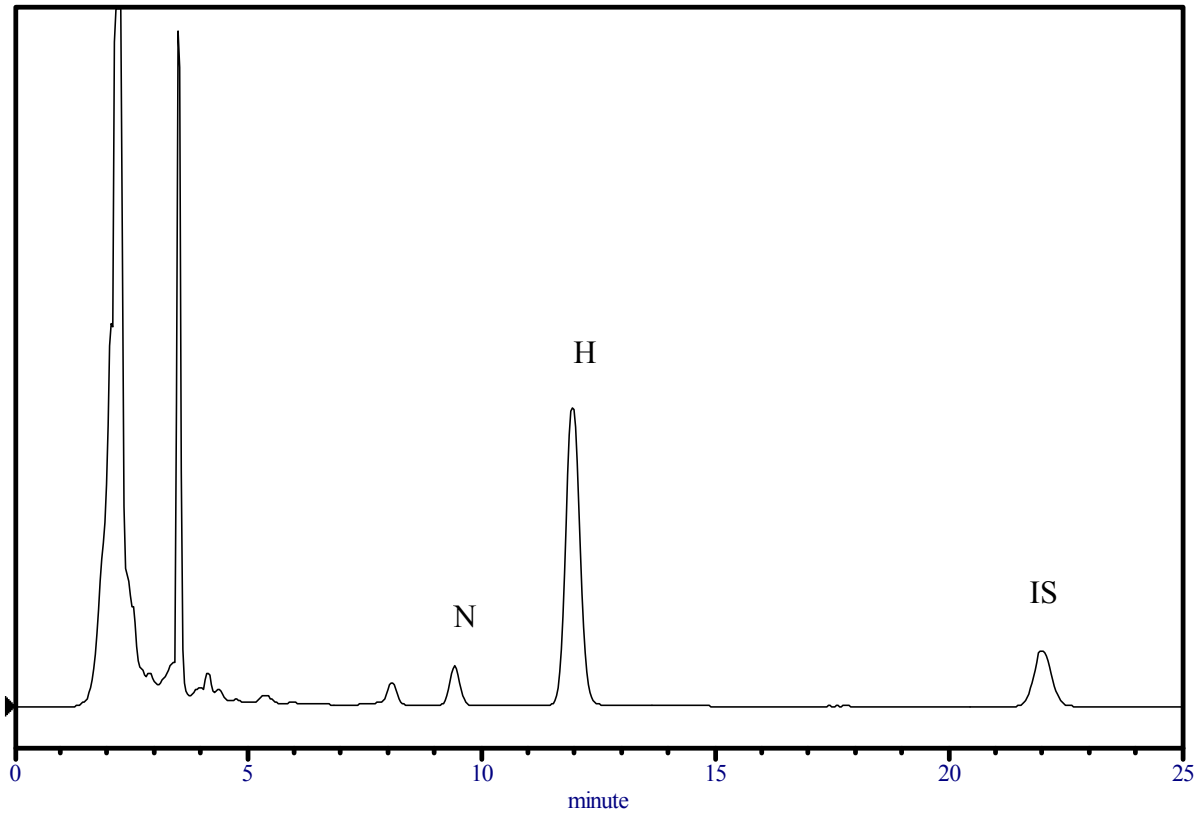


Fig. 3-1 Chromatogram of hesperidin, narirutin and the internal standard in orange juice.
H: hesperidin, N: narirutin, IS: 6,7-dimethoxycoumarin.

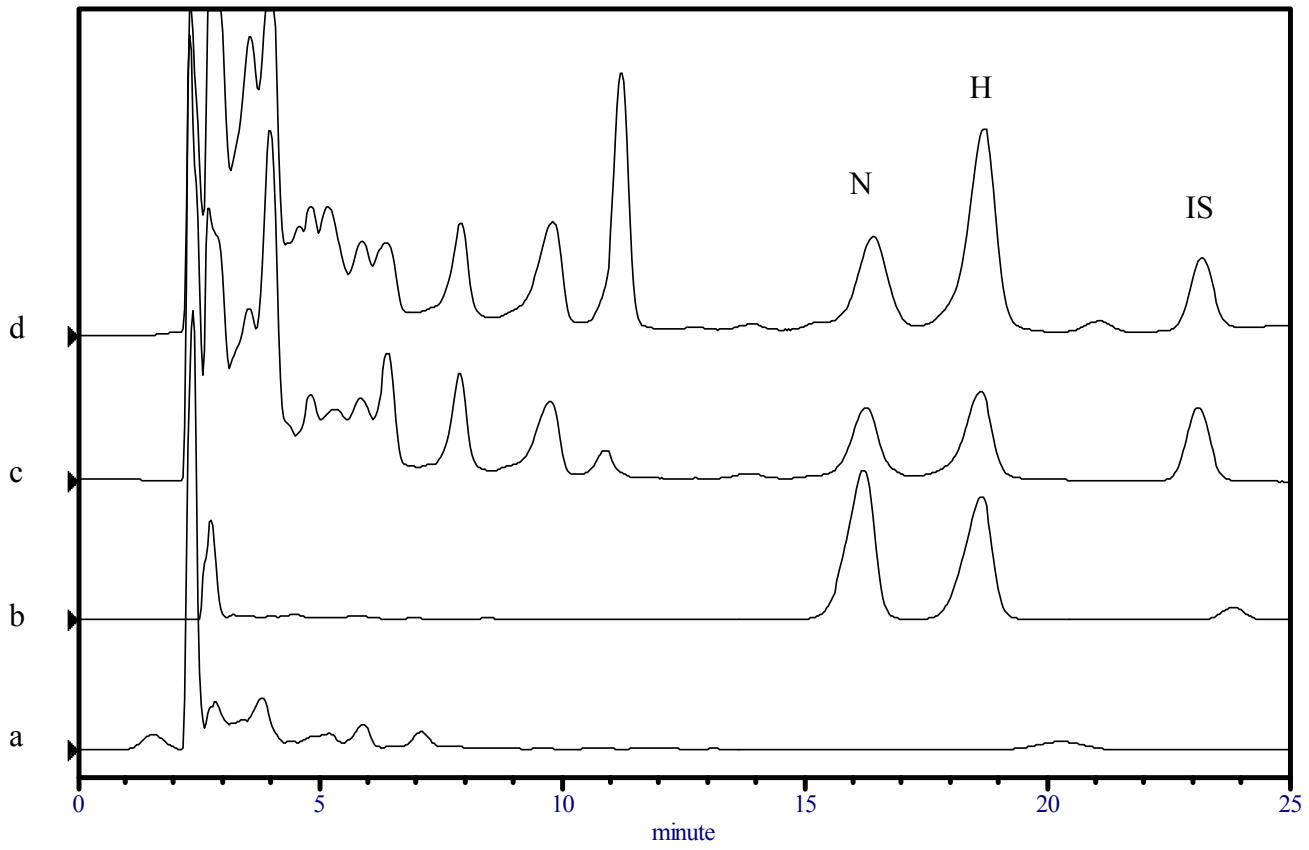


Fig. 3-2 Chromatograms of hesperetin, naringenin and the internal standard in human urine.

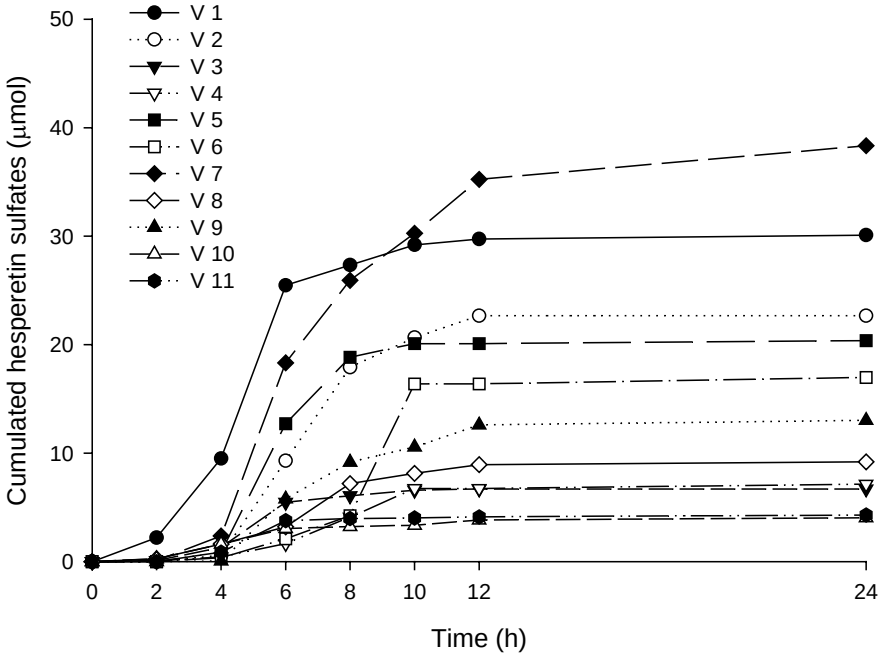
(a): blank urine,

(b): urine spiked with hesperetin (10.0 μg/mL), naringenin (10.0 μg/mL) and the internal standard,

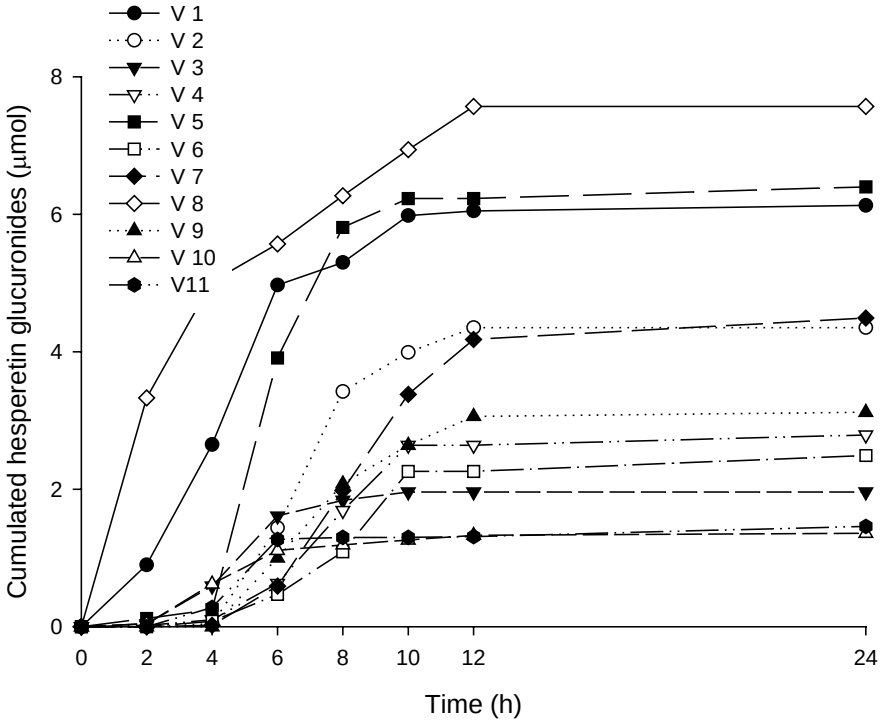
(c): an urine sample hydrolyzed with glucuronidase,

(d): an urine sample hydrolyzed with sulfatase.

H: hesperetin, N: naringenin, IS: 5,7- dimethoxycoumarin.

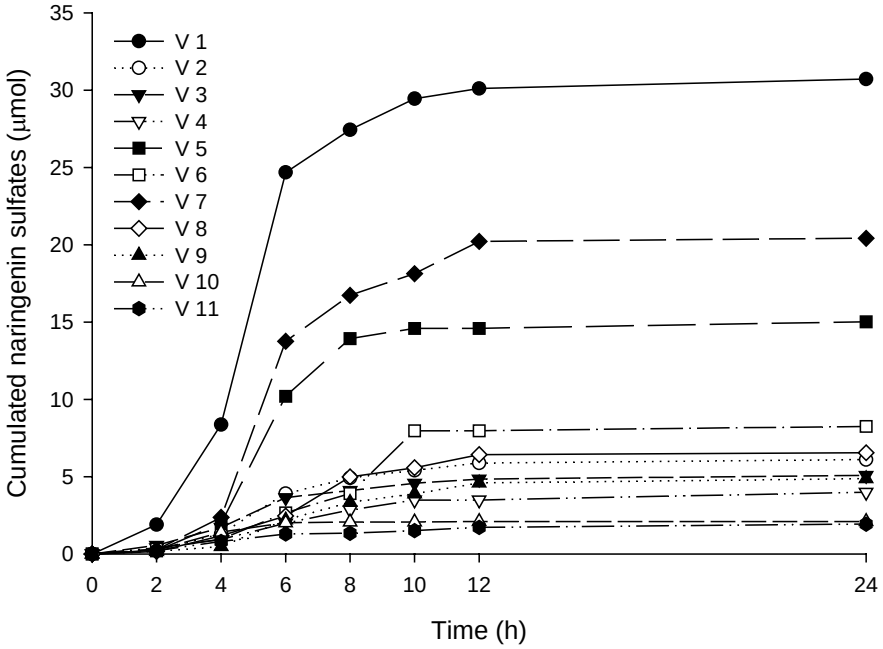


(a)

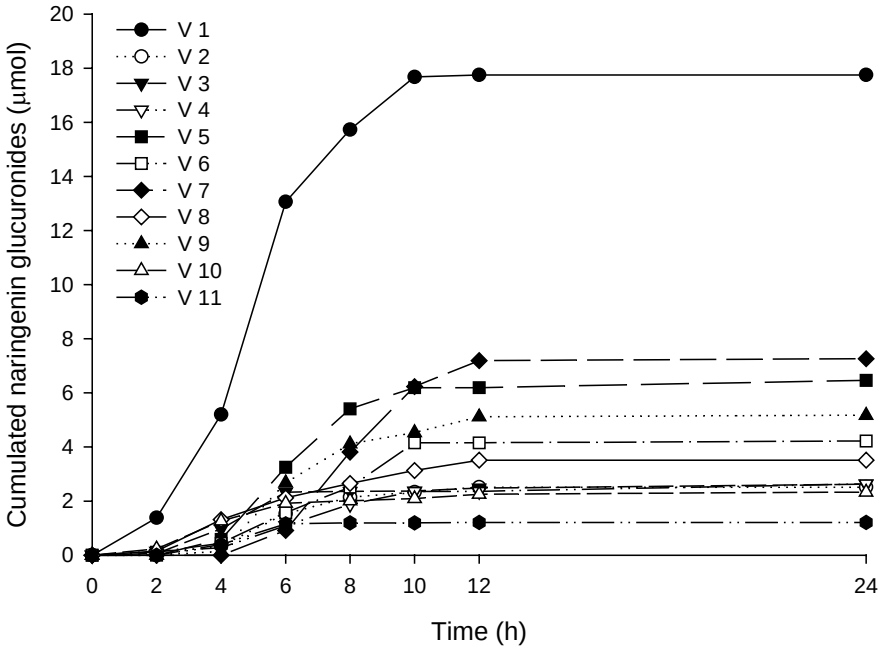


(b)

Fig. 3-3 Cumulated urinary excretion of (a): hesperetin sulfates and (b): hesperetin glucuronides after oral administration of orange juice (1L/volunteer) to eleven volunteers.



(a)



(b)

Fig. 3-4 Cumulated urinary excretion of (a): naringenin sulfates and (b): naringenin glucuronides after oral administration of orange juice (1L/volunteer) to eleven volunteers.

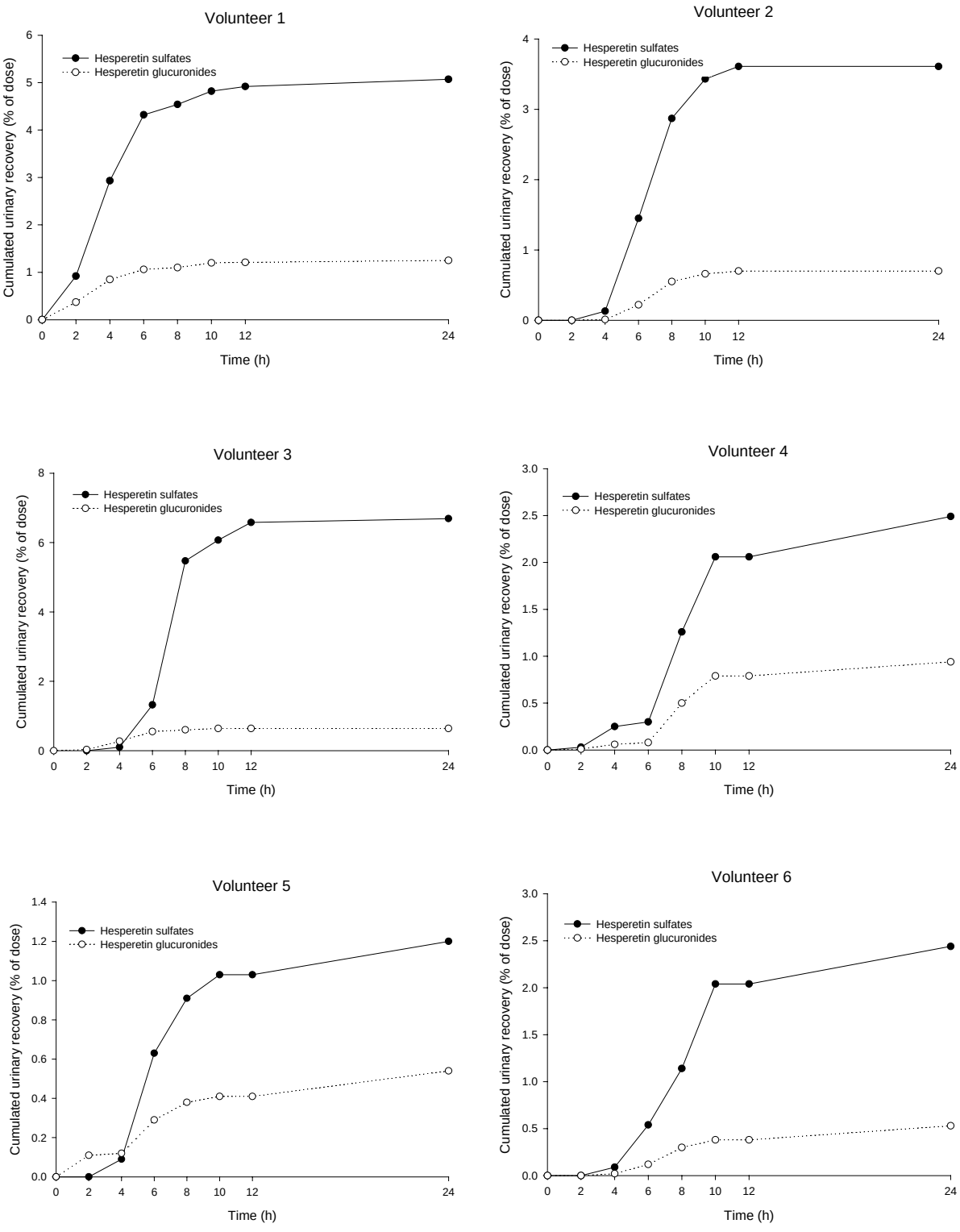
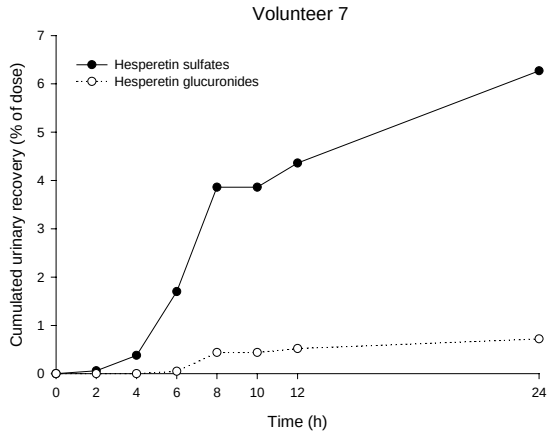
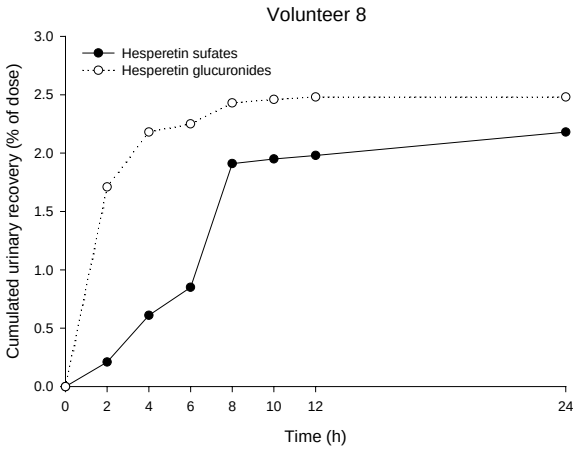
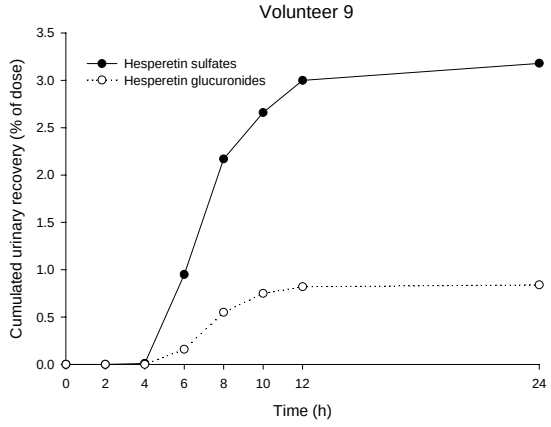
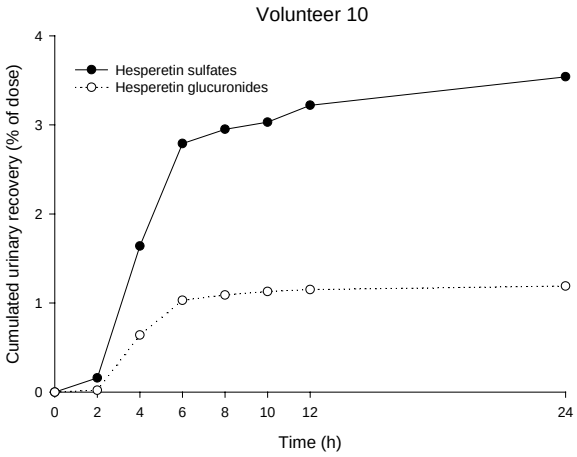


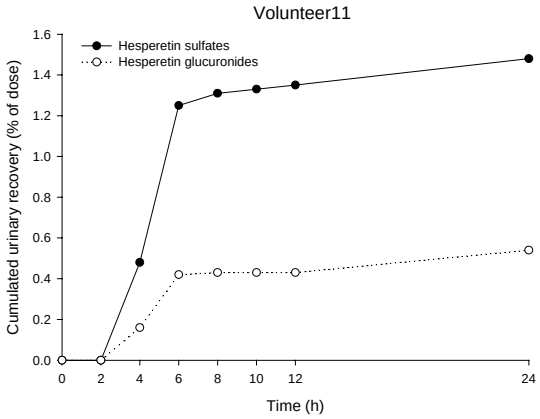
Fig. 3-5 Individual cumulated urinary recoveries (% of dose) of hesperetin in eleven volunteers after oral administration of orange juice (1L/volunteer).


Volunteer 7
Hesperetin sulfates
Hesperetin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)


Volunteer 8
Hesperetin sufates
Hesperetin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)


Volunteer 9
Hesperetin sulfates
Hesperetin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)


Volunteer 10
Hesperetin sulfates
Hesperetin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)


Volunteer11
Hesperetin sulfates
Hesperetin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)

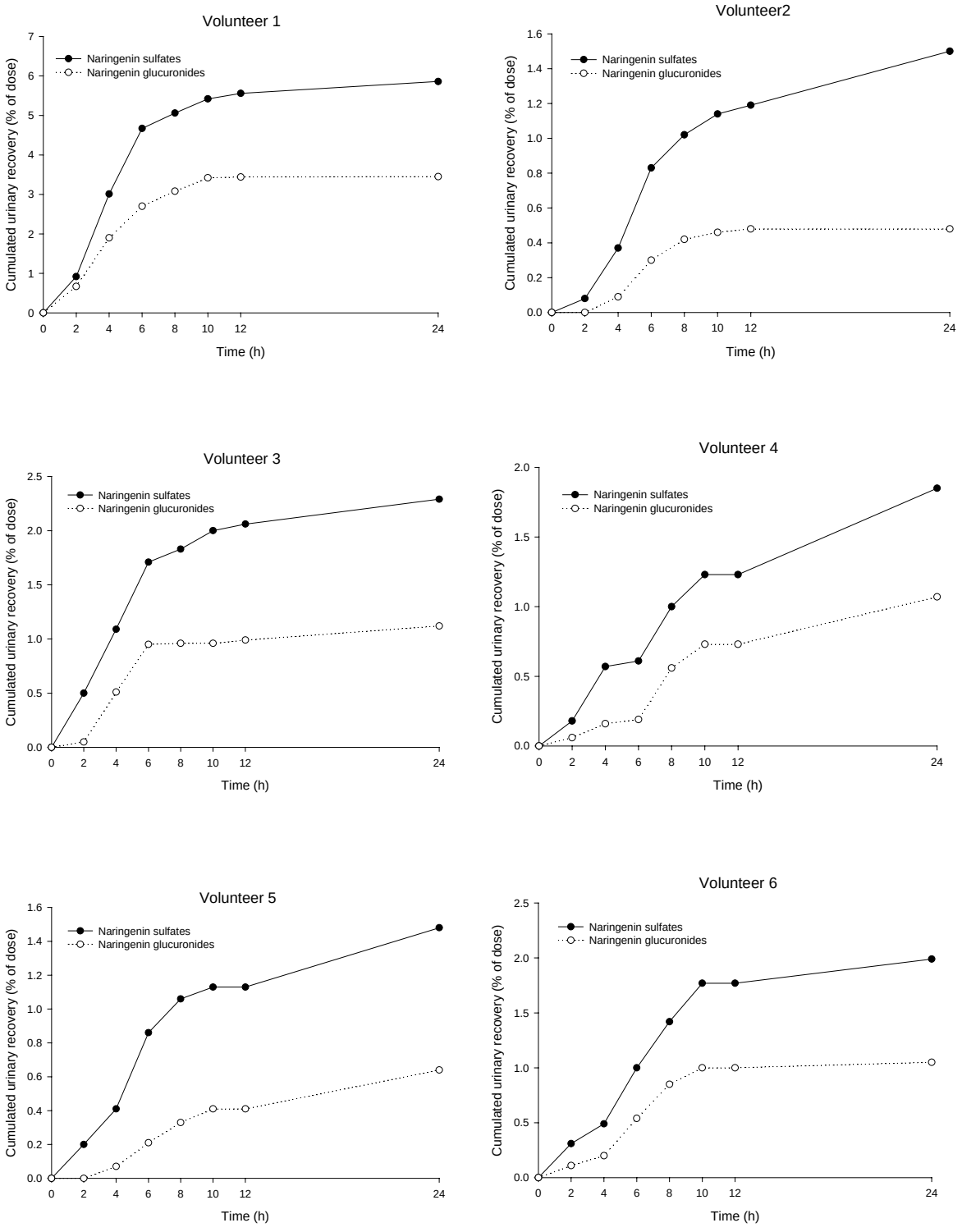
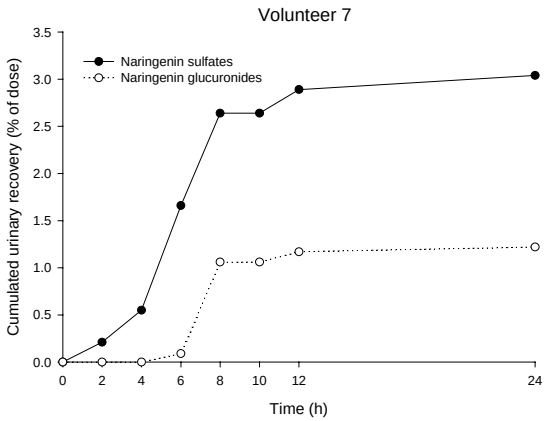
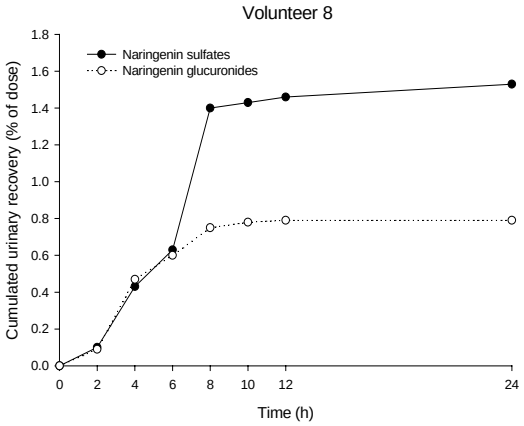
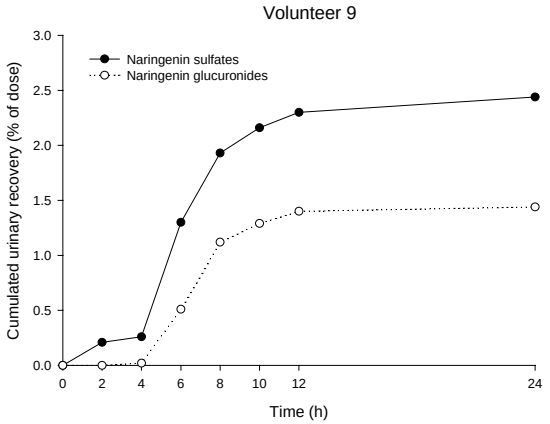
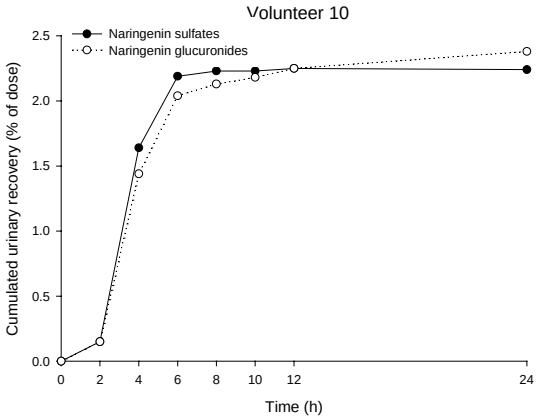


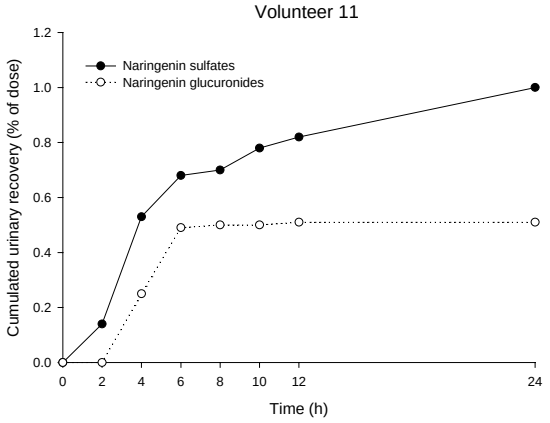
Fig. 3-6 Individual cumulated urinary recoveries (% of dose) of naringenin in eleven volunteers after oral administration of orange juice (1L/volunteer).


Volunteer 7
Naringenin sulfates
Naringenin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)


Volunteer 8
Naringenin sulfates
Naringenin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)


Volunteer 9
Naringenin sulfates
Naringenin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)


Volunteer 10
Naringenin sulfates
Naringenin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)


Volunteer 11
Naringenin sulfates
Naringenin glucuronides
Cumulated urinary recovery (% of dose)
Time (h)

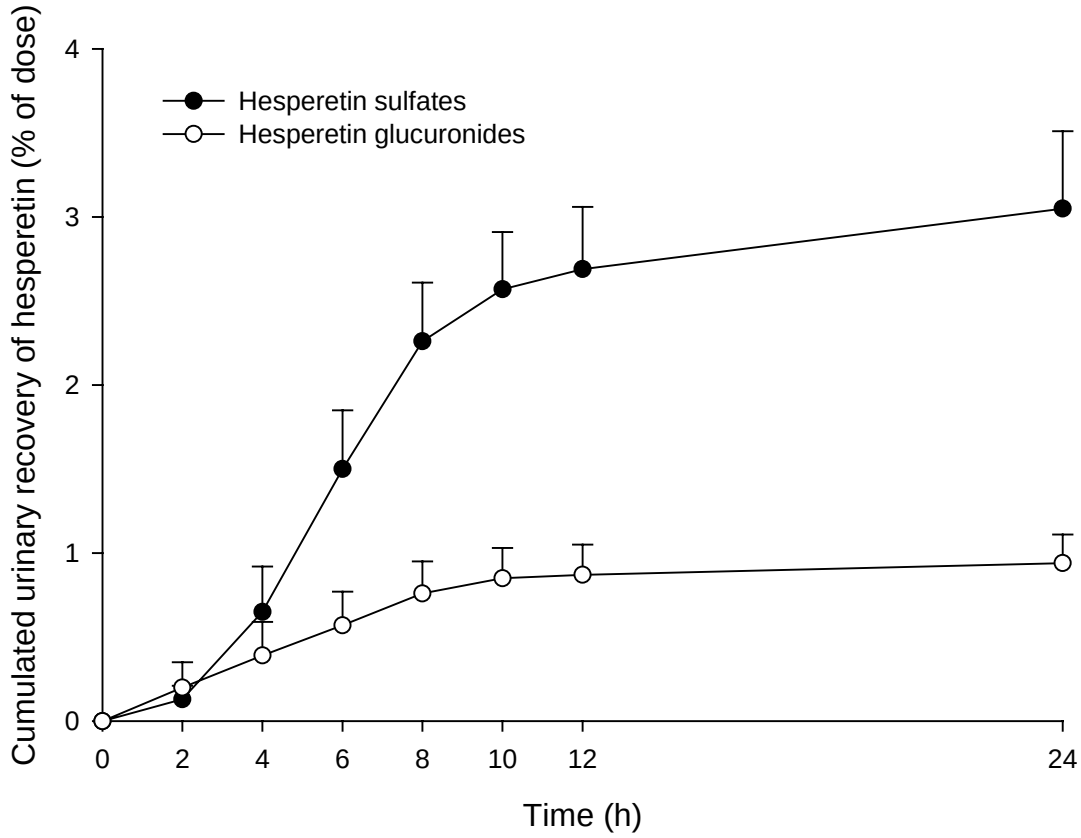


Fig. 3-7 Cumulated urinary recoveries (% of dose) of hesperetin sulfates and glucuronides in eleven volunteers after oral administration of orange juice.

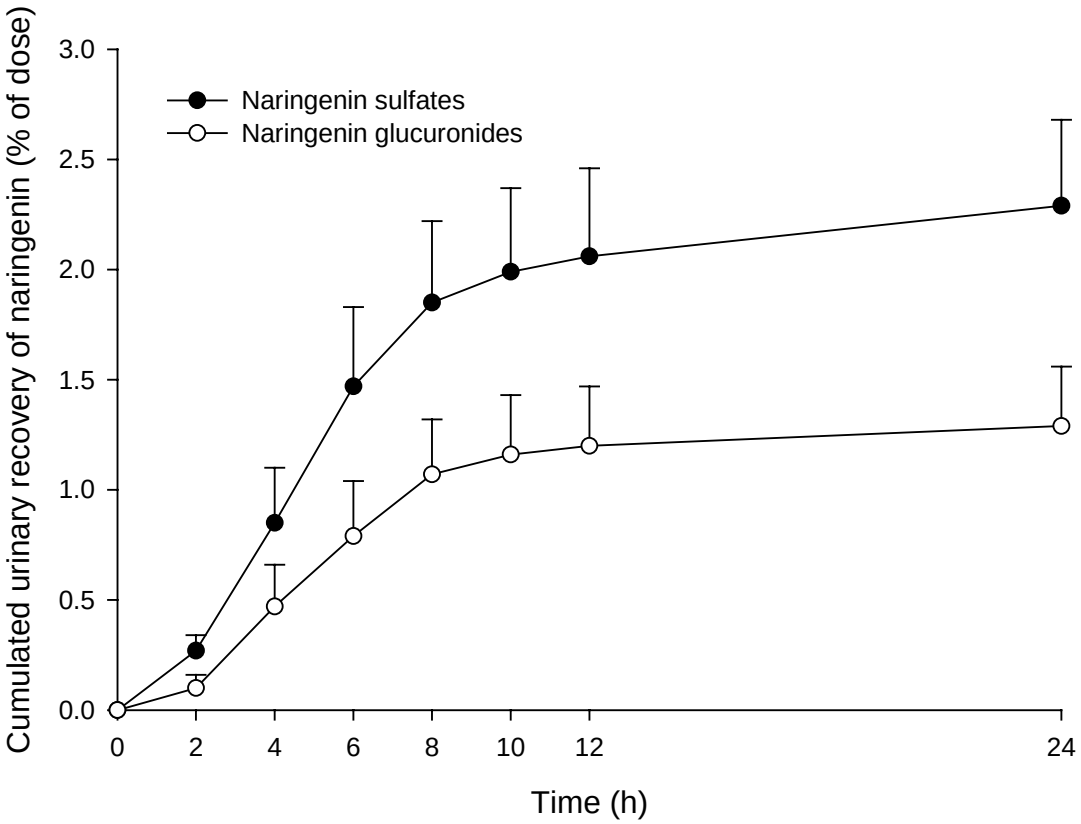
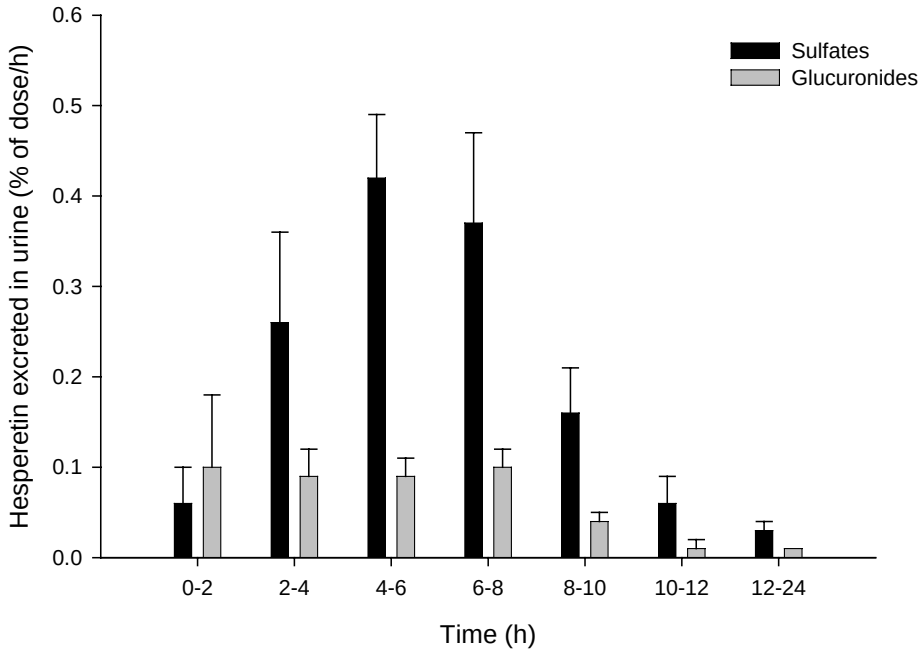
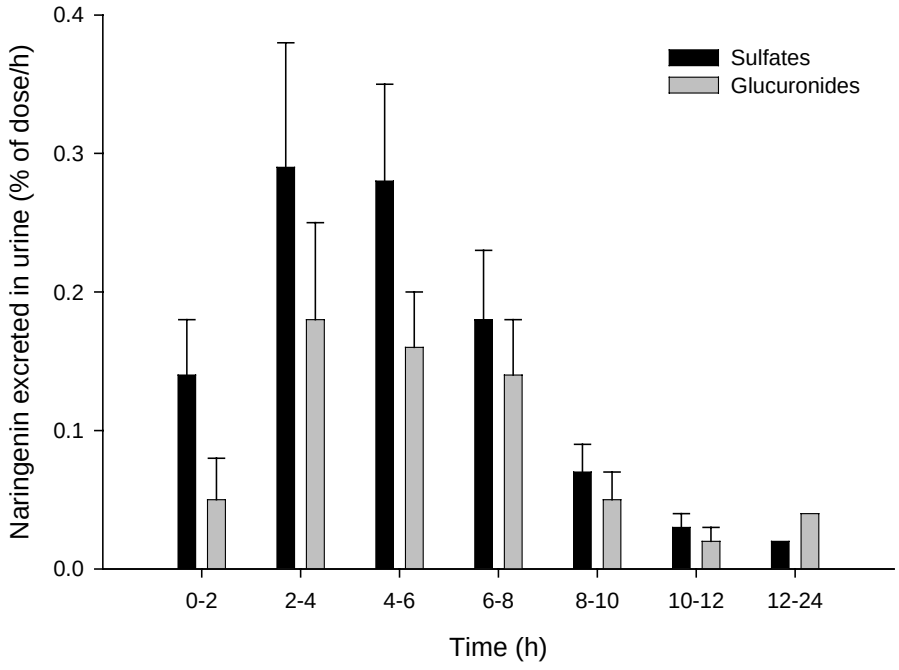


Fig. 3-8 Cumulated urinary recoveries (% of dose) of naringenin sulfates and glucuronides in eleven volunteers after oral administration of orange juice.



(a)



(b)

Fig. 3-9 Mean (± S.E.) urinary recovery (% dose /h) of sulfates and glucuronides of (a): hesperetin and (b): naringenin in each time interval after administration of orange juice (1L/volunteer) to eleven volunteers.

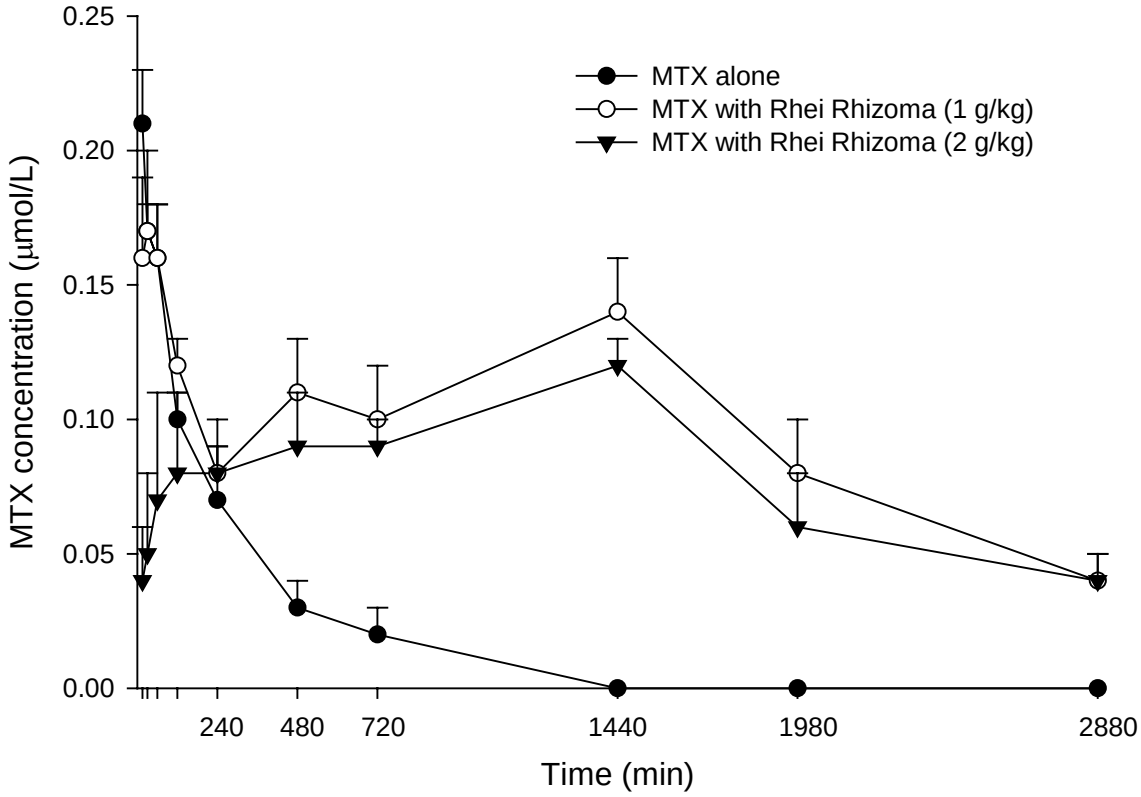
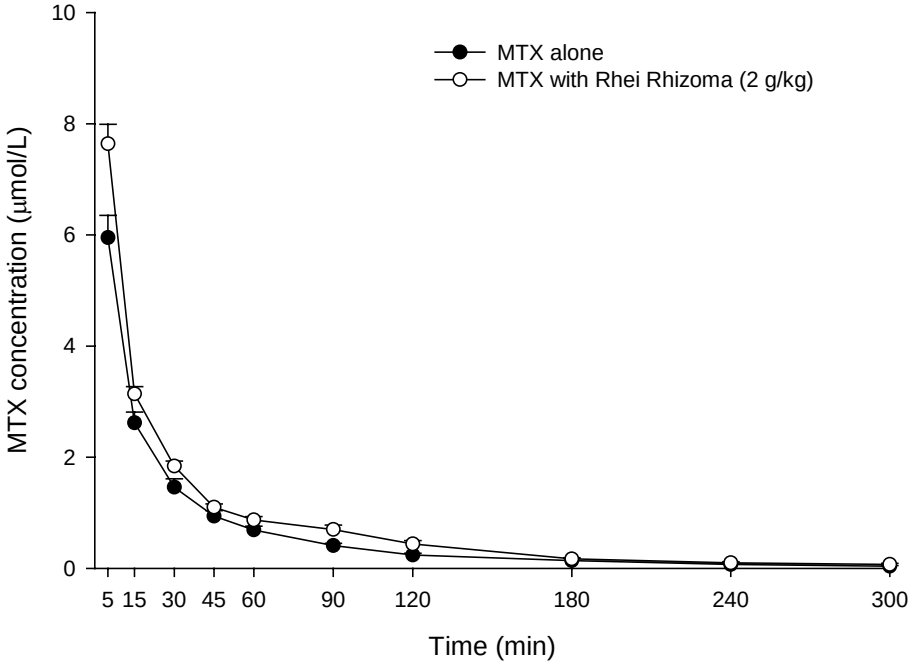
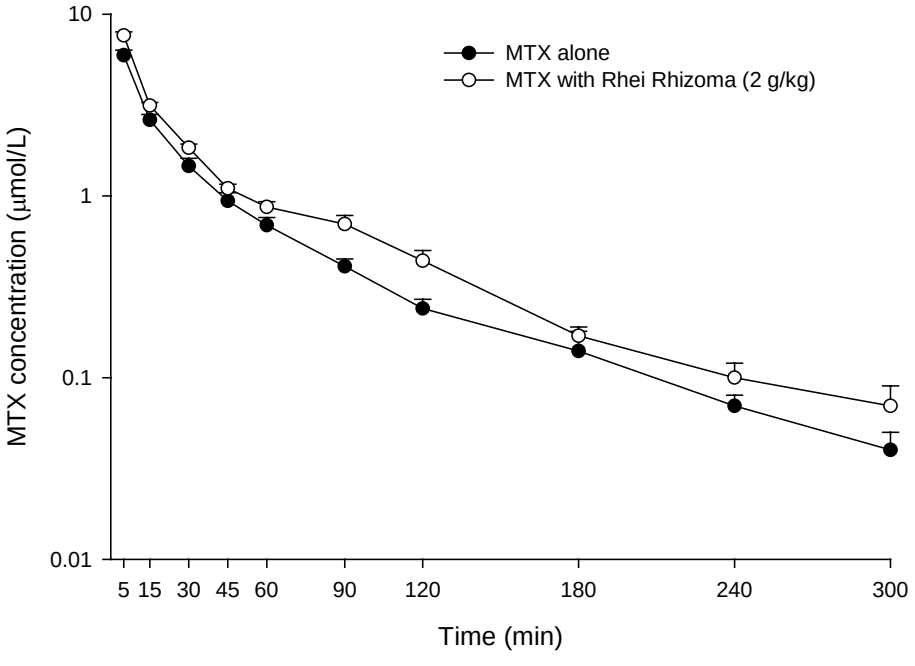


Fig. 4-1 Mean (± S.E.) serum concentration-time profiles of methotrexate after oral methotrexate alone (●) and coadministration with 1.0 g/kg (○), and 2.0 g/kg (▼) of Rhei Rhizoma decoction (n=8).



(a)



(b)

Fig. 4-2 (a) Mean (± S.E.) serum concentration-time profiles of methotrexate after intravenous methotrexate alone (●) and coadministration with 2.0 g/kg of Rhei Rhizoma decoction (○) and (b): the semi-log diagram of (a) (n=8).

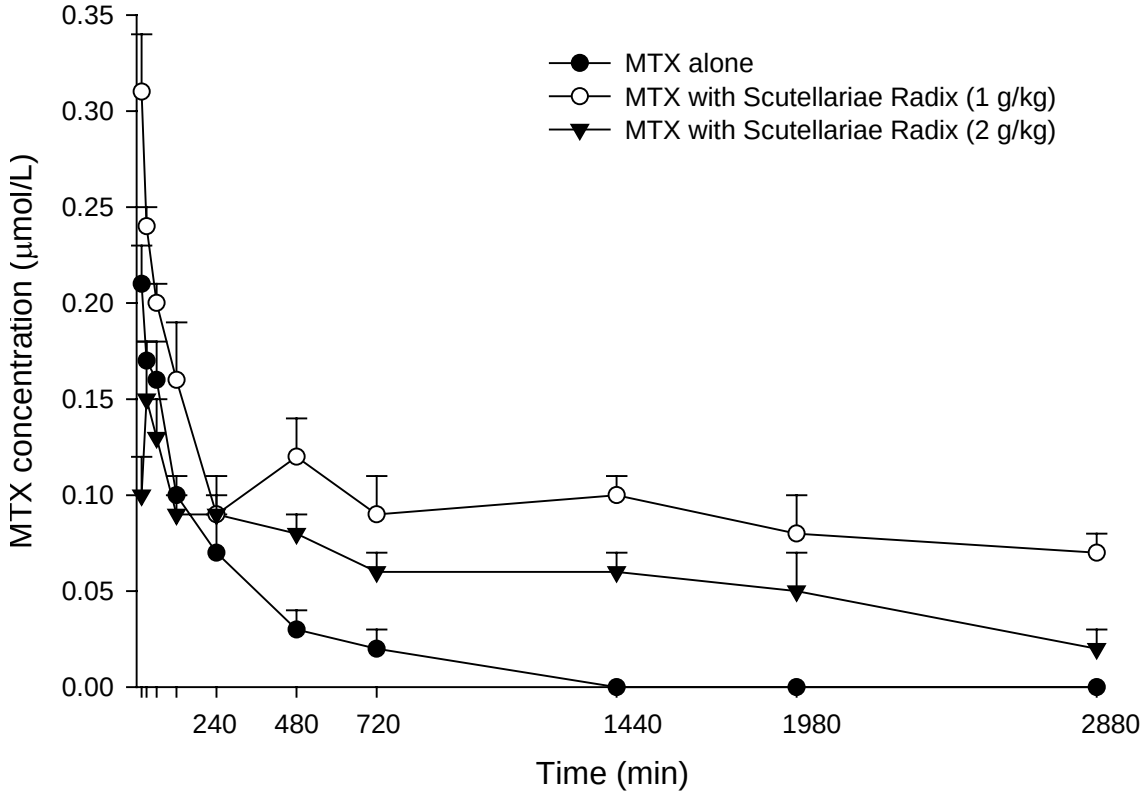
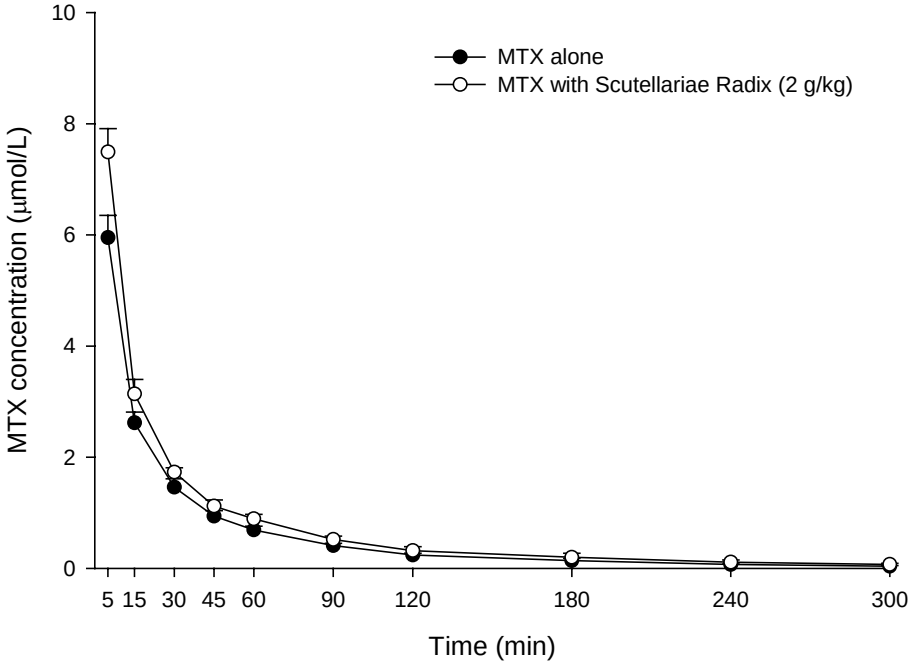
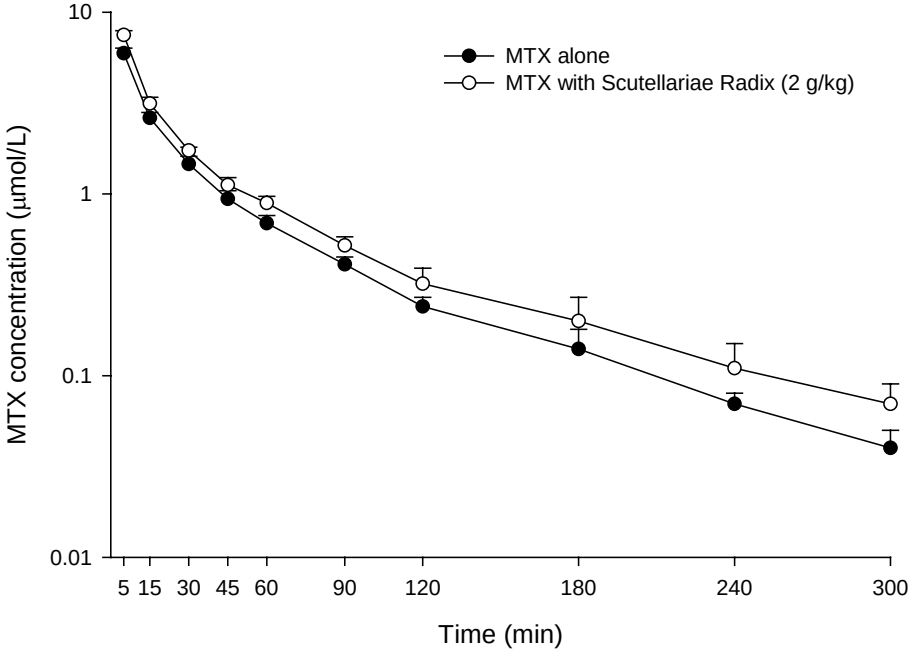


Fig. 4-3 Mean (± S.E.) serum concentration-time profiles of methotrexate after oral methotrexate alone (●) and coadministration with 1.0 g/kg (○), 2.0 g/kg (▼) of Scutellariae Radix decoction (n=8).



(a)



(b)

Fig. 4-4 (a) Mean (± S.E.) serum concentration-time profiles of methotrexate after intravenous methotrexate alone (●) and coadministration with 2.0 g/kg of Scutellariae Radix decoction (○) and (b): the semi-log diagram of (a) (n=8).