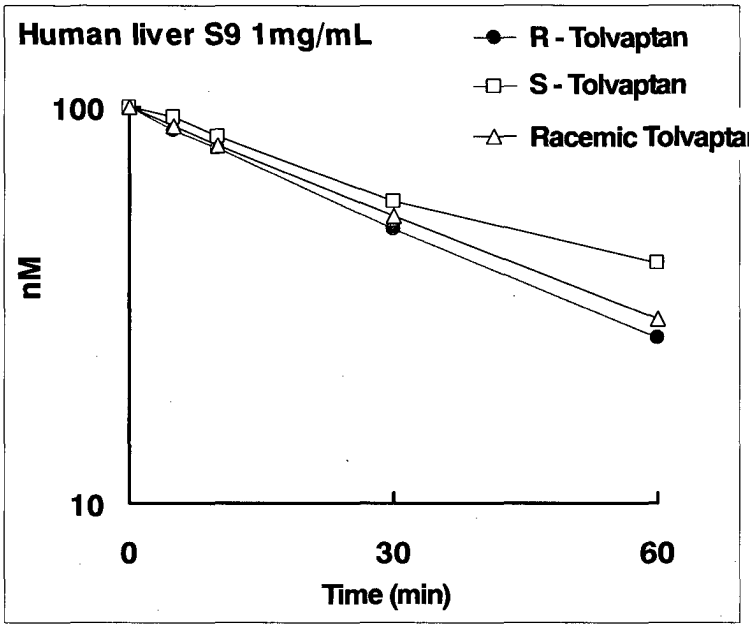
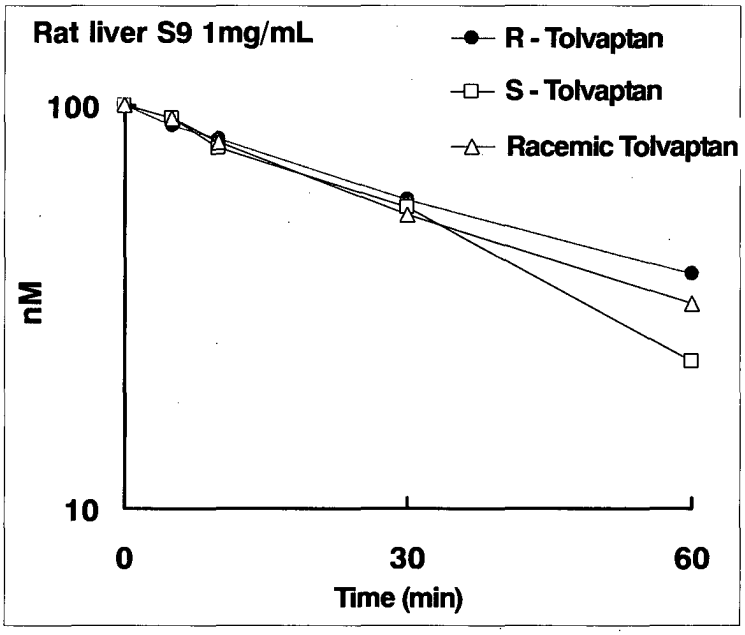
[Fig. 1]

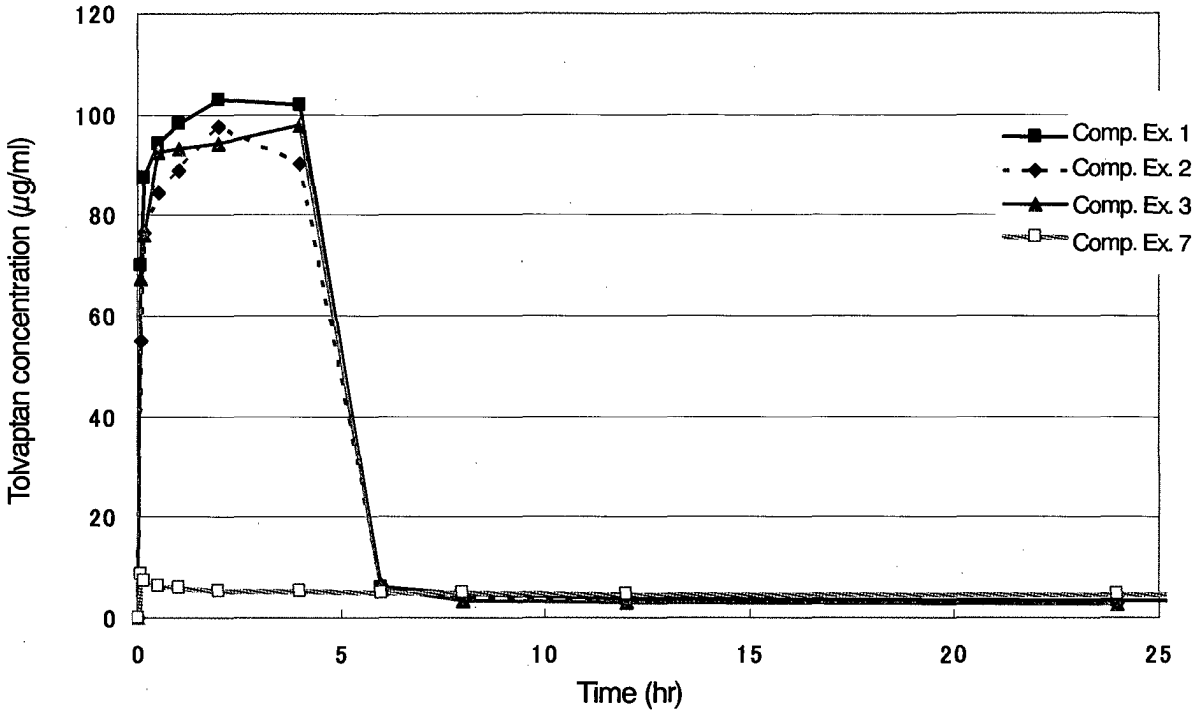
(1)


Human liver S9 1mg/mL
R - Tolvaptan
S - Tolvaptan
Racemic Tolvaptan
100
nM
10
0
30
60
Time (min)

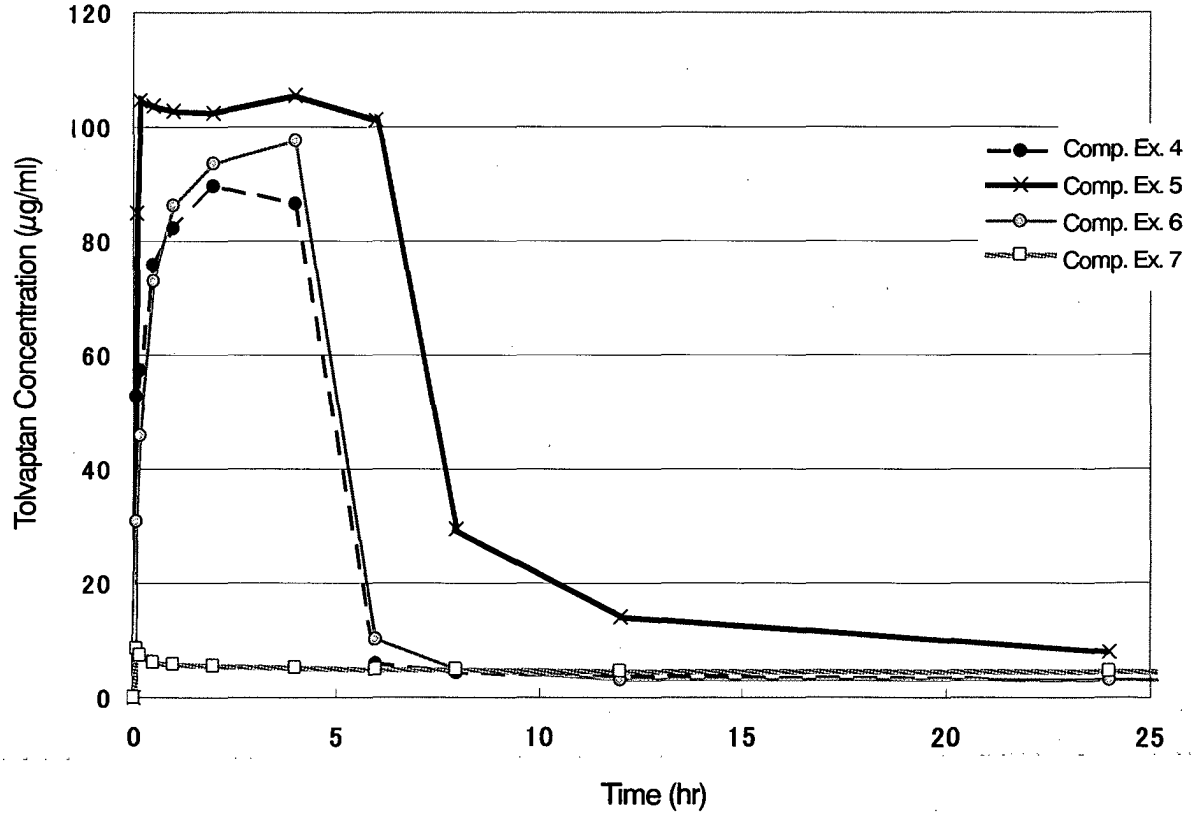
(2)


Rat liver S9 1mg/mL
R - Tolvaptan
S - Tolvaptan
Racemic Tolvaptan
100
nM
10
0
30
60
Time (min)

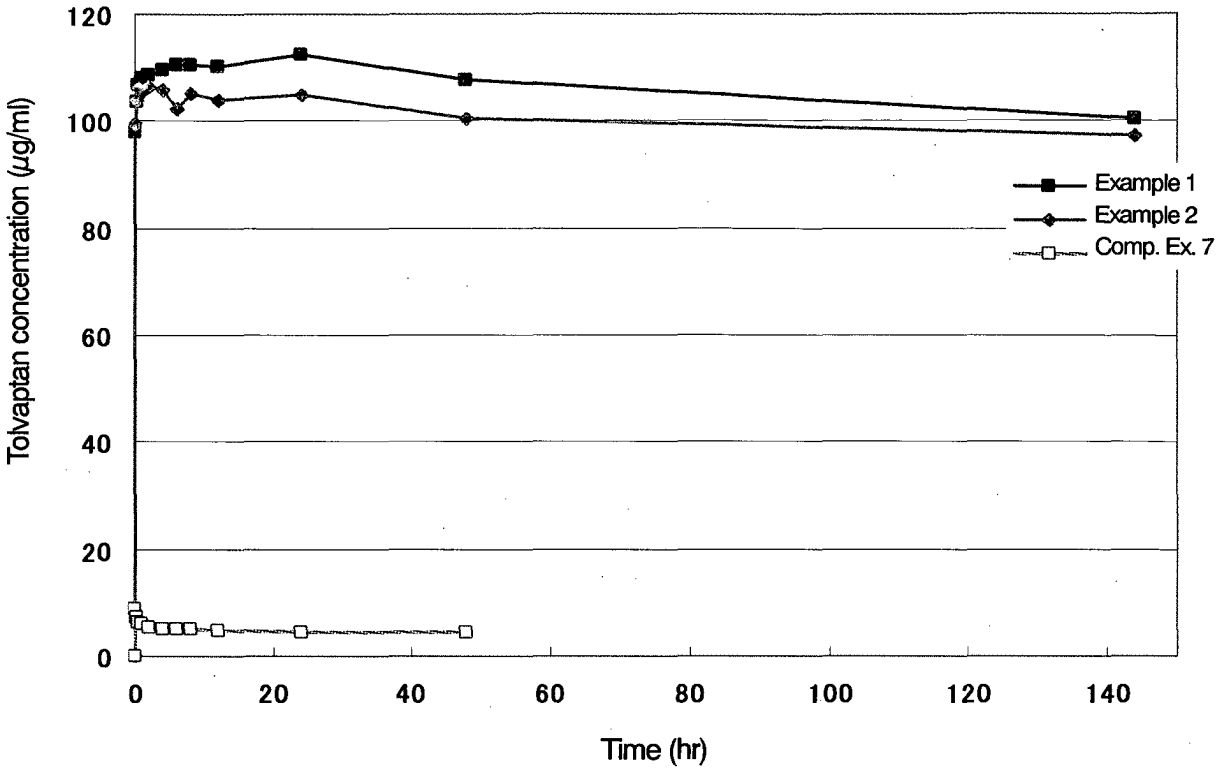
[Fig. 2]


120
100
80
60
40
20
0
Tolvaptan concentration (μg/ml)
0
5
10
15
20
25
Time (hr)
Comp. Ex. 1
Comp. Ex. 2
Comp. Ex. 3
Comp. Ex. 7

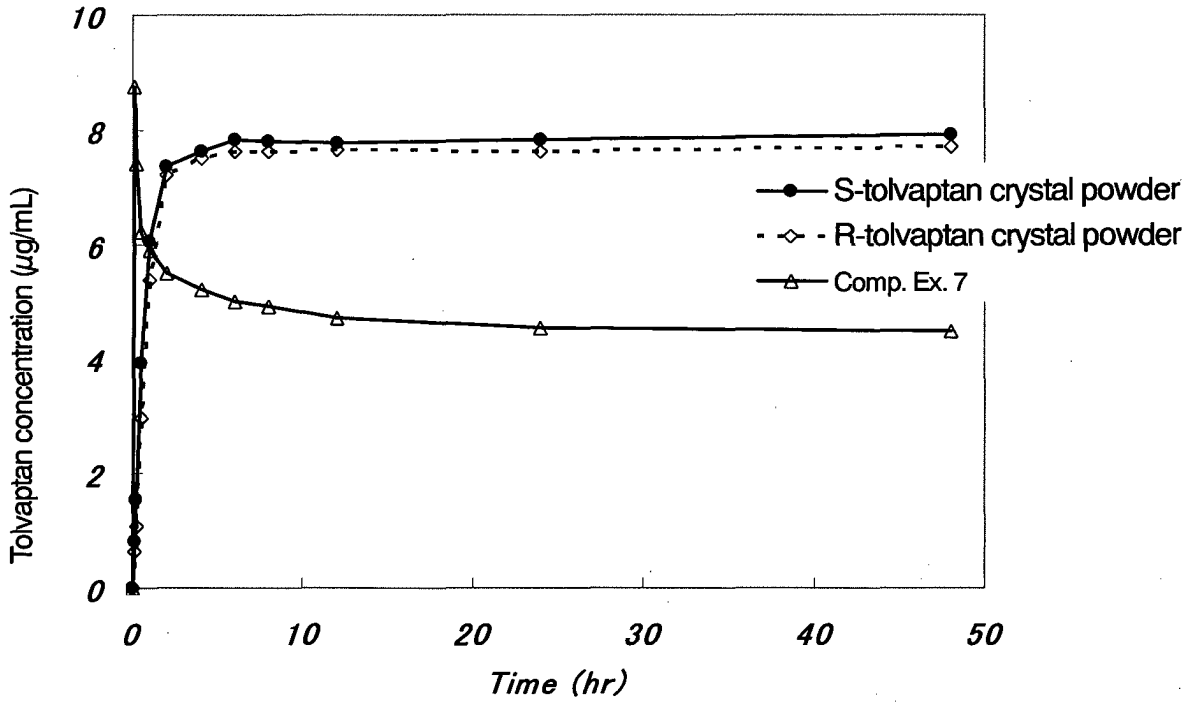
[Fig. 3]


120
100
80
60
40
20
0
Tolvaptan Concentration (μg/ml)
0
5
10
15
20
25
Time (hr)
Comp. Ex. 4
Comp. Ex. 5
Comp. Ex. 6
Comp. Ex. 7

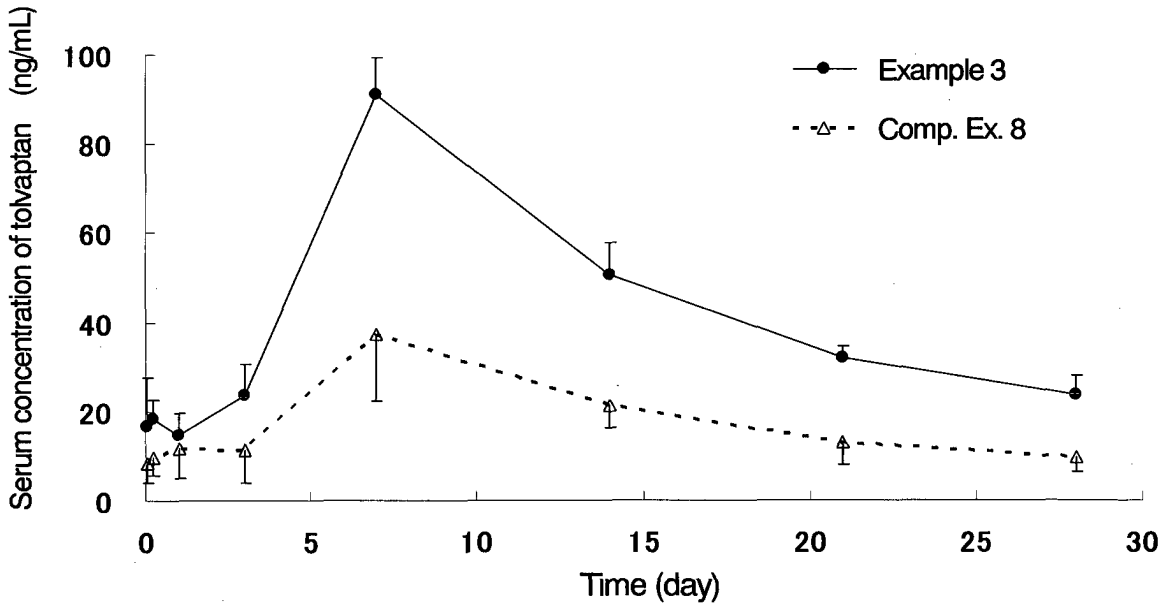
[Fig. 4]


120
100
80
60
40
20
0
Tolvaptan concentration (μg/ml)
0
20
40
60
80
100
120
140
Time (hr)
Example 1
Example 2
Comp. Ex. 7

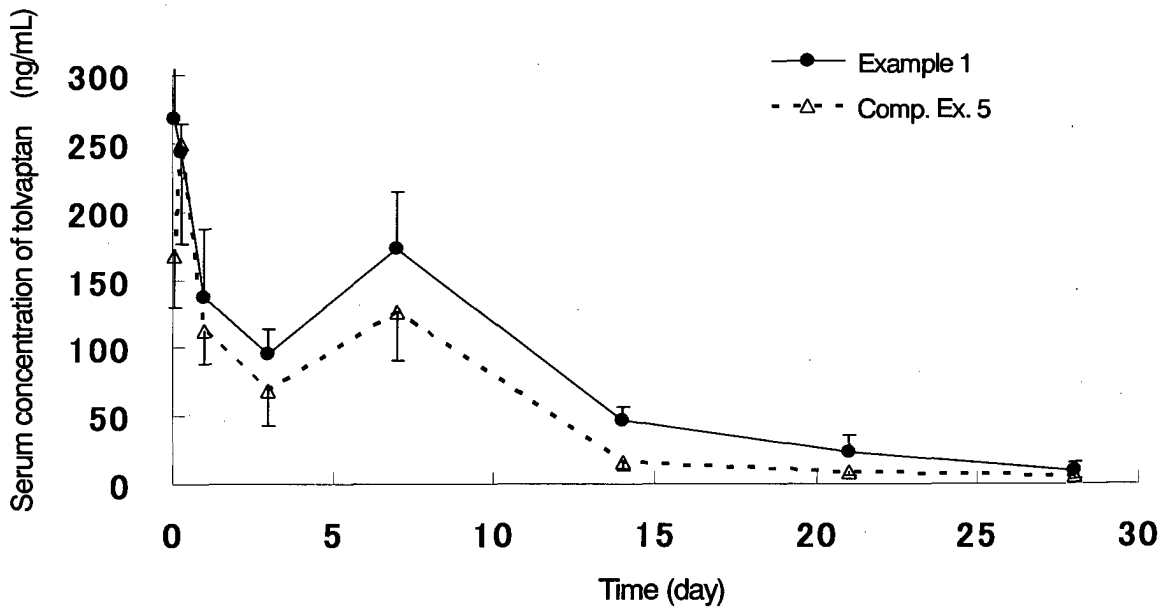
[Fig. 5]


10
8
6
4
2
0
Tolvaptan concentration (μg/mL)
0
10
20
30
40
50
Time (hr)
S-tolvaptan crystal powder
R-tolvaptan crystal powder
Comp. Ex. 7

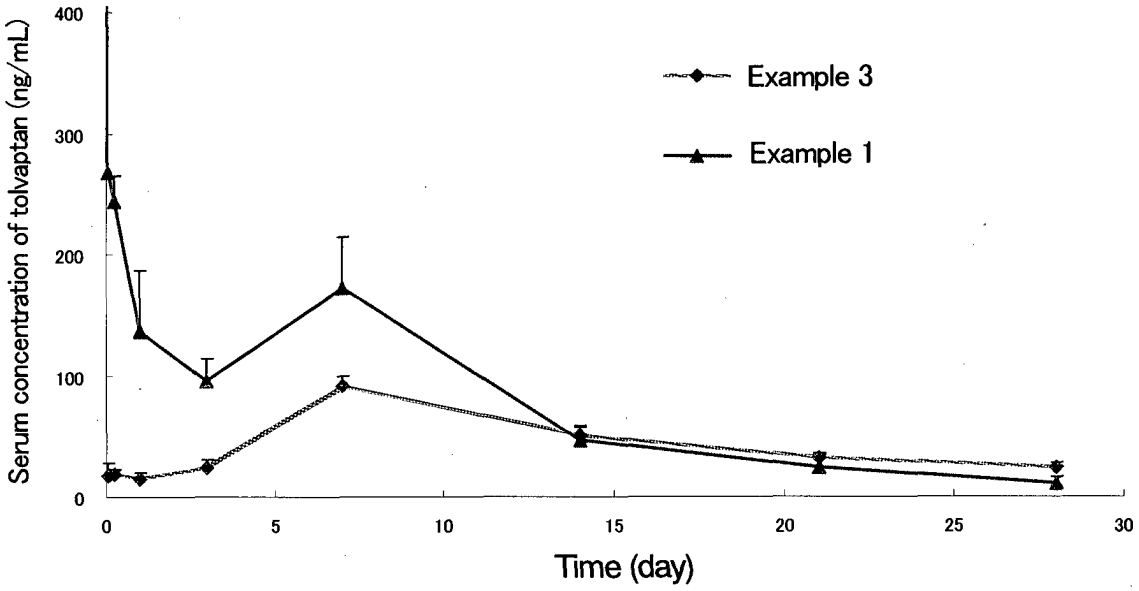
[Fig. 6]


Serum concentration of tolvaptan (ng/mL)
100
80
60
40
20
0
0
5
10
15
20
25
30
Time (day)
Example 3
Comp. Ex. 8

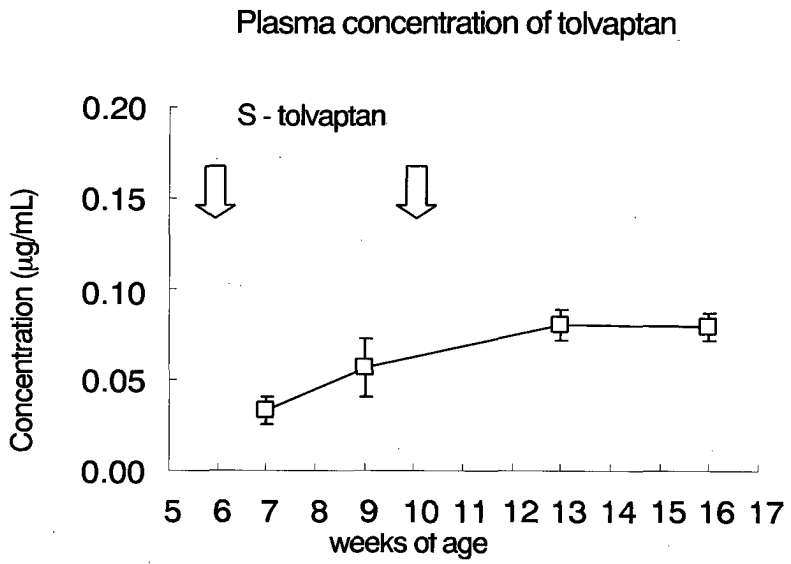
[Fig. 7]


Serum concentration of tolvaptan (ng/mL)
300
250
200
150
100
50
0
0
5
10
15
20
25
30
Time (day)
Example 1
Comp. Ex. 5

[Fig. 8]

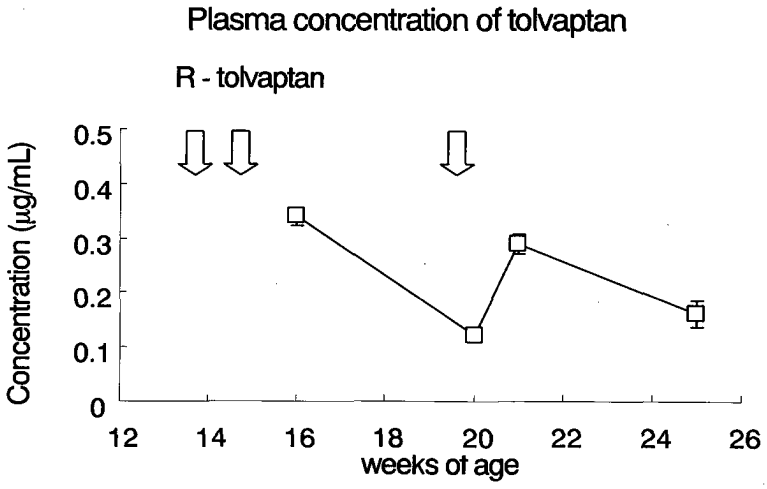

Serum concentration of tolvaptan (ng/mL)
400
300
200
100
0
0
5
10
15
20
25
30
Time (day)
Example 3
Example 1

[Fig. 9]



S-tolvaptan was subcutaneously injected twice, i.e., at 6 weeks of age and 10 weeks of age. Each value indicates the mean value ± SEM. (n=3-10)

[Fig. 10]



R-tolvaptan was intramuscularly injected three times, i.e., at 14 weeks of age, 15 weeks of age, and 20 weeks of age. Each value indicates the mean value ± SEM. (n=9)