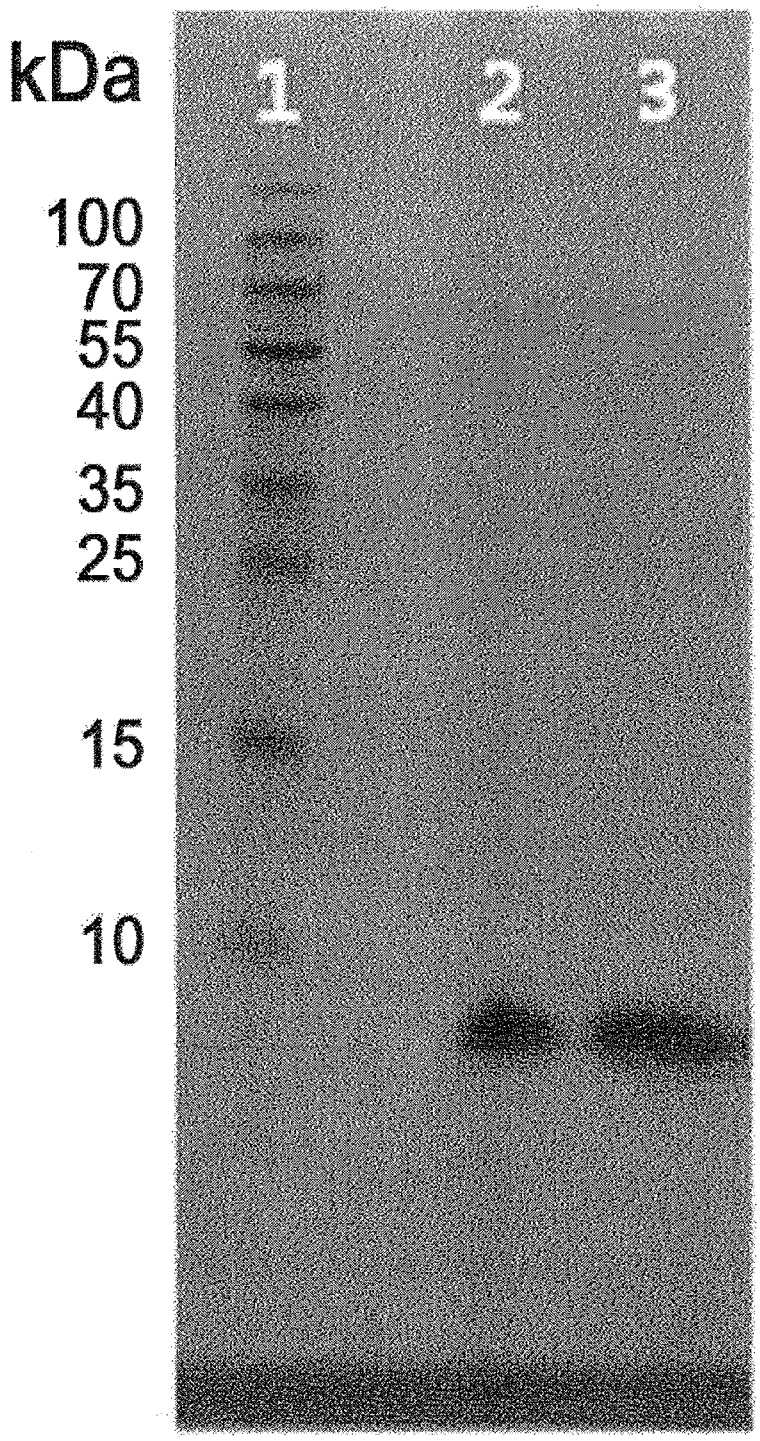
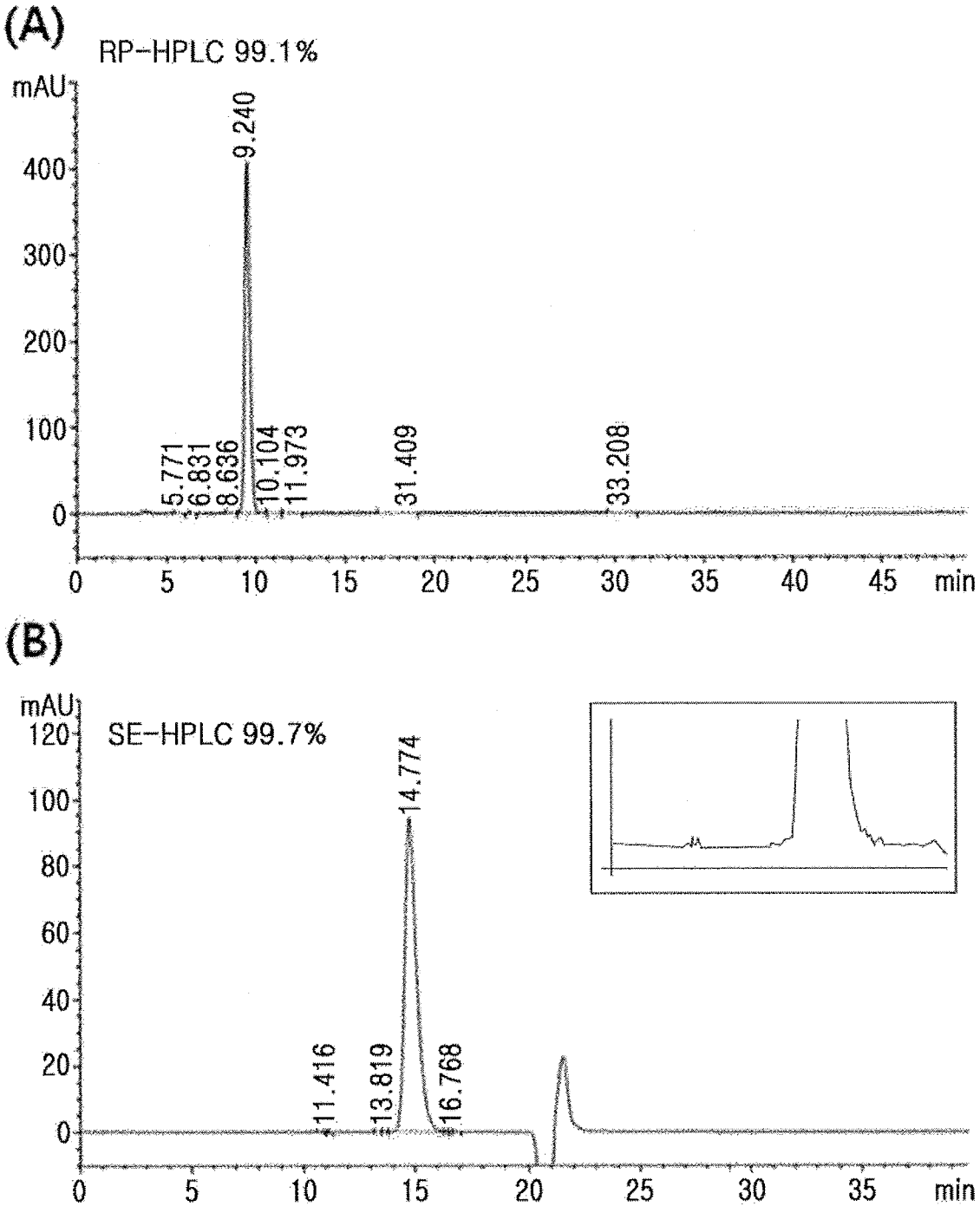
[DRAWINGS]

[FIG. 1]

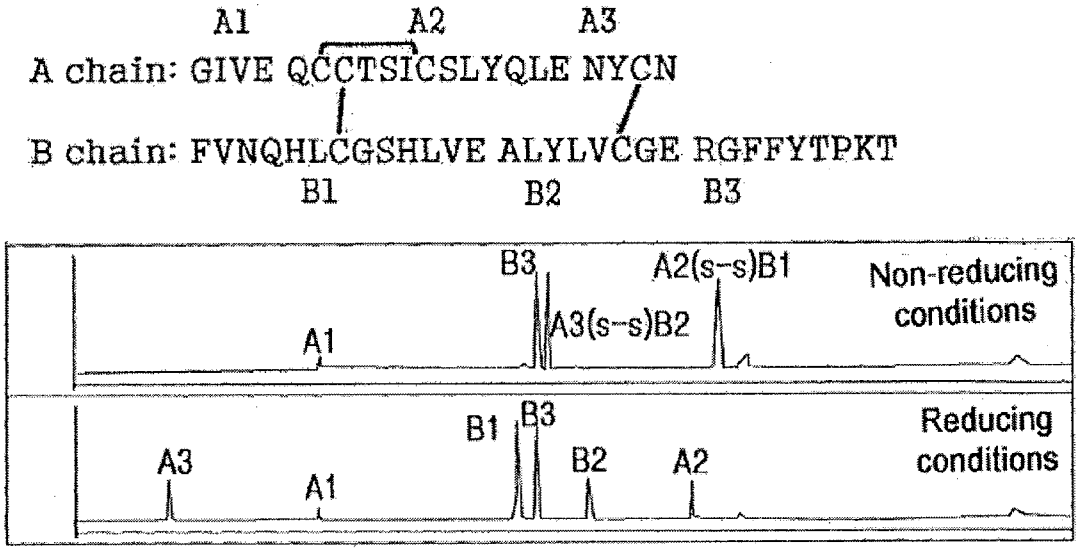


[FIG. 2]

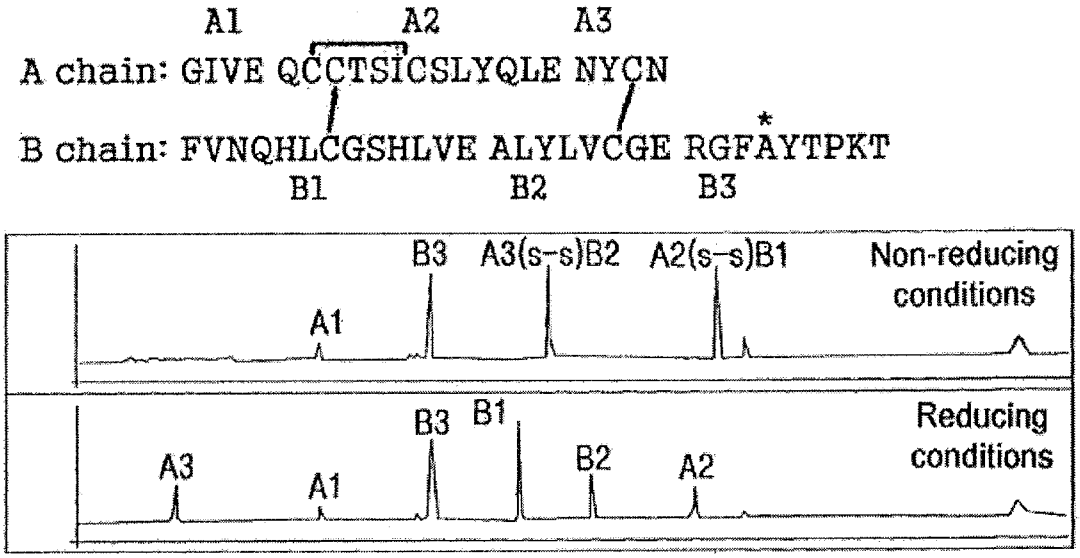

(A)
RP-HPLC 99.1%
mAU
400
300
200
100
0
9.240
5.771
6.831
8.636
10.104
11.973
31.409
33.208
0
5
10
15
20
25
30
35
40
45
min
(B)
mAU
120
100
80
60
40
20
0
SE-HPLC 99.7%
14.774
11.416
13.819
16.768
0
5
10
15
20
25
30
35
min

[FIG. 3]

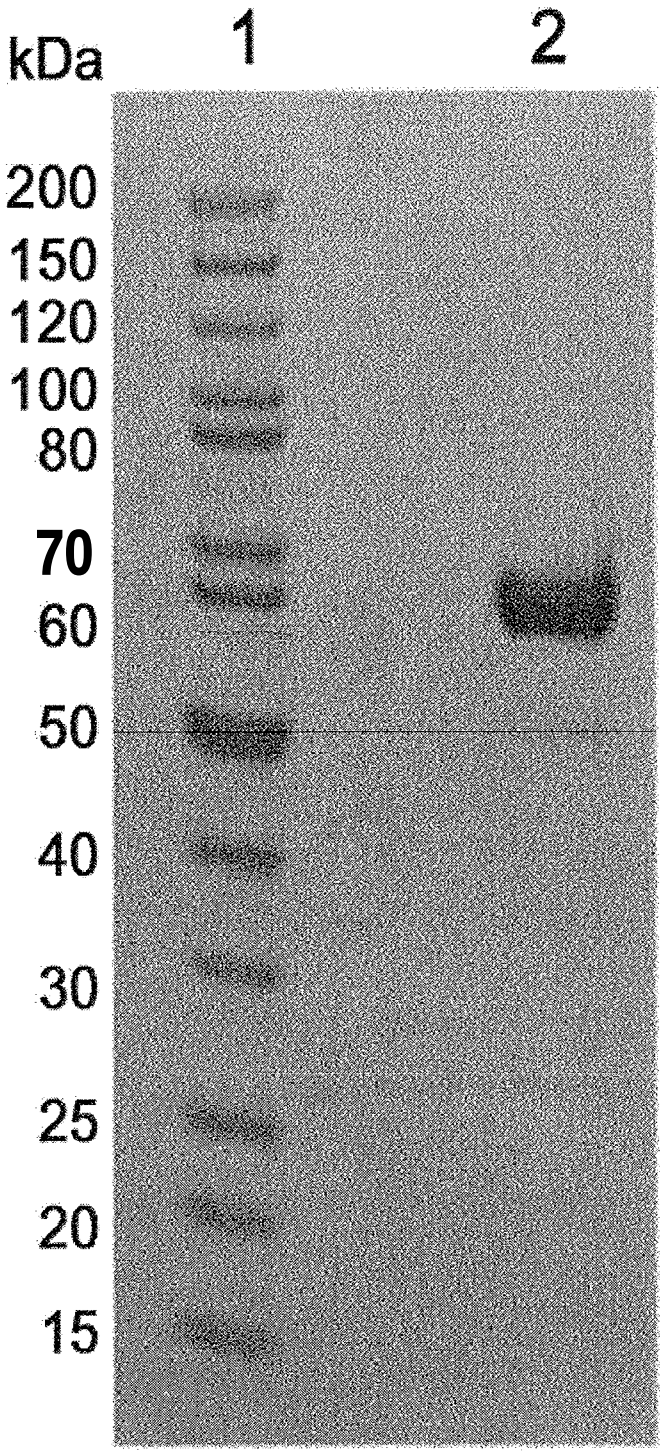
(A) Glu-C cleavage fragment of native insulin sequence



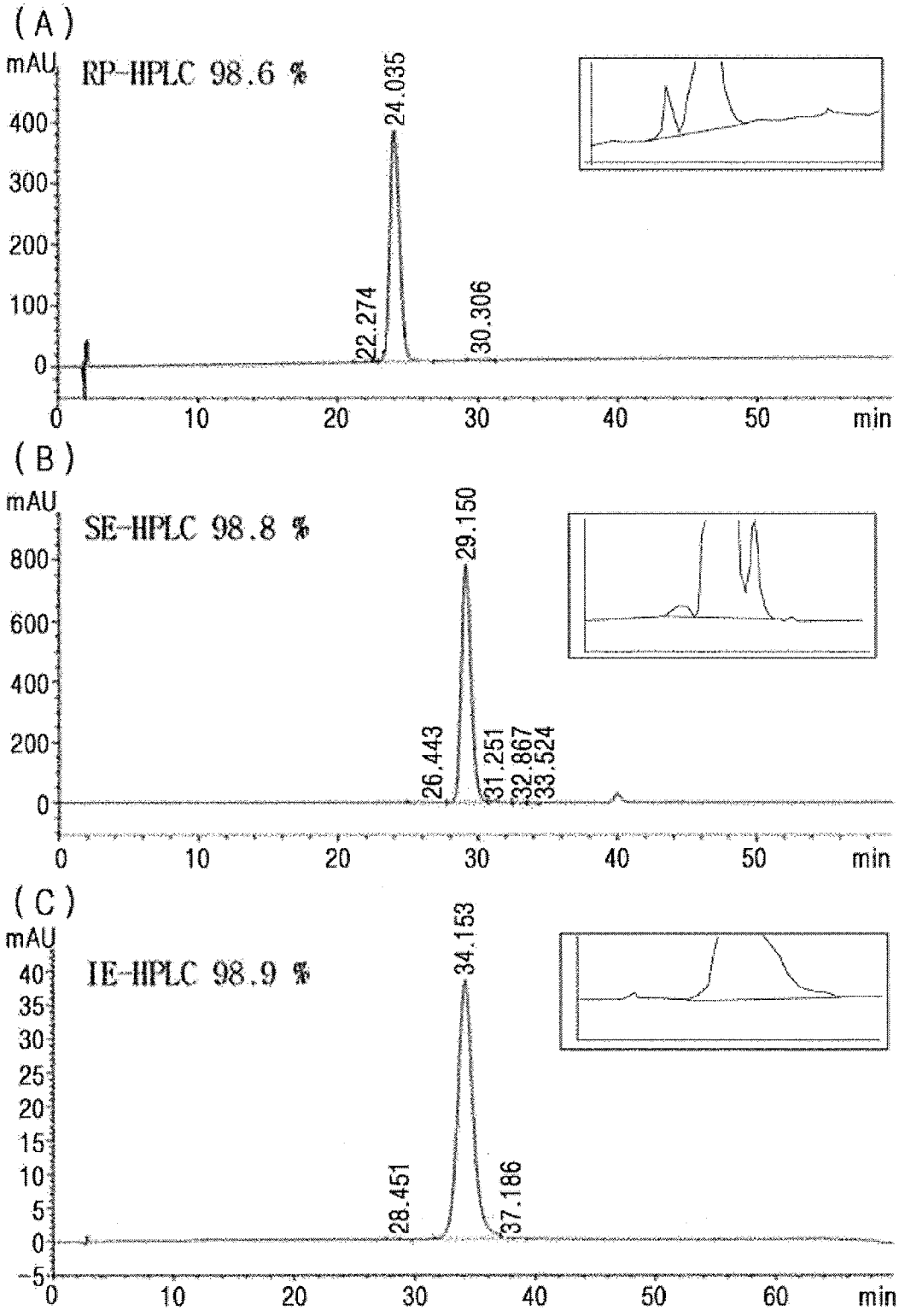
(B) Glu-C cleavage fragment of insulin analog (No. 7) sequence



[FIG. 4]

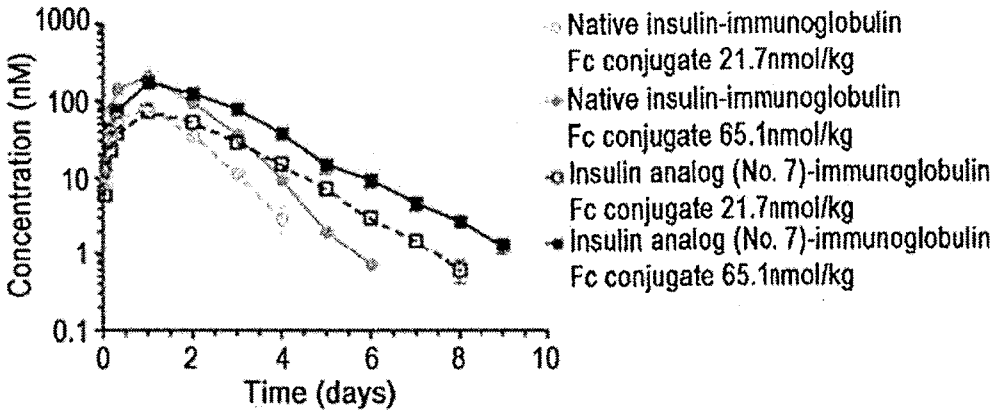


[FIG. 5]

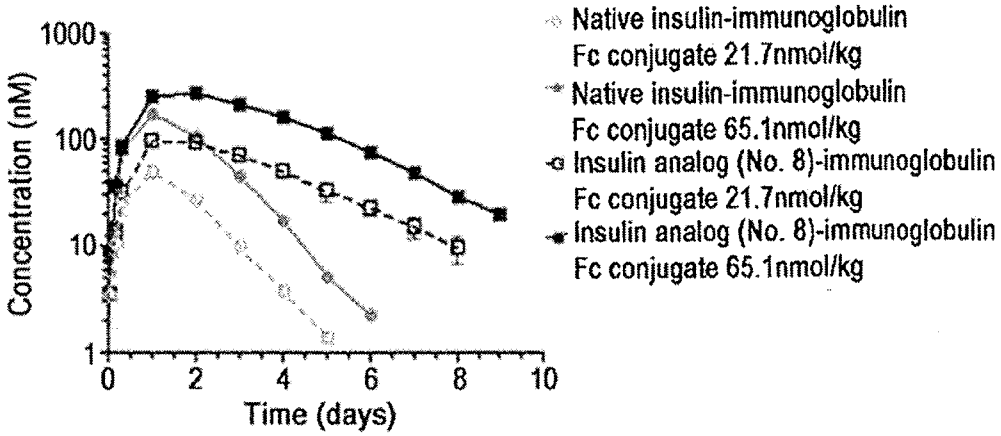

(A)
mAU
RP-HPLC 98.6 %
24.035
22.274
30.306
400
300
200
100
0
0
10
20
30
40
50
min
(B)
mAU
SE-HPLC 98.8 %
29.150
26.443
31.251
32.867
33.524
800
600
400
200
0
0
10
20
30
40
50
min
(C)
mAU
IE-HPLC 98.9 %
34.153
28.451
37.186
40
35
30
25
20
15
10
5
0
-5
0
10
20
30
40
50
60
min

[FIG. 6]

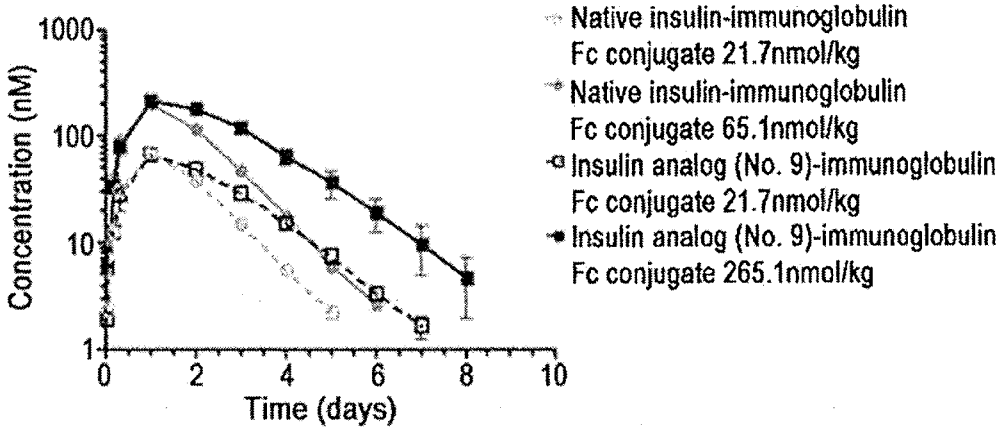
(A)


1000
100
10
1
0.1
Concentration (nM)
0
2
4
6
8
10
Time (days)
Native insulin-immunoglobulin Fc conjugate 21.7nmol/kg
Native insulin-immunoglobulin Fc conjugate 65.1nmol/kg
Insulin analog (No. 7)-immunoglobulin Fc conjugate 21.7nmol/kg
Insulin analog (No. 7)-immunoglobulin Fc conjugate 65.1nmol/kg

(B)


1000
100
10
1
Concentration (nM)
0
2
4
6
8
10
Time (days)
Native insulin-immunoglobulin Fc conjugate 21.7nmol/kg
Native insulin-immunoglobulin Fc conjugate 65.1nmol/kg
Insulin analog (No. 8)-immunoglobulin Fc conjugate 21.7nmol/kg
Insulin analog (No. 8)-immunoglobulin Fc conjugate 65.1nmol/kg

(C)


1000
100
10
1
Concentration (nM)
0
2
4
6
8
10
Time (days)
Native insulin-immunoglobulin Fc conjugate 21.7nmol/kg
Native insulin-immunoglobulin Fc conjugate 65.1nmol/kg
Insulin analog (No. 9)-immunoglobulin Fc conjugate 21.7nmol/kg
Insulin analog (No. 9)-immunoglobulin Fc conjugate 265.1nmol/kg