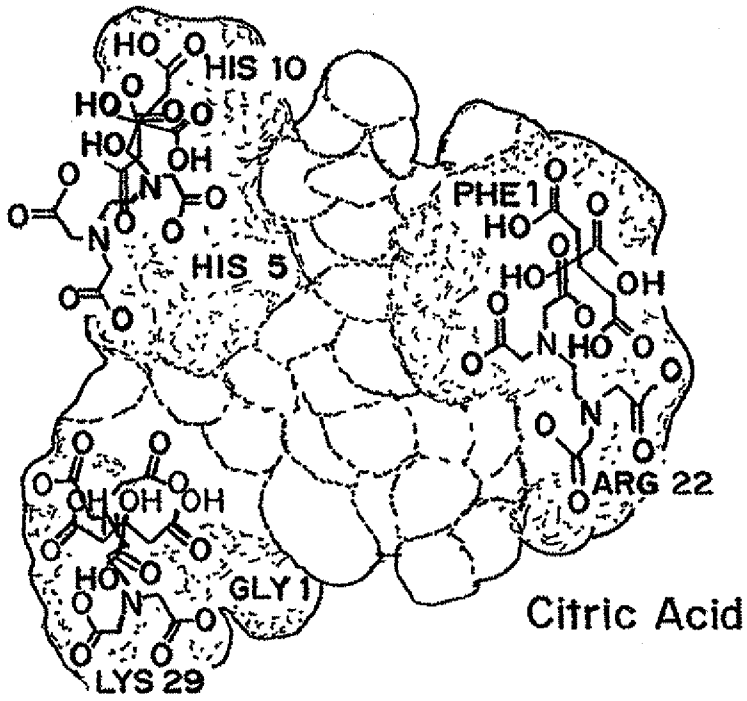

HIS 10
HIS 5
PHE 1
ARG 22
GLY 1
LYS 29
Citric Acid

FIG. 1

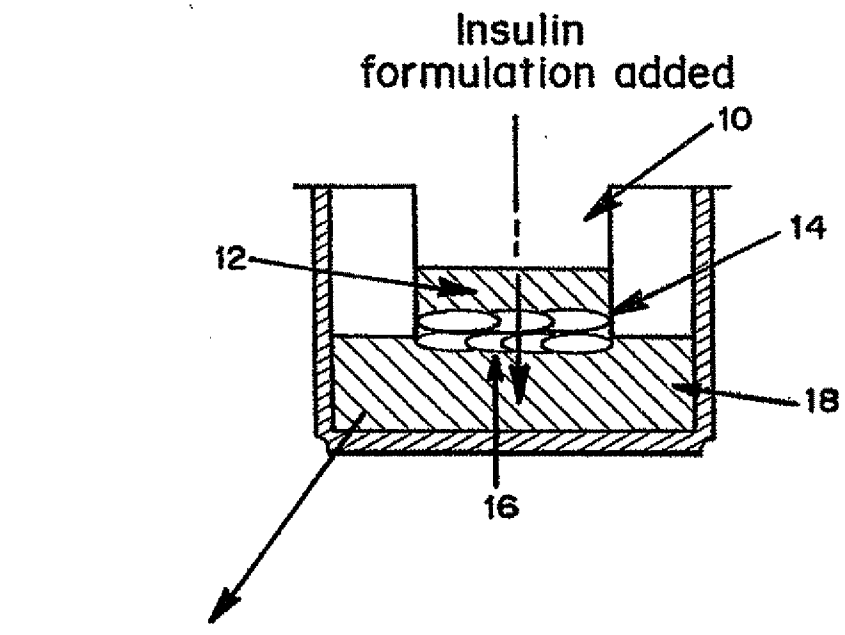

Insulin
formulation added
10
12
14
16
18
Sample withdrawn for ELISA

FIG. 2

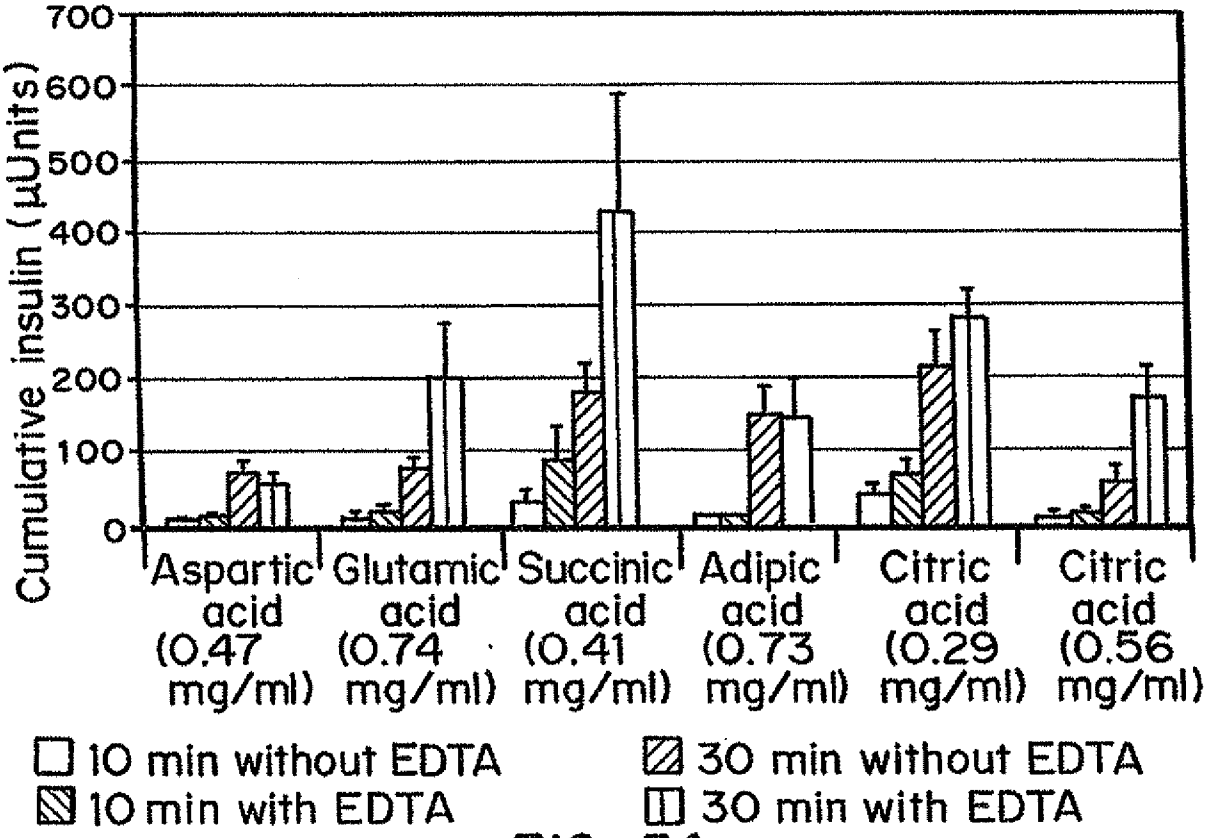

Cumulative insulin (µUnits)
700
600
500
400
300
200
100
0
Aspartic acid (0.47 mg/ml)
Glutamic acid (0.74 mg/ml)
Succinic acid (0.41 mg/ml)
Adipic acid (0.73 mg/ml)
Citric acid (0.29 mg/ml)
Citric acid (0.56 mg/ml)
10 min without EDTA
10 min with EDTA
30 min without EDTA
30 min with EDTA

FIG. 3A

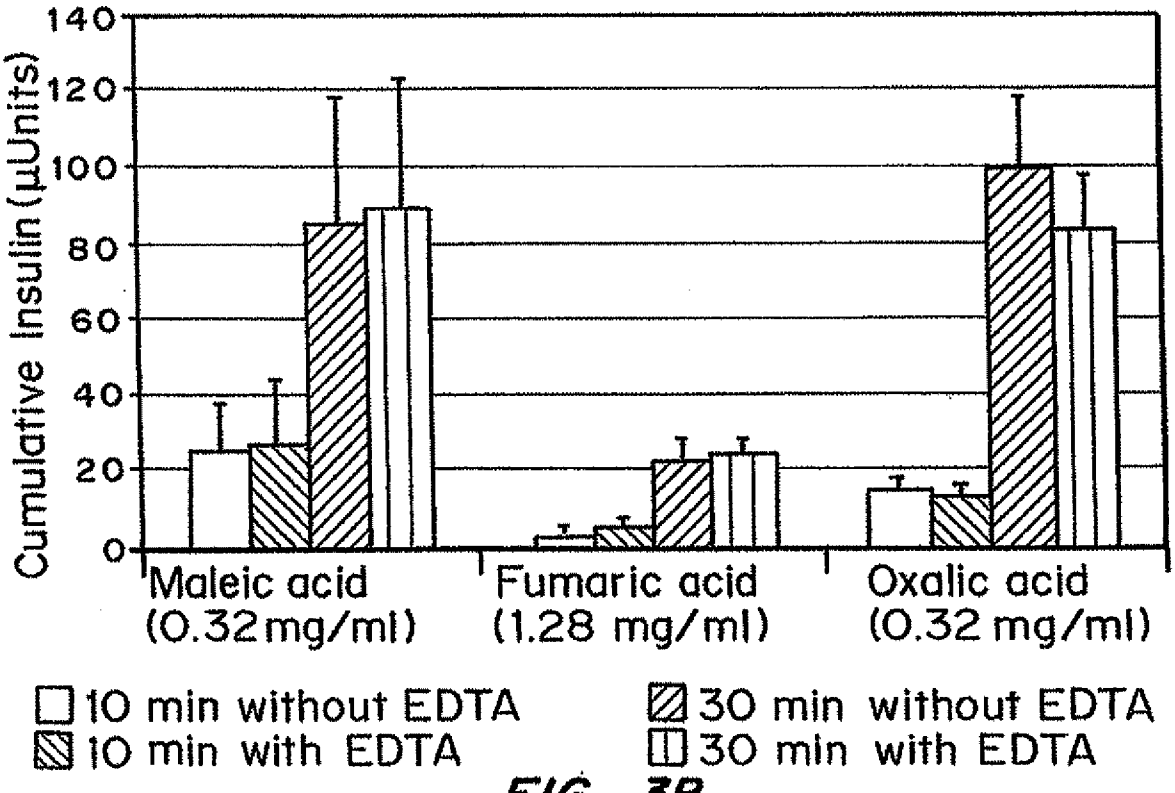

Cumulative Insulin (µUnits)
140
120
100
80
60
40
20
0
Maleic acid (0.32mg/ml)
Fumaric acid (1.28 mg/ml)
Oxalic acid (0.32 mg/ml)
10 min without EDTA
10 min with EDTA
30 min without EDTA
30 min with EDTA

FIG. 3B

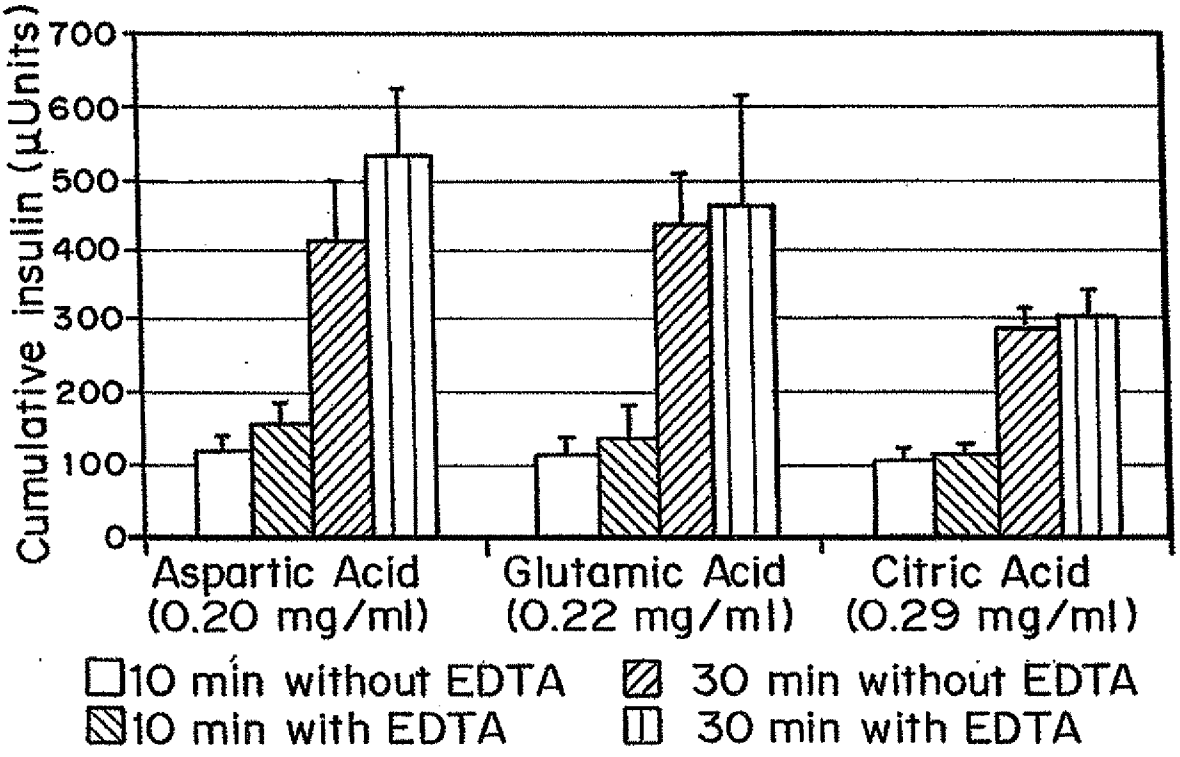

Cumulative insulin (µUnits)
700
600
500
400
300
200
100
0
Aspartic Acid (0.20 mg/ml)
Glutamic Acid (0.22 mg/ml)
Citric Acid (0.29 mg/ml)
10 min without EDTA
10 min with EDTA
30 min without EDTA
30 min with EDTA

FIG. 4A

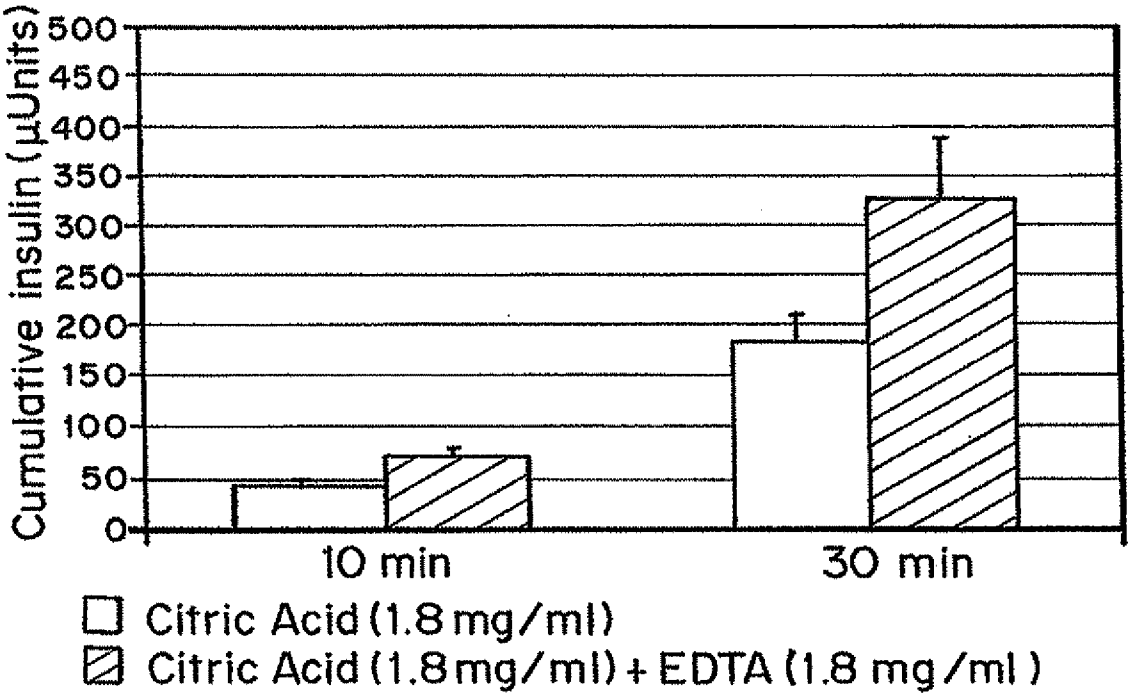

Cumulative insulin (µUnits)
500
450
400
350
300
250
200
150
100
50
0
10 min
30 min
Citric Acid (1.8 mg/ml)
Citric Acid (1.8 mg/ml) + EDTA (1.8 mg/ml)

FIG. 4B

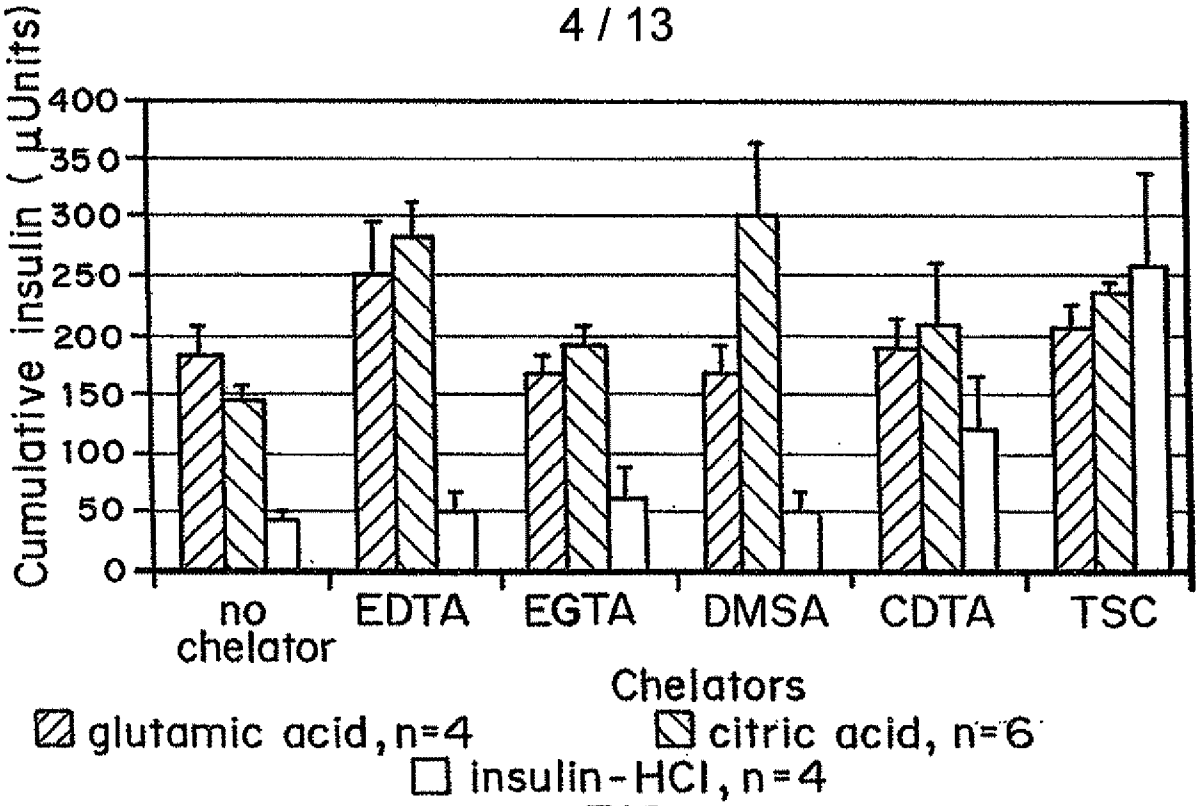

Cumulative insulin (μUnits)
400
350
300
250
200
150
100
50
0
no chelator
EDTA
EGTA
DMSA
CDTA
TSC
Chelators
glutamic acid, n=4
citric acid, n=6
insulin-HCl, n=4

FIG. 5

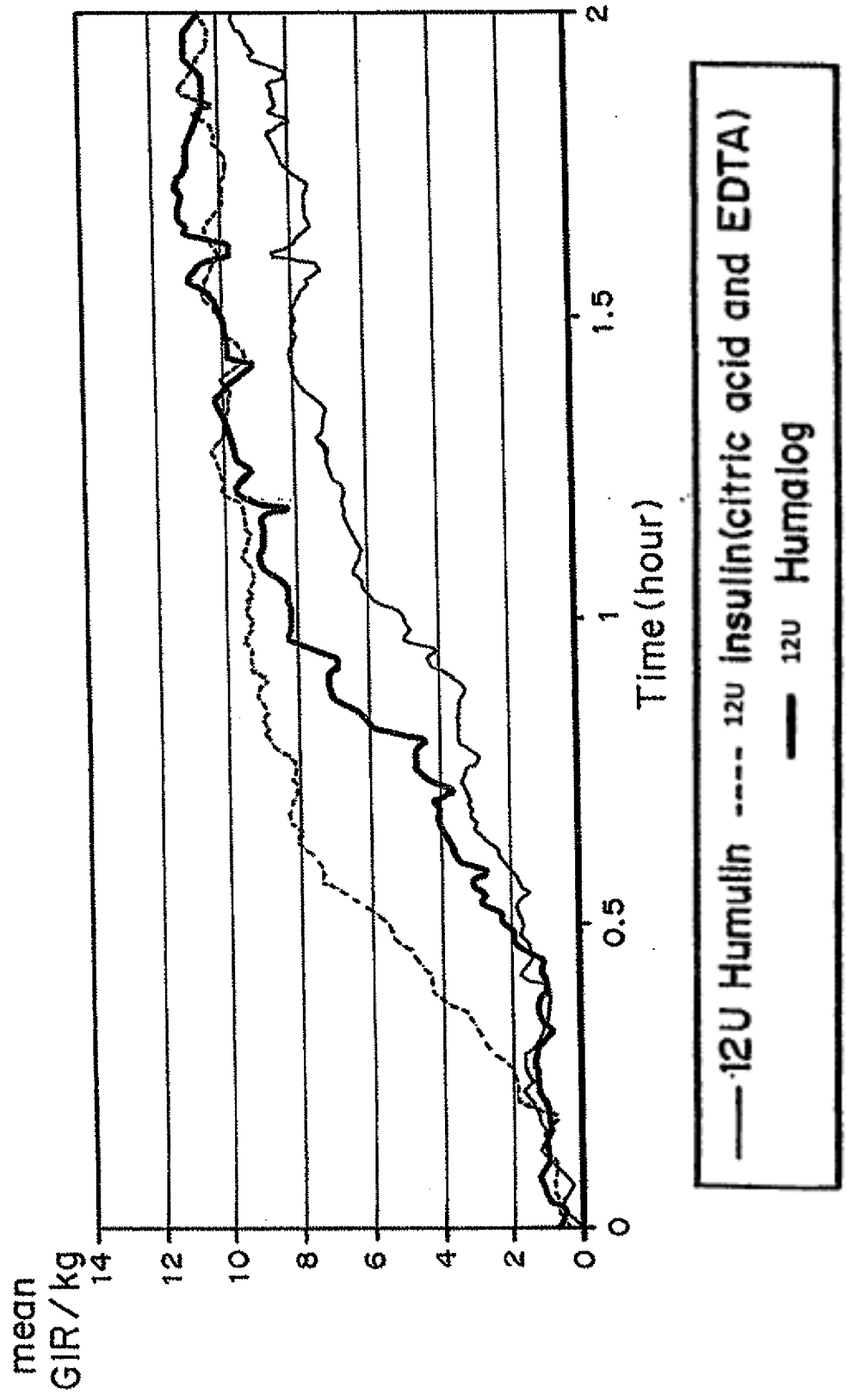

mean GIR/kg
14
12
10
8
6
4
2
0
0
0.5
1
1.5
2
Time (hour)
12U Humulin ---- 12U Insulin(citric acid and EDTA)
12U Humalog

FIGURE 6

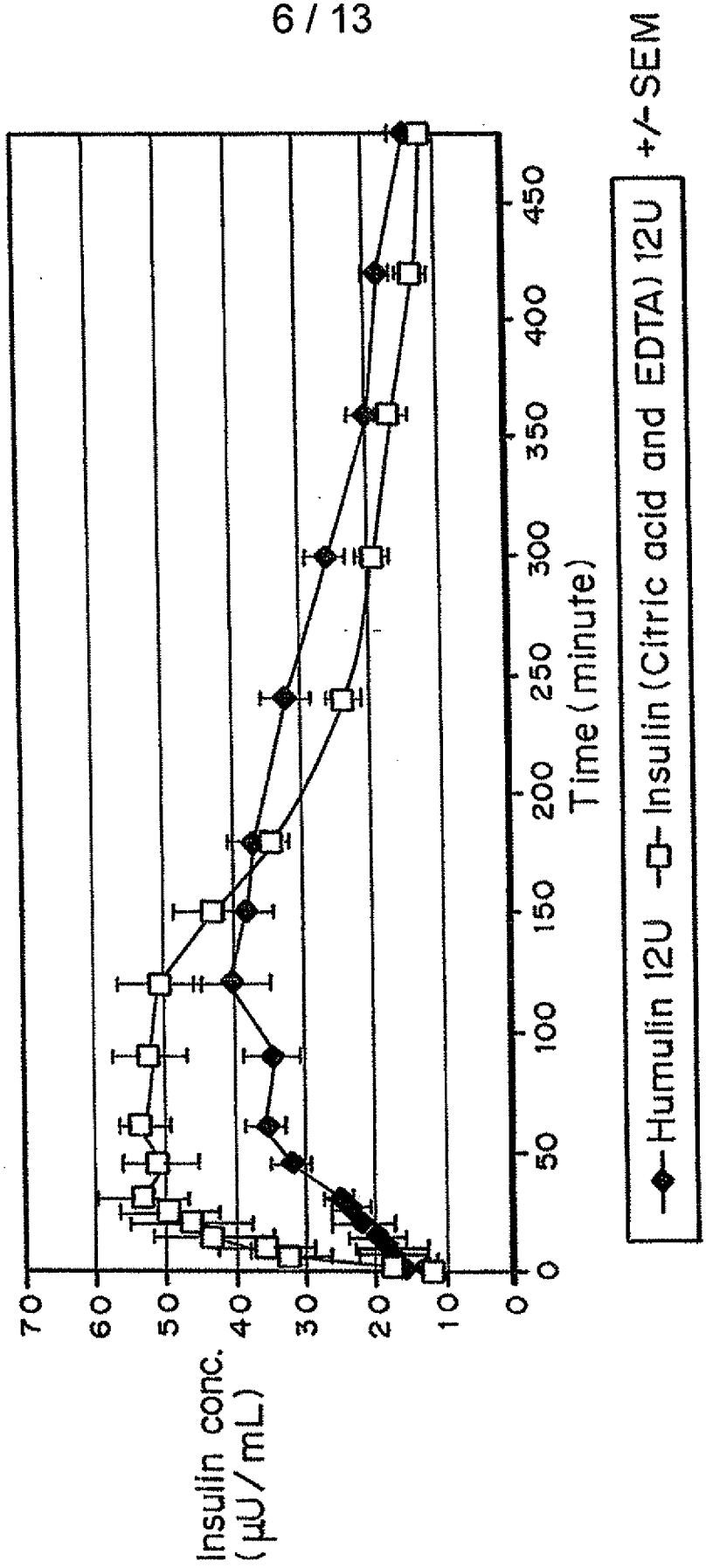

Insulin conc. (μU/mL)
70
60
50
40
30
20
10
0
0
50
100
150
200
250
300
350
400
450
Time (minute)
Humulin 12U
Insulin (Citric acid and EDTA) 12U
+/- SEM

FIGURE 7

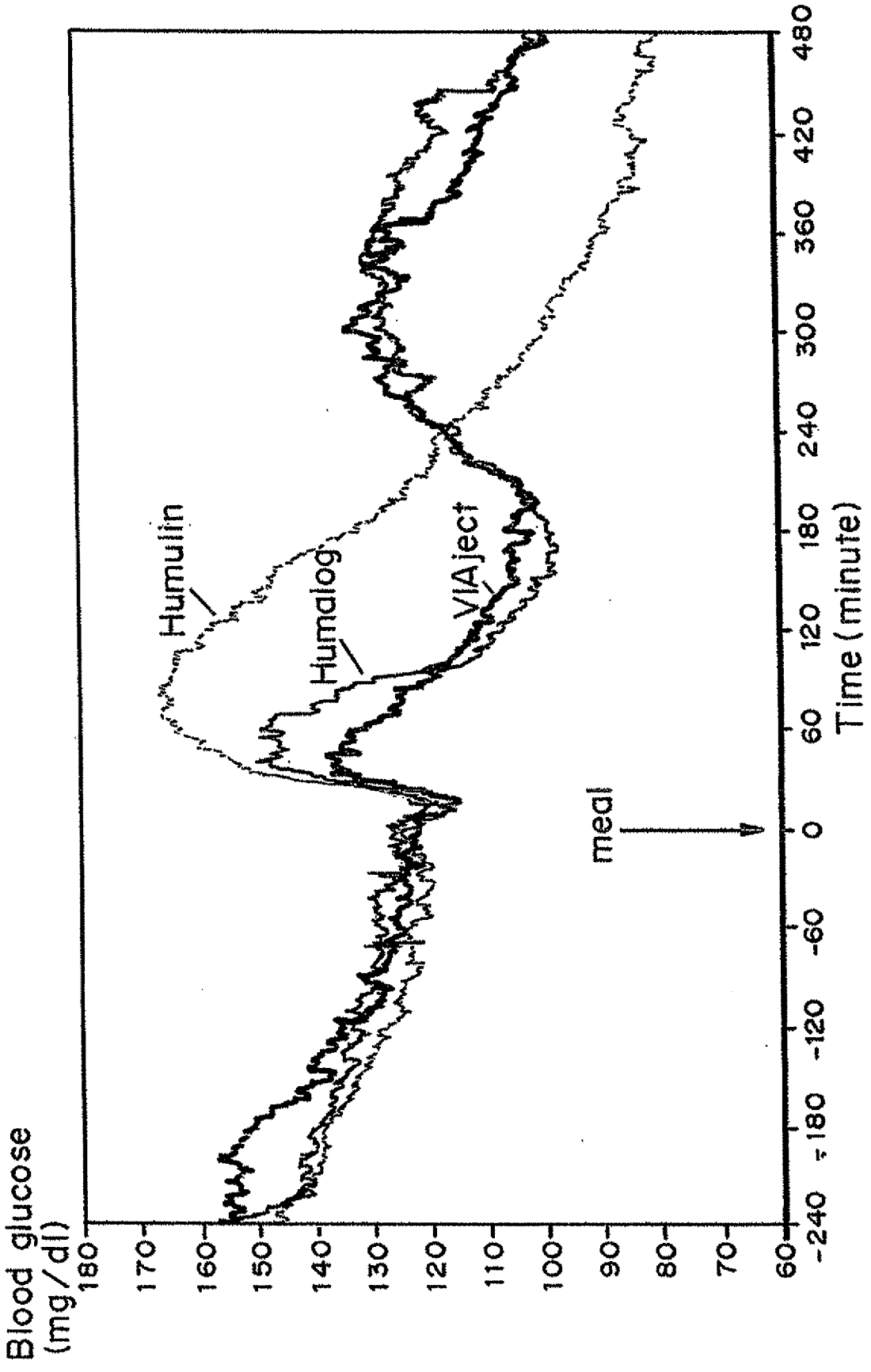

Blood glucose (mg/dl)
180
170
160
150
140
130
120
110
100
90
80
70
60
-240
-180
-120
-60
0
60
120
180
240
300
360
420
480
Time (minute)
Humulin
Humalog
VIAject
meal

FIGURE 8

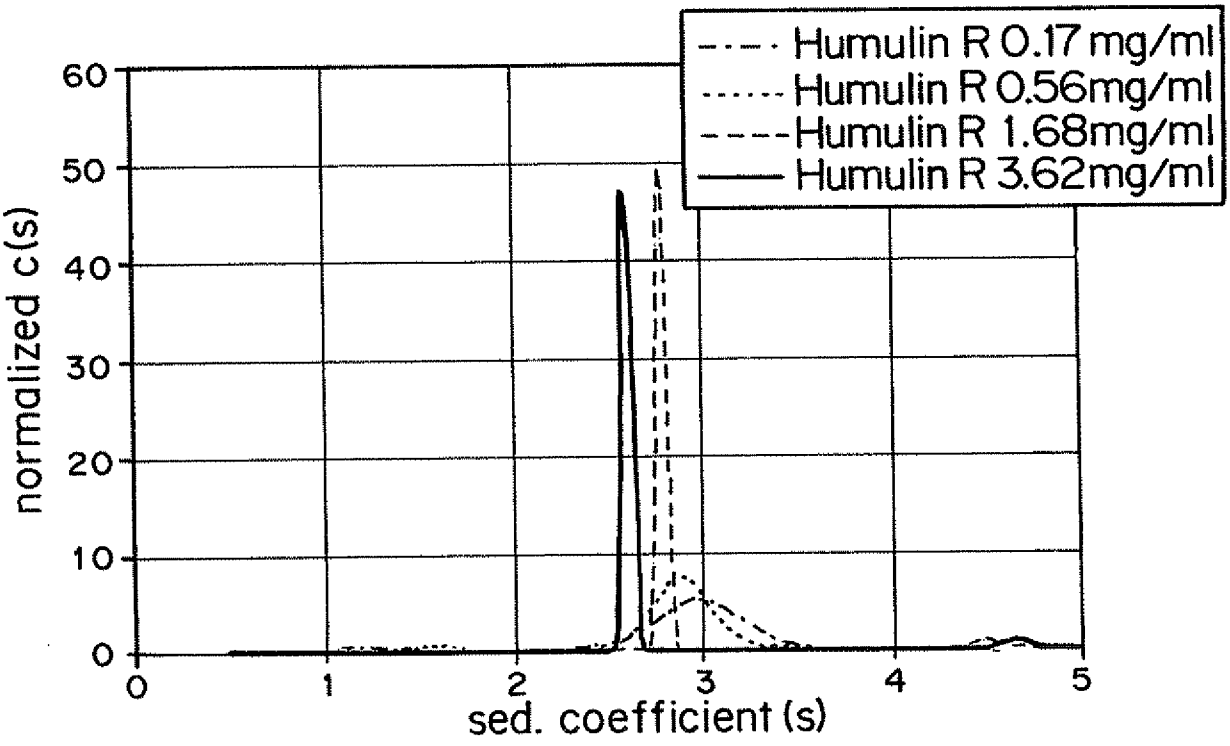

Humulin R 0.17 mg/ml
Humulin R 0.56mg/ml
Humulin R 1.68mg/ml
Humulin R 3.62mg/ml
normalized c(s)
60
50
40
30
20
10
0
0
1
2
3
4
5
sed. coefficient (s)

FIG. 9A

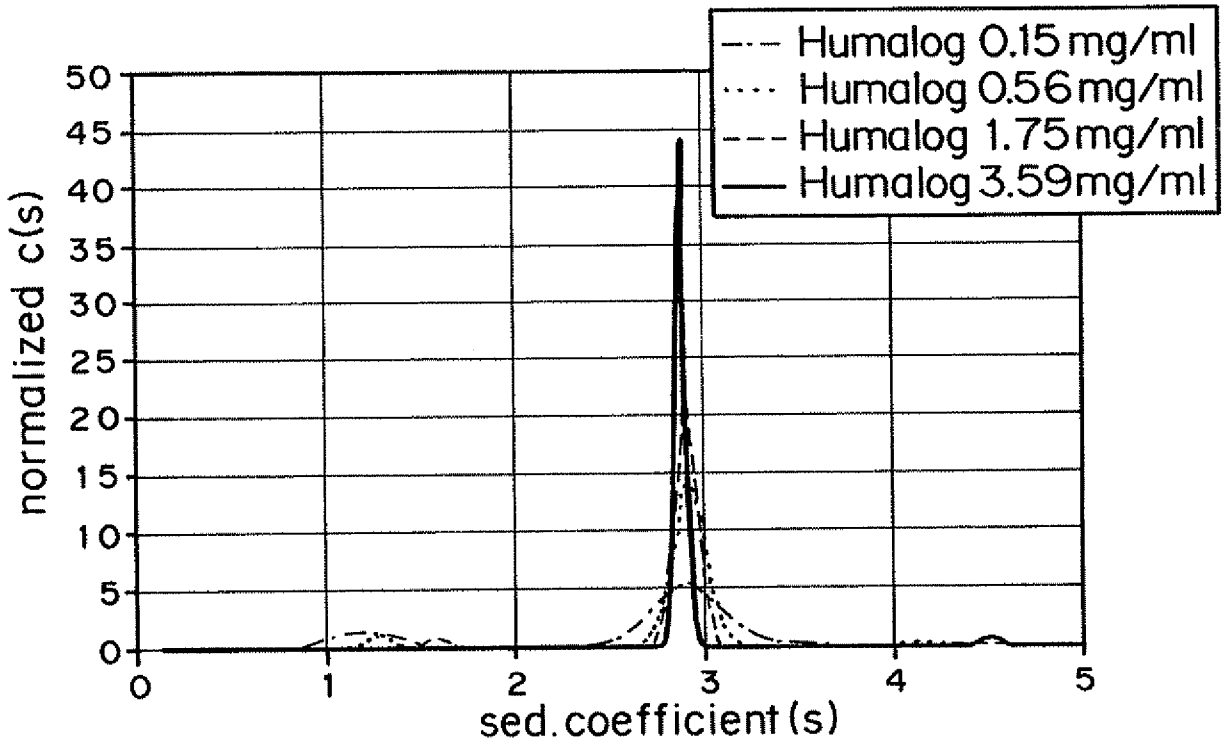

Humalog 0.15 mg/ml
Humalog 0.56 mg/ml
Humalog 1.75 mg/ml
Humalog 3.59mg/ml
normalized c(s)
50
45
40
35
30
25
20
15
10
5
0
0
1
2
3
4
5
sed.coefficient (s)

FIG. 9B

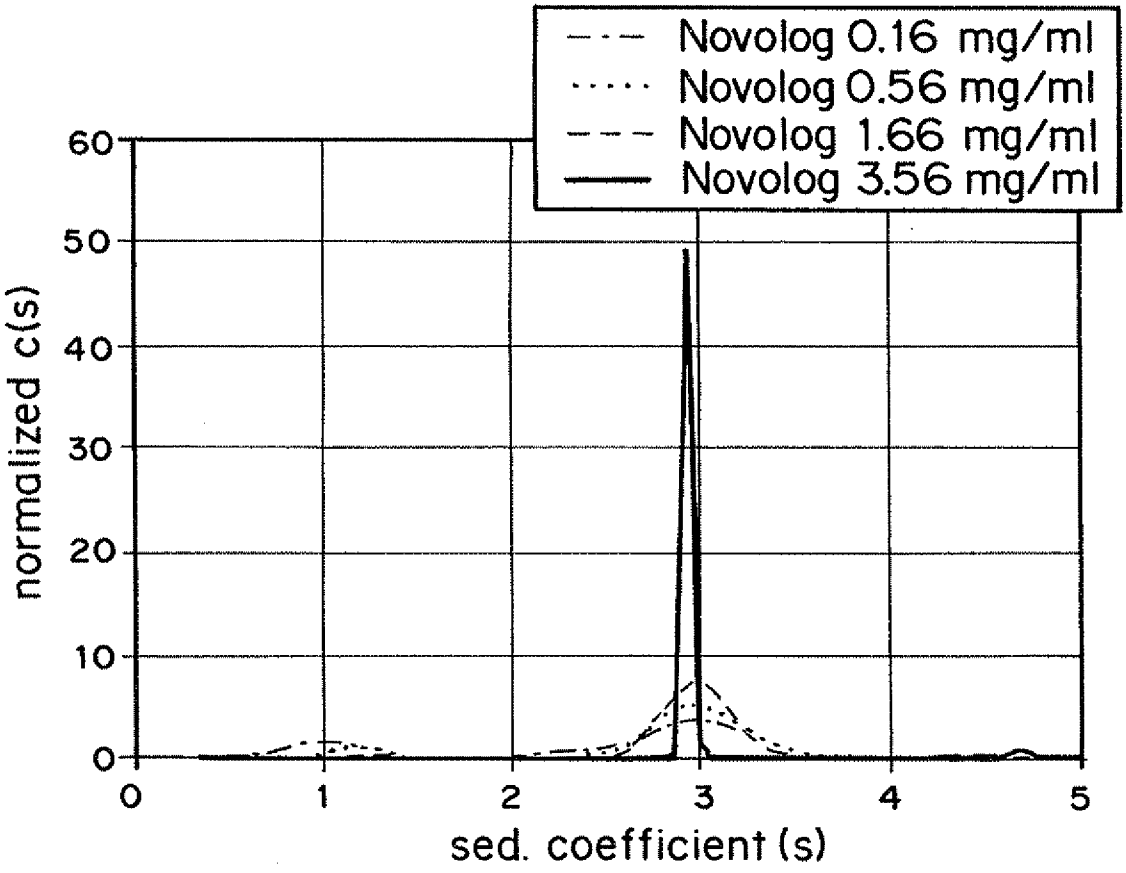

Novolog 0.16 mg/ml
Novolog 0.56 mg/ml
Novolog 1.66 mg/ml
Novolog 3.56 mg/ml
normalized c(s)
60
50
40
30
20
10
0
0
1
2
3
4
5
sed. coefficient (s)

FIG. 9C

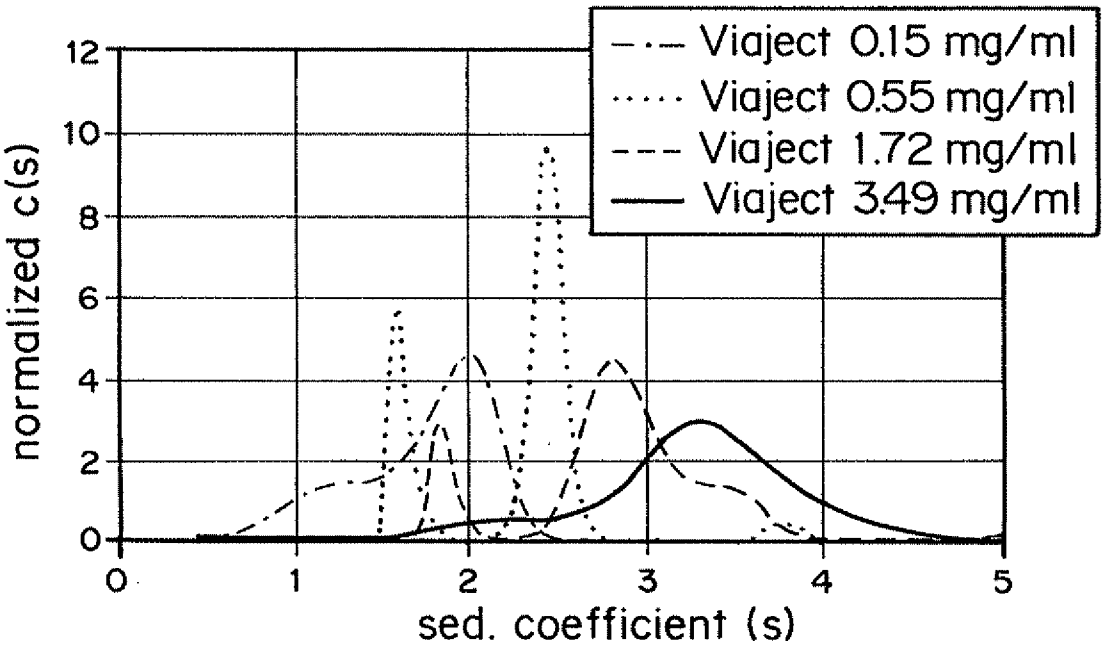

Viaject 0.15 mg/ml
Viaject 0.55 mg/ml
Viaject 1.72 mg/ml
Viaject 3.49 mg/ml
normalized c(s)
12
10
8
6
4
2
0
0
1
2
3
4
5
sed. coefficient (s)

FIG. 9D

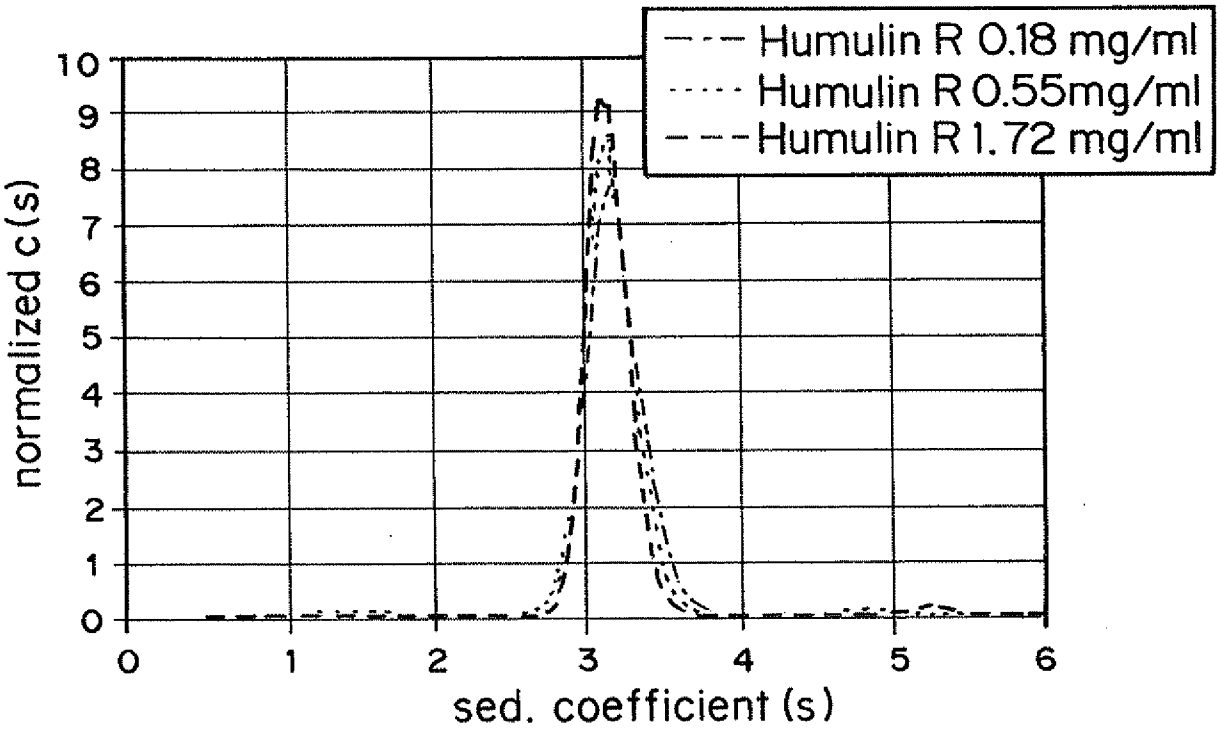


FIG. 10A

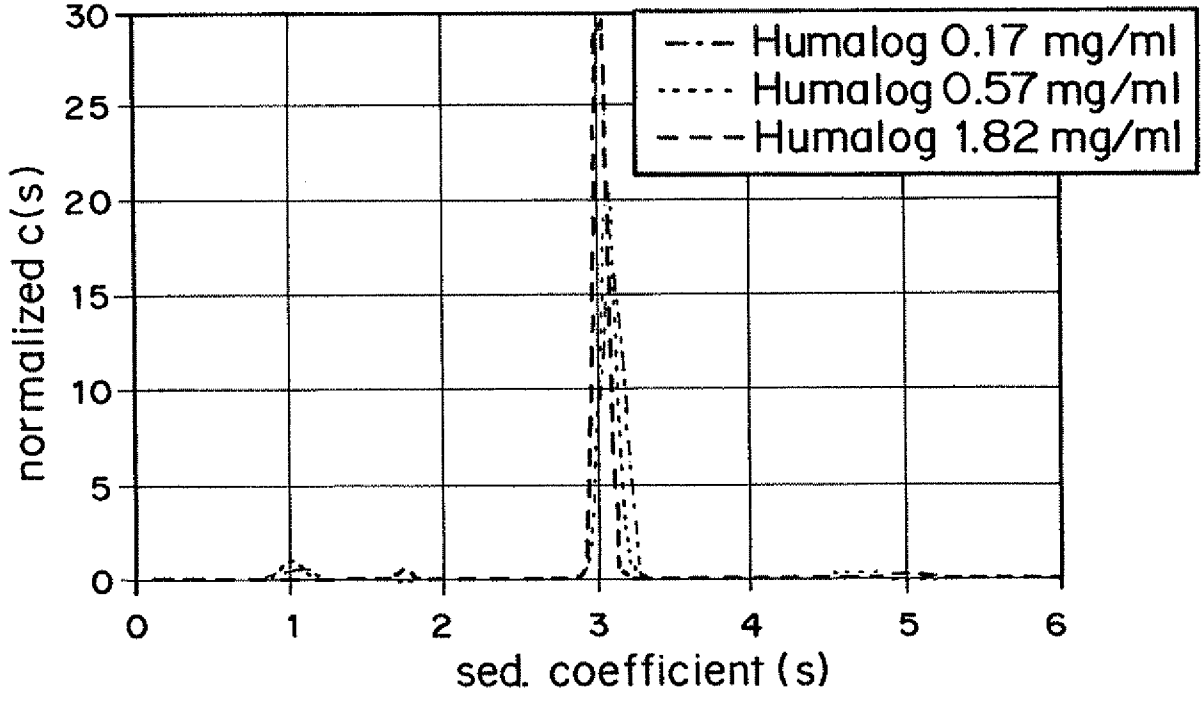


FIG. 10B

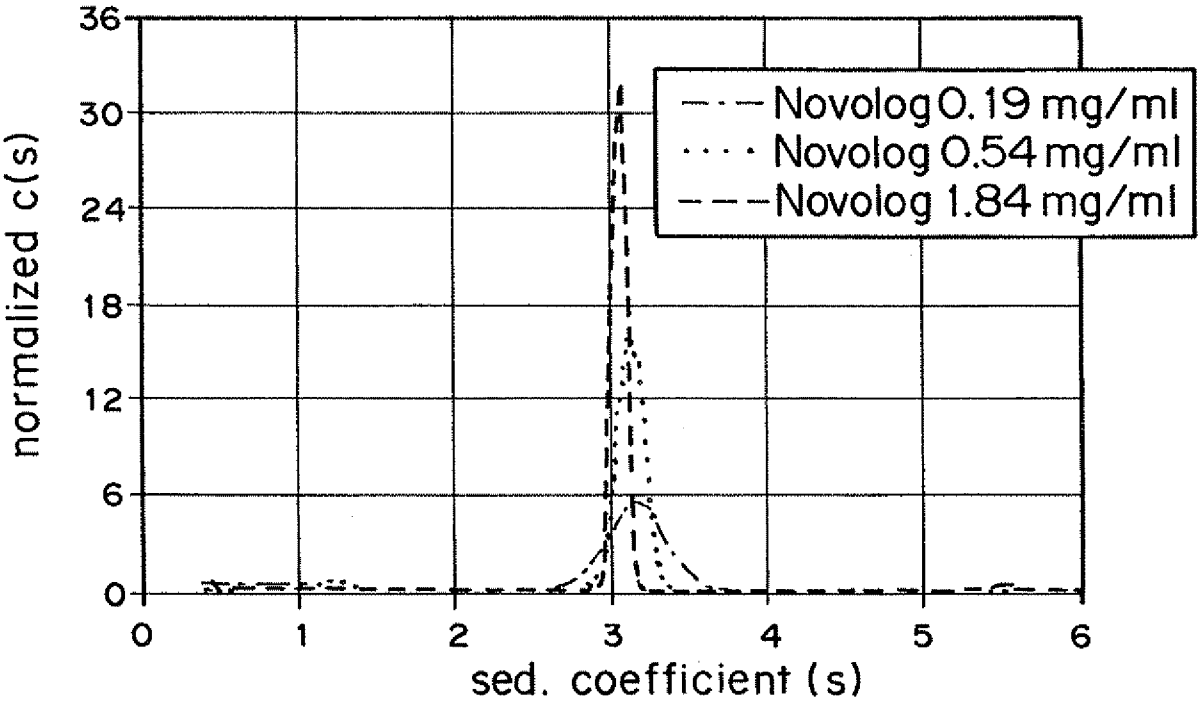


FIG. 10C

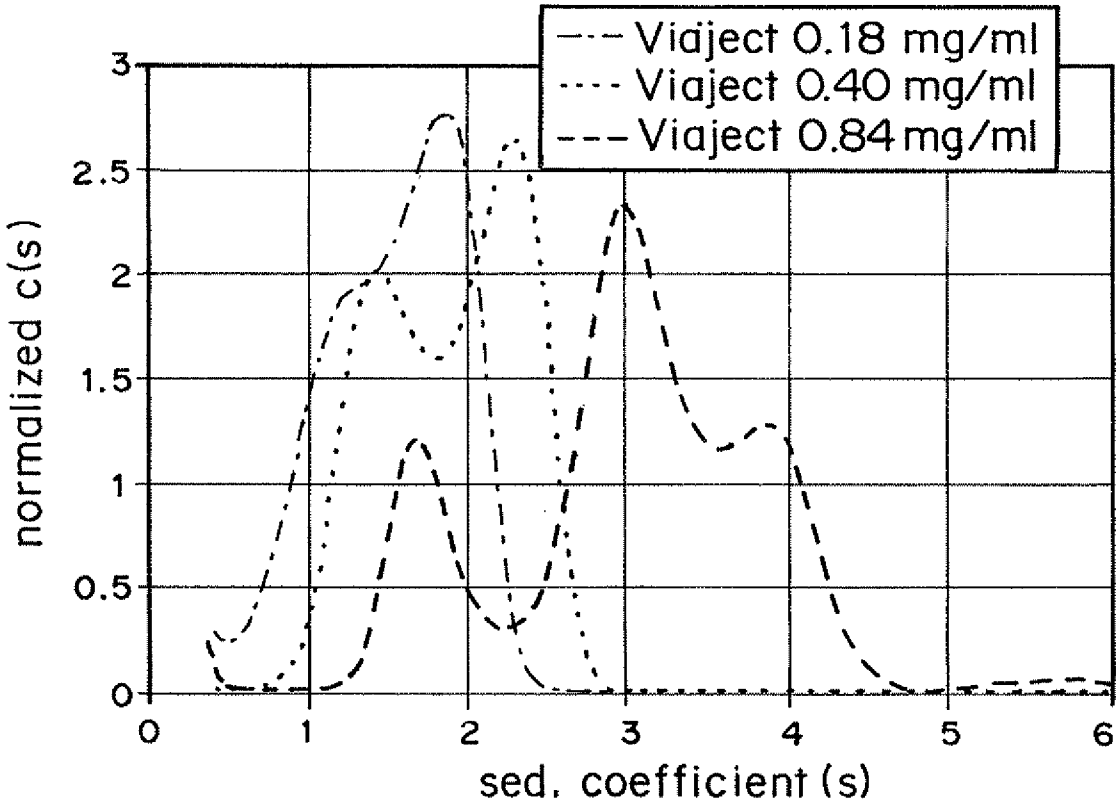


FIG. 10D

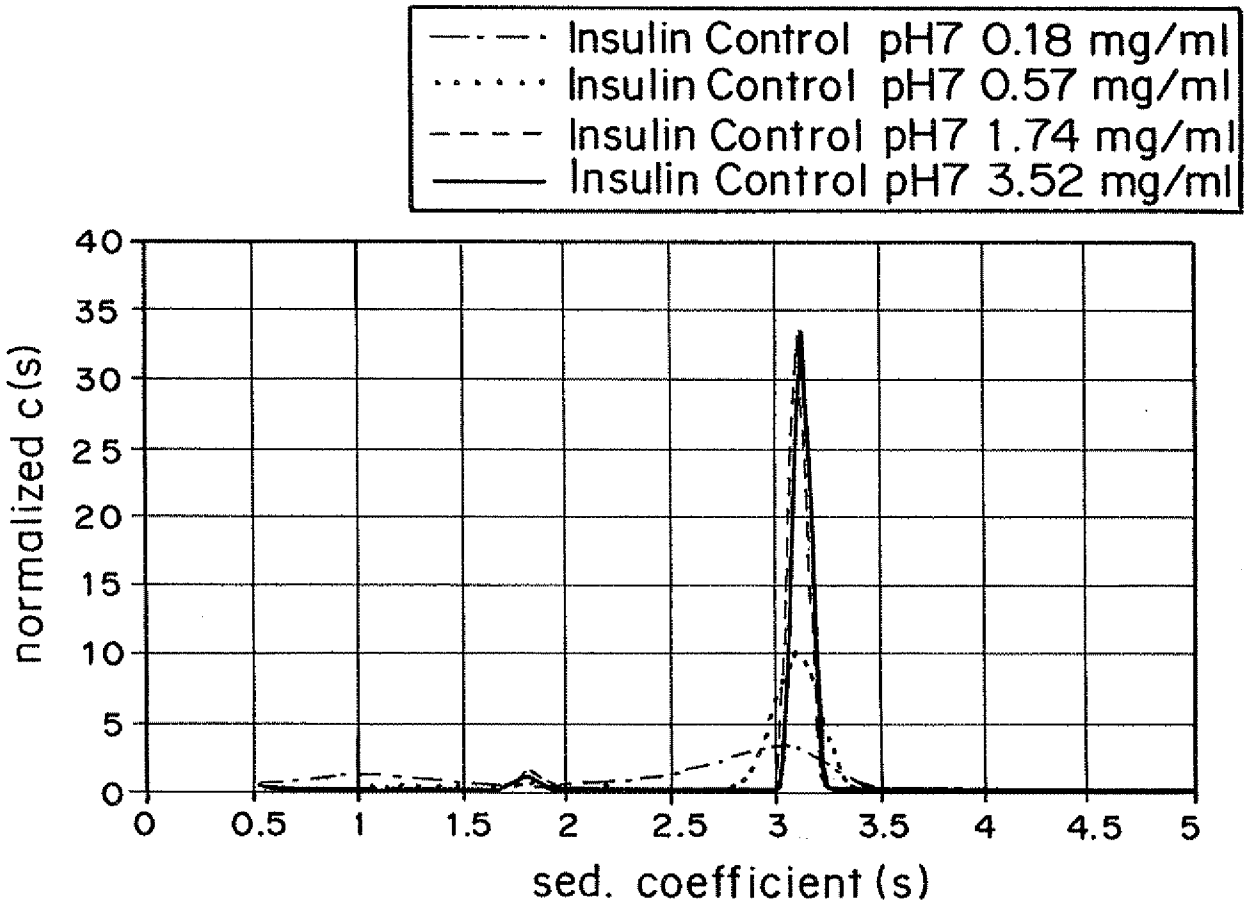

Insulin Control pH7 0.18 mg/ml
Insulin Control pH7 0.57 mg/ml
Insulin Control pH7 1.74 mg/ml
Insulin Control pH7 3.52 mg/ml
normalized c(s)
0
5
10
15
20
25
30
35
40
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
sed. coefficient (s)

FIG. 11

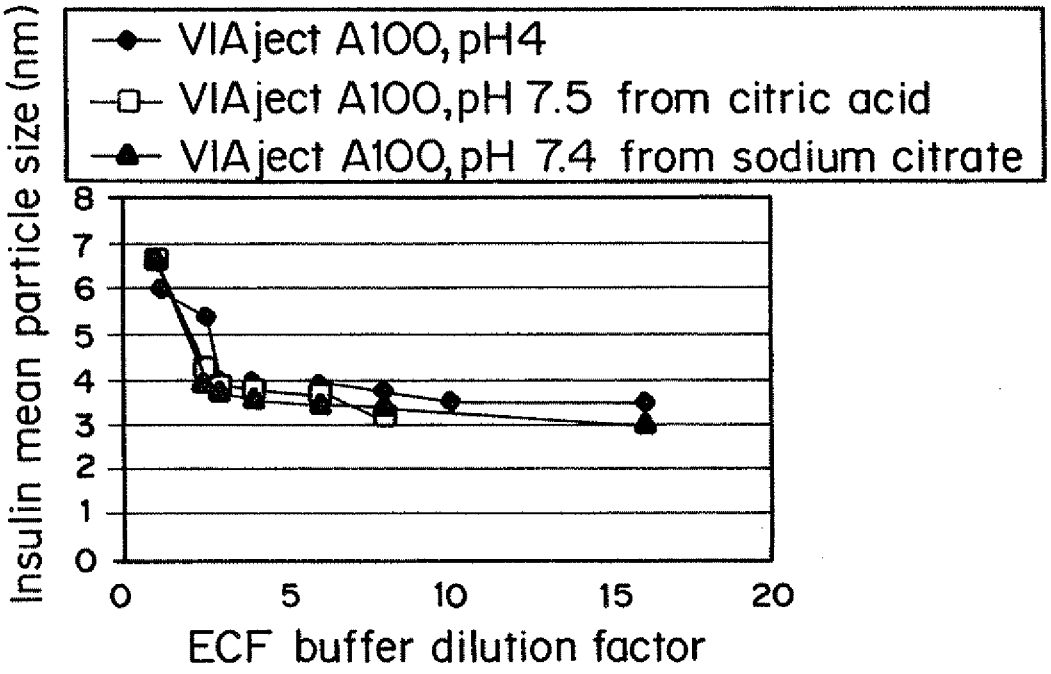

VIAject A100, pH4
VIAject A100, pH 7.5 from citric acid
VIAject A100, pH 7.4 from sodium citrate
Insulin mean particle size (nm)
0
1
2
3
4
5
6
7
8
0
5
10
15
20
ECF buffer dilution factor

FIG. 12

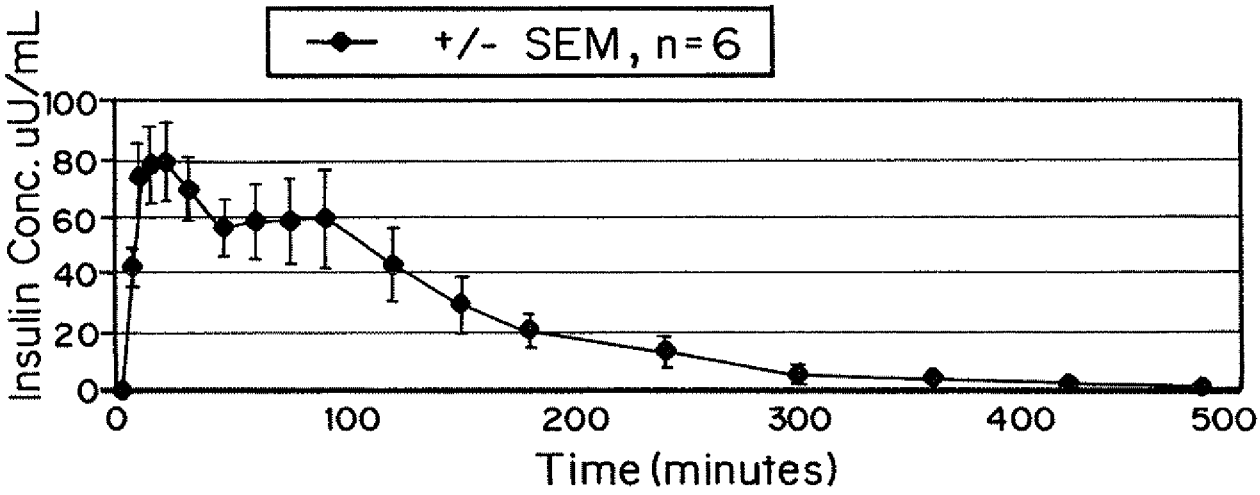

+/- SEM, n=6
Insulin Conc. uU/mL
0
20
40
60
80
100
0
100
200
300
400
500
Time (minutes)

FIG. 13