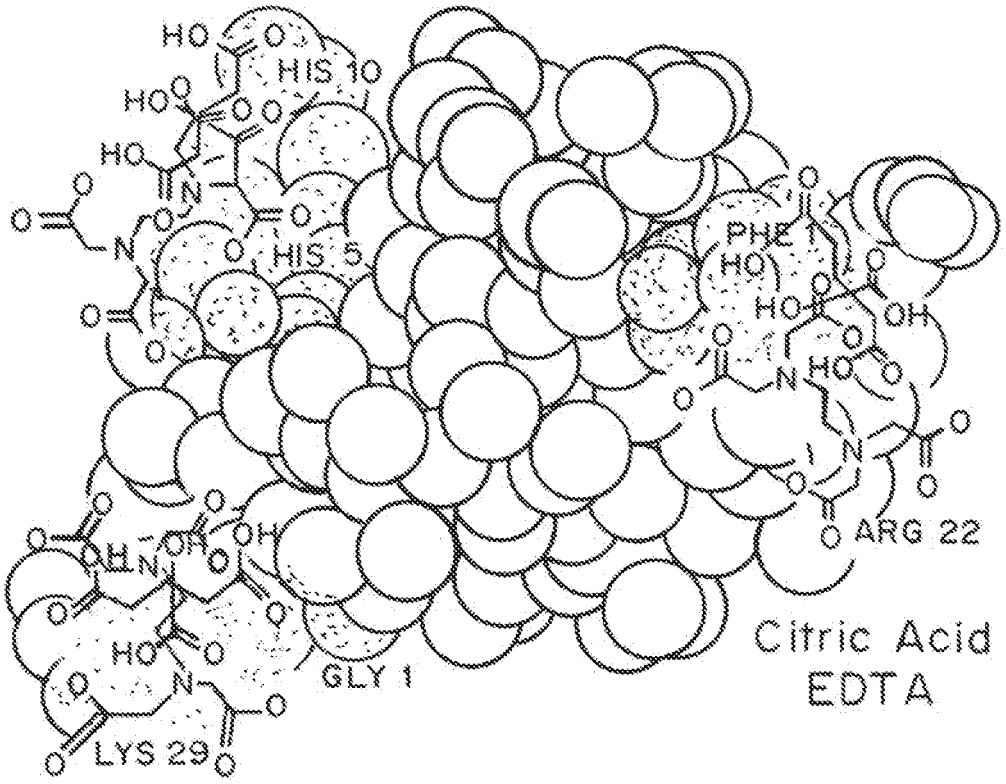
Insulin Charge Distribution



- Cationic residues on insulin are clustered
- Multivalent anions may neutralize (mask) the charge

FIG. 1

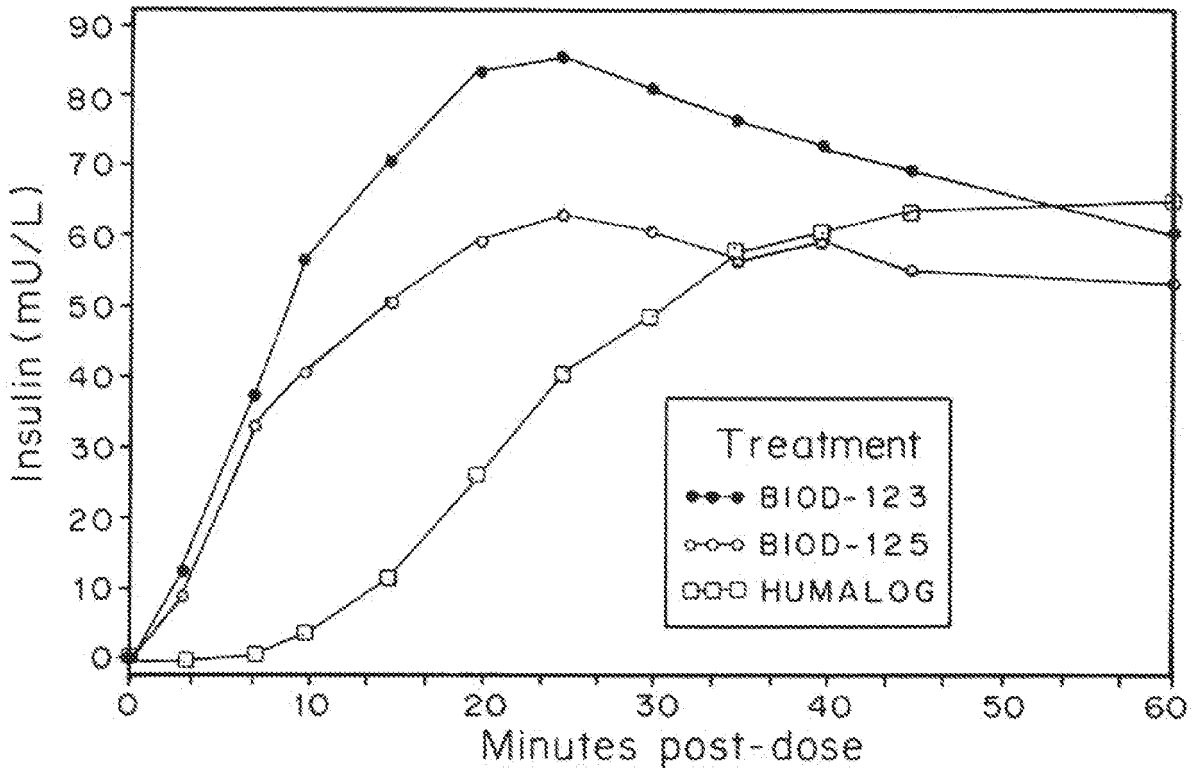

Insulin (mU/L)
0
10
20
30
40
50
60
70
80
90
Minutes post-dose
0
10
20
30
40
50
60
Treatment
BIOD-123
BIOD-125
HUMALOG

FIG. 2

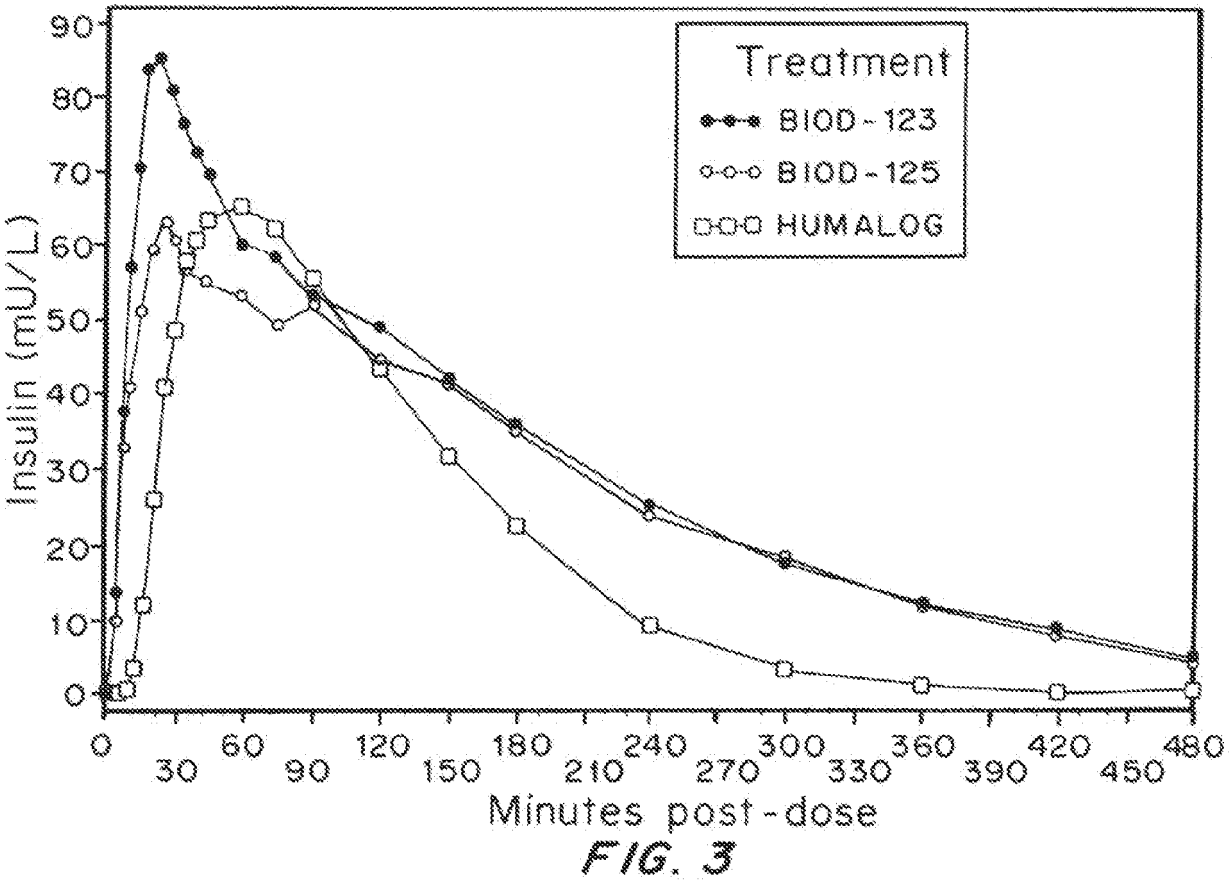

Insulin (mU/L)
0
10
20
30
40
50
60
70
80
90
Minutes post-dose
0
30
60
90
120
150
180
210
240
270
300
330
360
390
420
450
480
Treatment
BIOD-123
BIOD-125
HUMALOG

FIG. 3

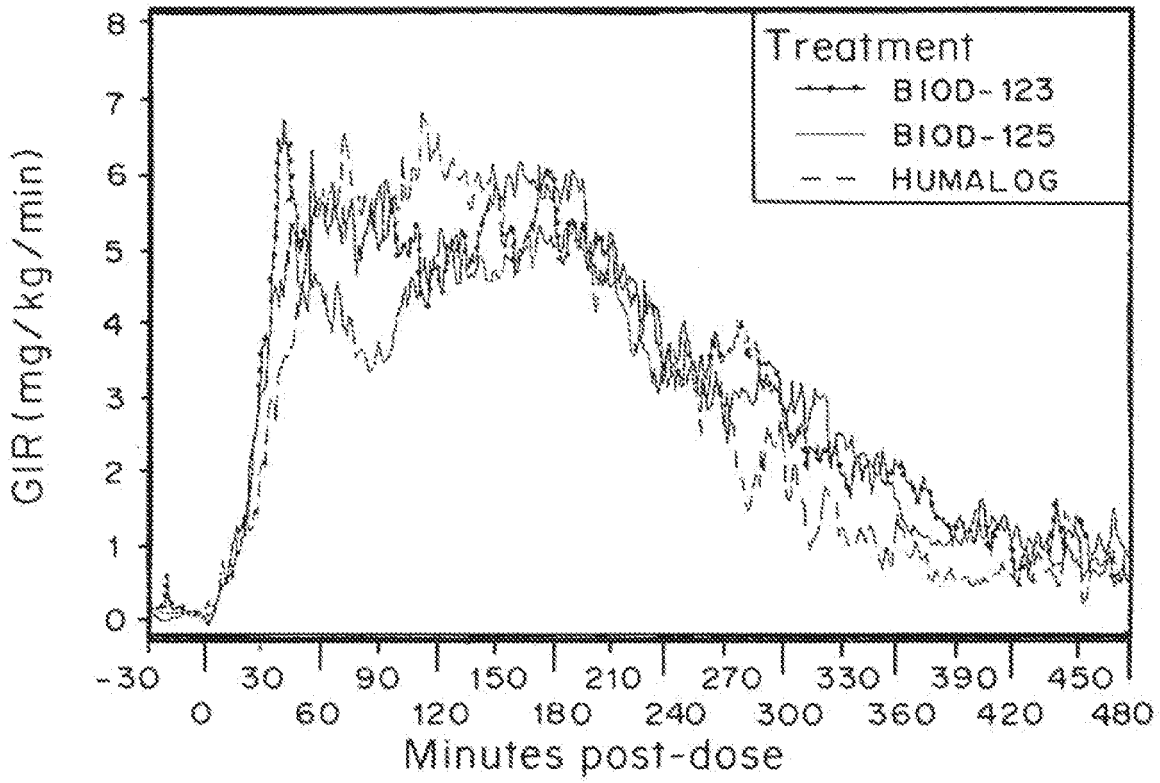

Treatment
BIOD-123
BIOD-125
HUMALOG
GIR (mg/kg/min)
0
1
2
3
4
5
6
7
8
-30
0
30
60
90
120
150
180
210
240
270
300
330
360
390
420
450
480
Minutes post-dose

FIG. 4

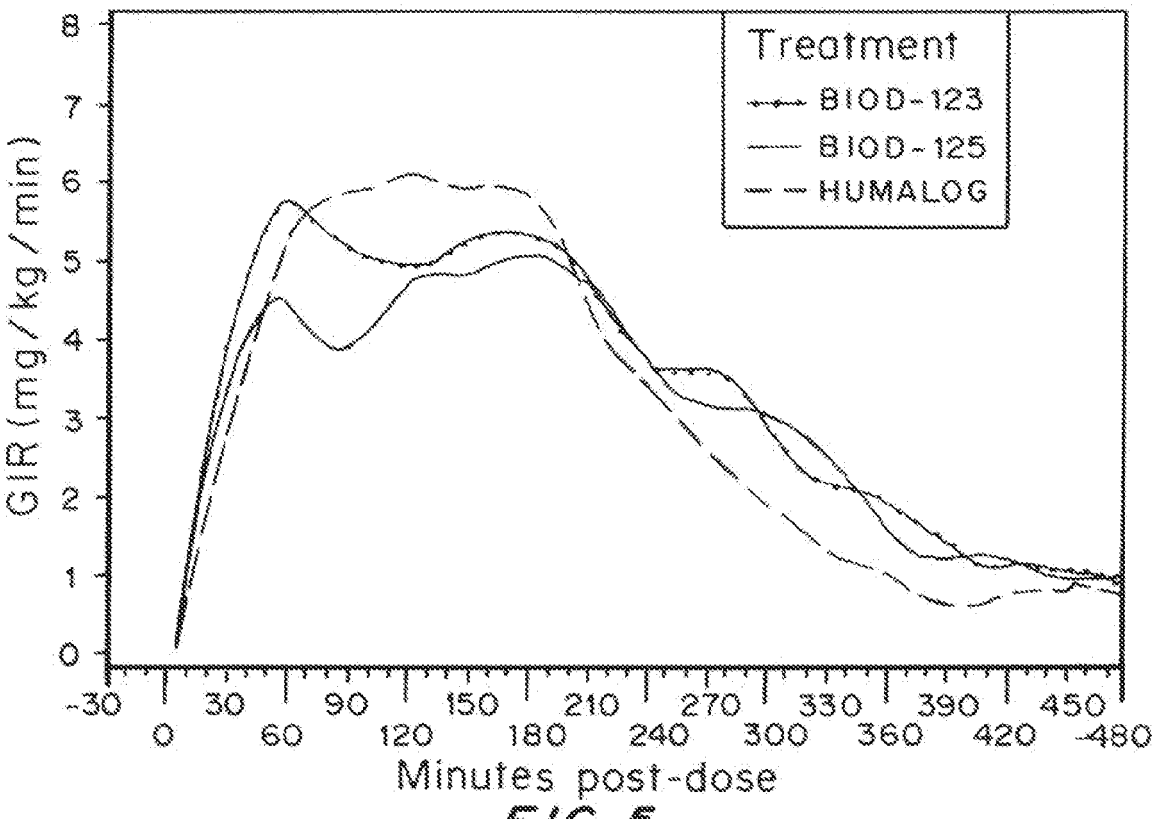

Treatment
BIOD-123
BIOD-125
HUMALOG
GIR (mg/kg/min)
0
1
2
3
4
5
6
7
8
-30
0
30
60
90
120
150
180
210
240
270
300
330
360
390
420
450
480
Minutes post-dose

FIG. 5

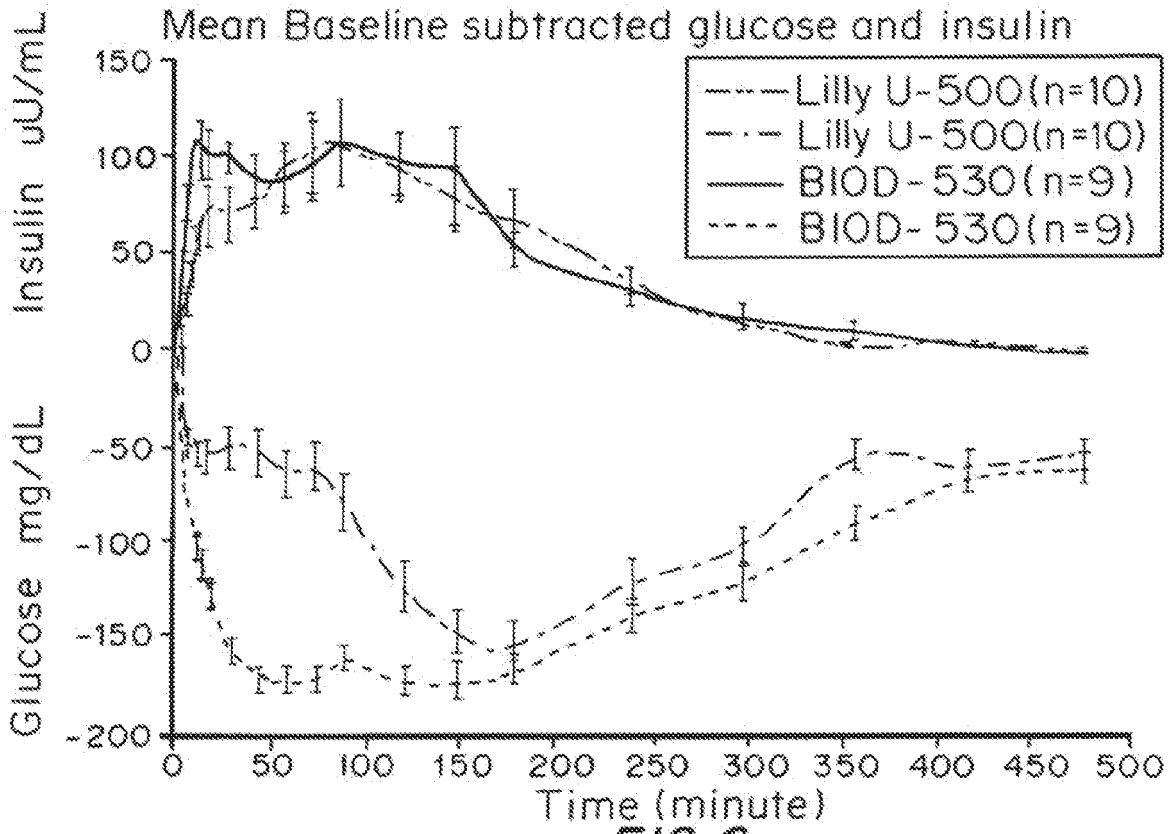

Mean Baseline subtracted glucose and insulin
Insulin uU/mL
Glucose mg/dL
Lilly U-500(n=10)
Lilly U-500(n=10)
BIOD-530(n=9)
BIOD-530(n=9)
150
100
50
0
-50
-100
-150
-200
0 50 100 150 200 250 300 350 400 450 500
Time (minute)

FIG. 6

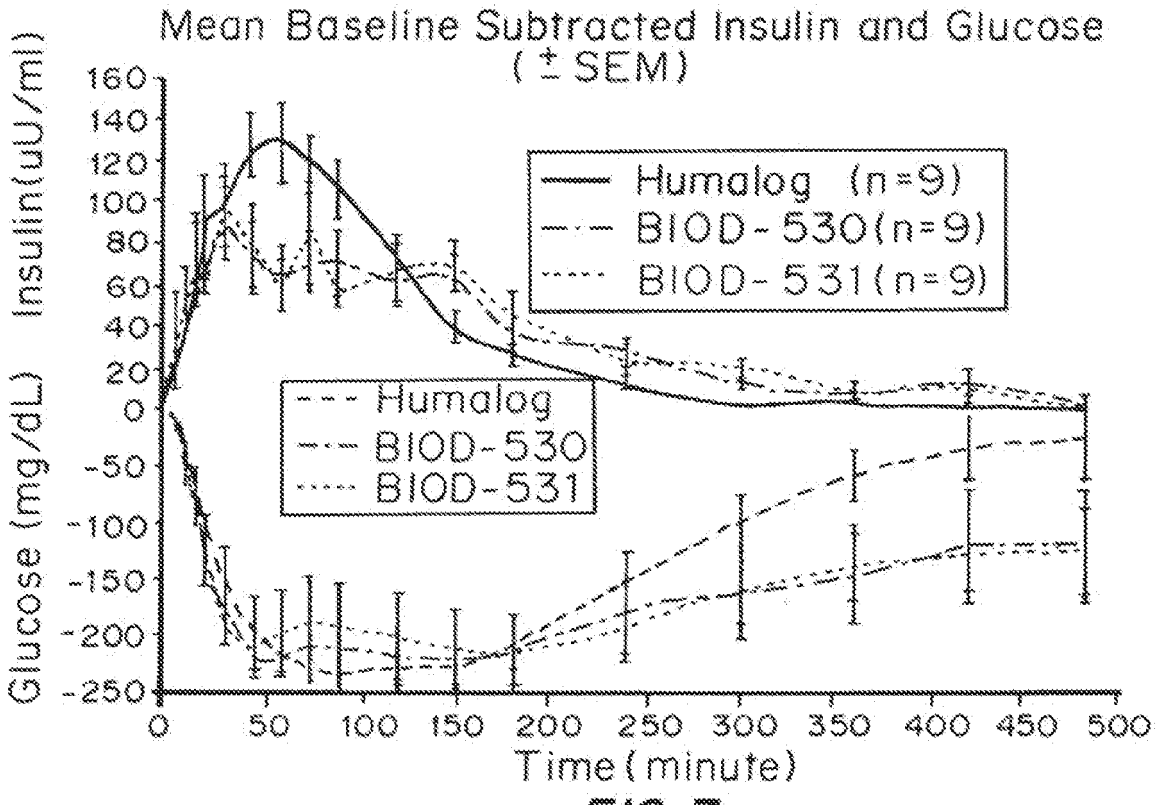

Mean Baseline Subtracted Insulin and Glucose
(± SEM)
Insulin(uU/ml)
Glucose (mg/dL)
Humalog (n=9)
BIOD-530(n=9)
BIOD-531(n=9)
Humalog
BIOD-530
BIOD-531
160
140
120
100
80
60
40
20
0
-50
-100
-150
-200
-250
0 50 100 150 200 250 300 350 400 450 500
Time (minute)

FIG. 7

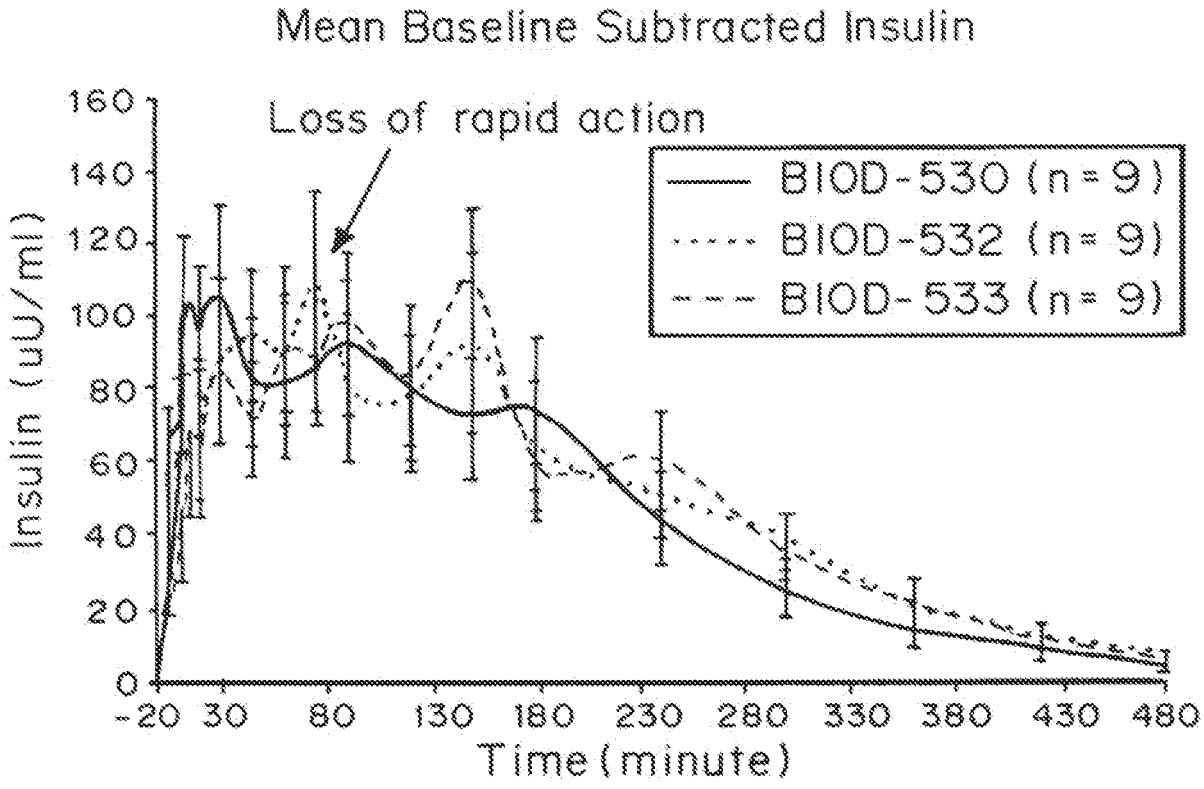

Mean Baseline Subtracted Insulin
Loss of rapid action
BIOD-530 (n=9)
BIOD-532 (n=9)
BIOD-533 (n=9)
Insulin (uU/ml)
160
140
120
100
80
60
40
20
0
-20 30 80 130 180 230 280 330 380 430 480
Time (minute)

FIG. 8

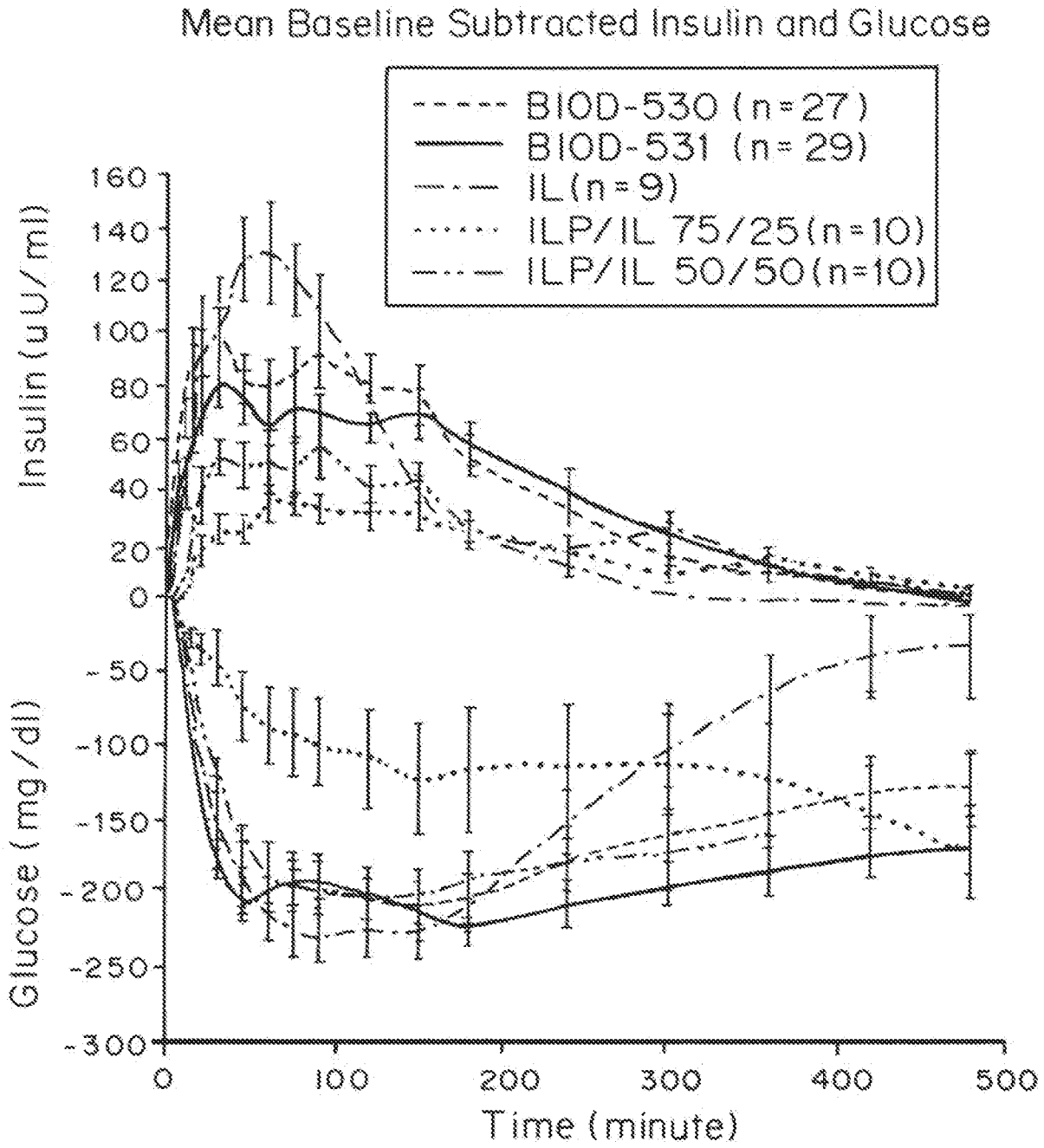

Mean Baseline Subtracted Insulin and Glucose
BIOD-530 (n=27)
BIOD-531 (n=29)
IL(n=9)
ILP/IL 75/25(n=10)
ILP/IL 50/50(n=10)
Insulin (uU/ml)
Glucose (mg/dl)
160
140
120
100
80
60
40
20
0
-50
-100
-150
-200
-250
-300
0
100
200
300
400
500
Time (minute)

FIG. 9