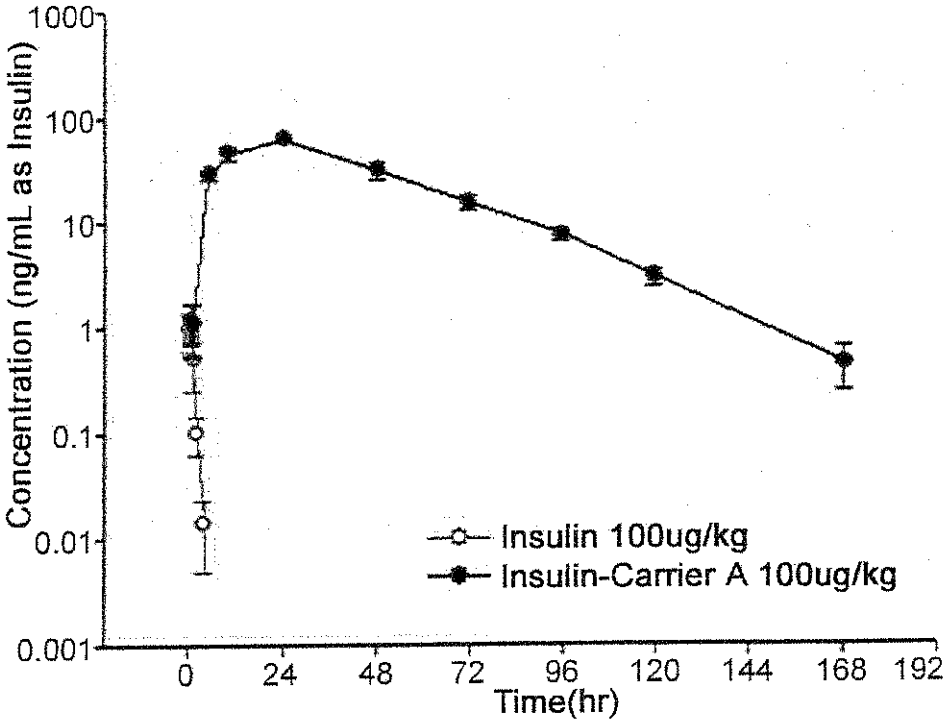
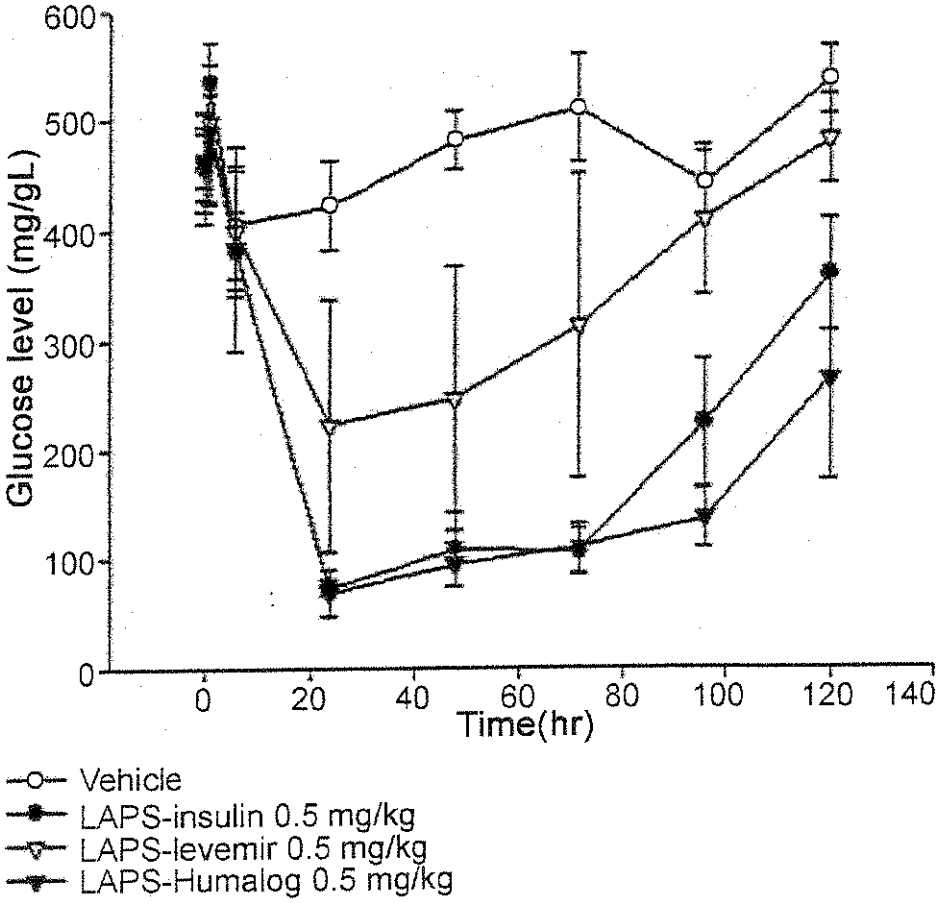
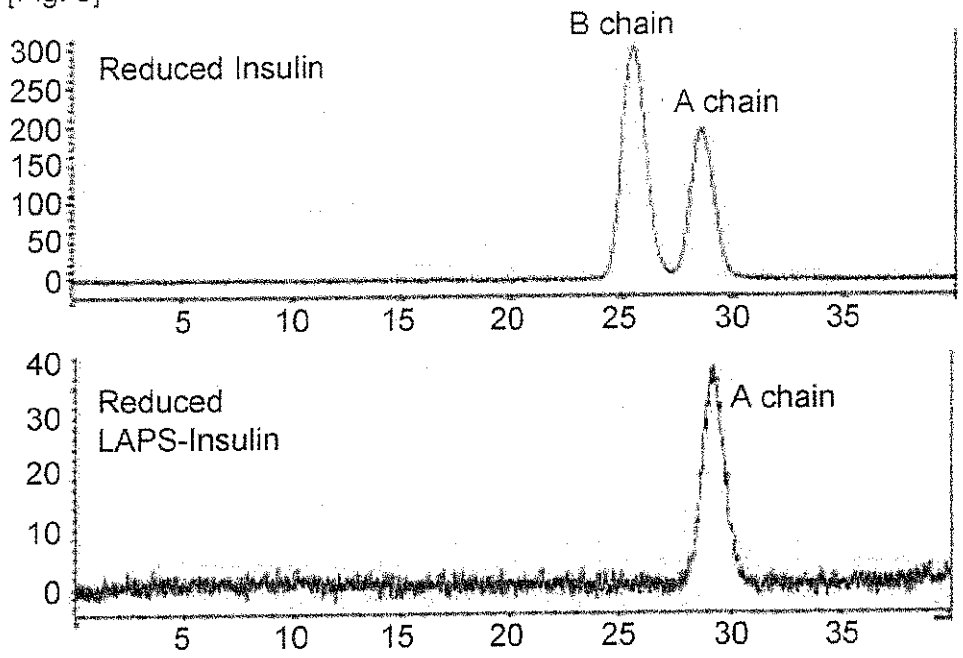
[Fig. 1]


Concentration (ng/mL as Insulin)
1000
100
10
1
0.1
0.01
0.001
0
24
48
72
96
120
144
168
192
Time(hr)
Insulin 100ug/kg
Insulin-Carrier A 100ug/kg

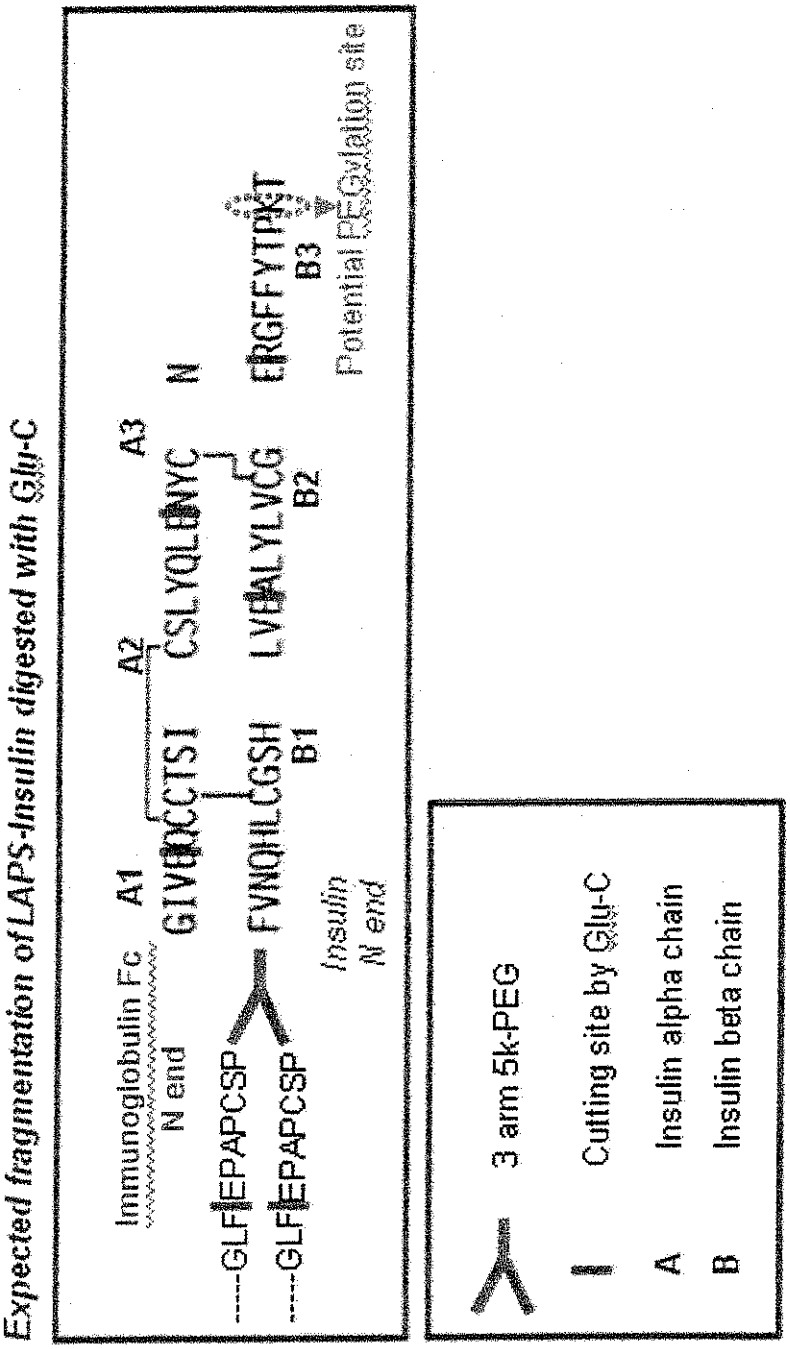
[Fig. 2]


Glucose level (mg/gL)
600
500
400
300
200
100
0
0
20
40
60
80
100
120
140
Time(hr)
Vehicle
LAPS-insulin 0.5 mg/kg
LAPS-levemir 0.5 mg/kg
LAPS-Humalog 0.5 mg/kg

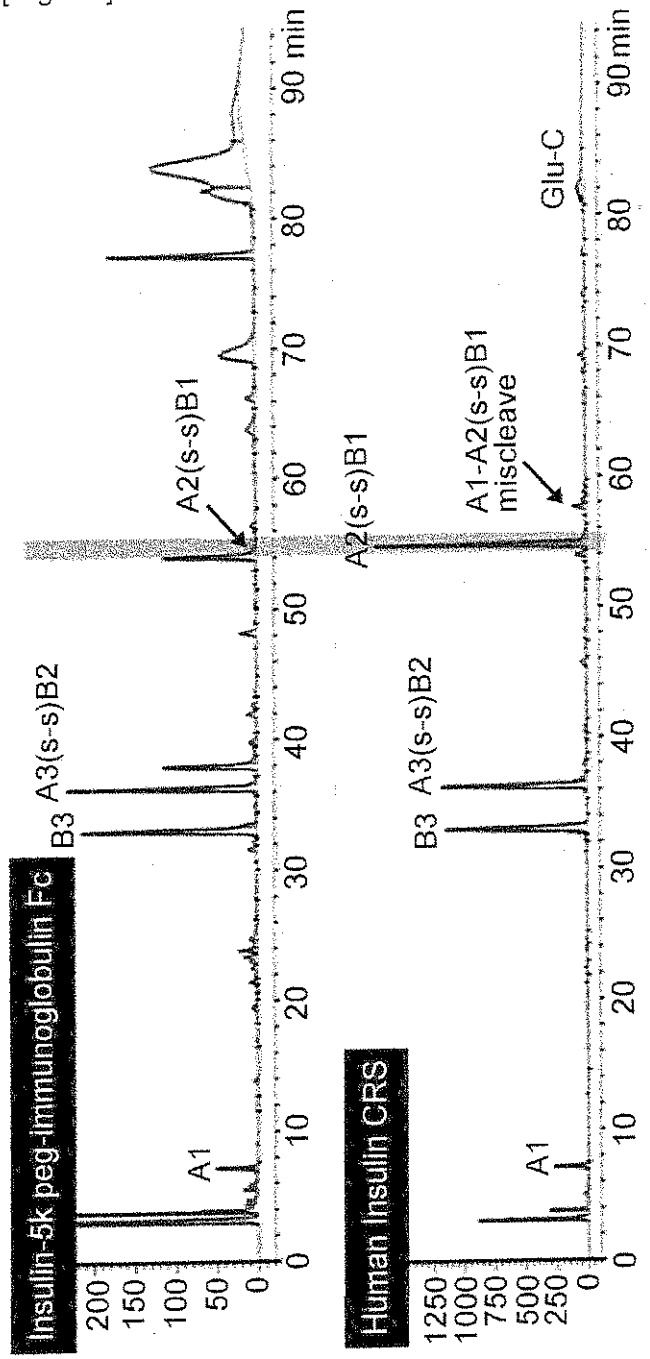
[Fig. 3]


B chain
A chain
Reduced Insulin
300
250
200
150
100
50
0
5
10
15
20
25
30
35
A chain
Reduced
LAPS-Insulin
40
30
20
10
0
5
10
15
20
25
30
35

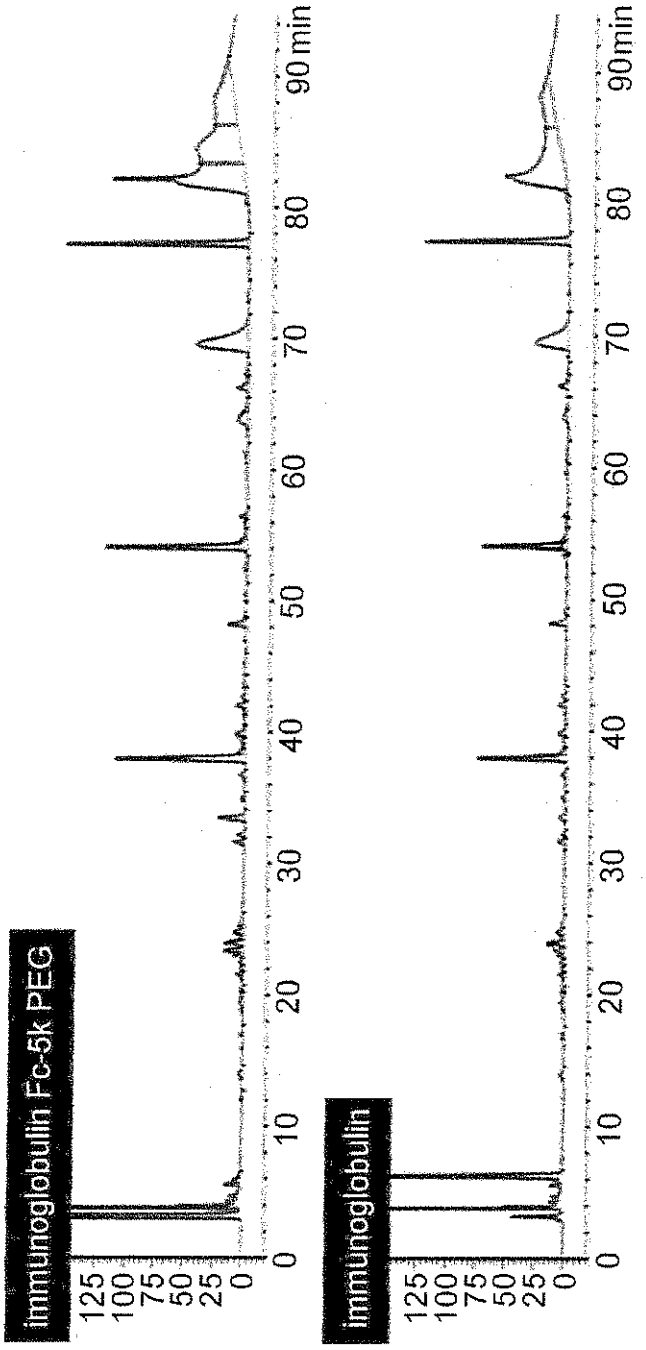
[Fig. 4a]


Expected fragmentation of LAPS-Insulin digested with Glu-C
Immunoglobulin Fc
N end
A1
A2
A3
N
GIVEQCCTSI
CSLYQLENYC
FVNQHLCGSH
LVEALYLVCG
ERGFFYTPKT
B1
B2
B3
Potential PEGylation site
Insulin
N end
-----GLFEPAPCSP
-----GLFEPAPCSP
3 arm 5k-PEG
Cutting site by Glu-C
A Insulin alpha chain
B Insulin beta chain

[Fig. 4b]


Insulin-5k peg-Immunoglobulin Fc
Human Insulin CRS
A1
B3
A3(s-s)B2
A2(s-s)B1
A1-A2(s-s)B1 miscleave
Glu-C
90 min

[Fig. 4c]


immunoglobulin Fc-5k PEG
125
100
75
50
25
0
0
10
20
30
40
50
60
70
80
90min
immunoglobulin
125
100
75
50
25
0
0
10
20
30
40
50
60
70
80
90min

<110> Hanmi Science Co., Ltd.

<120> An Insulin Conjugate Using an Immunoglobulin Fragment

<130> OPA11024

<150> KR10-2010-0030575
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1 5 10 15

Glu Asn Tyr Cys Asn
20

<210> 2
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<213> Homo sapiens

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1 5 10 15

Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Thr
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