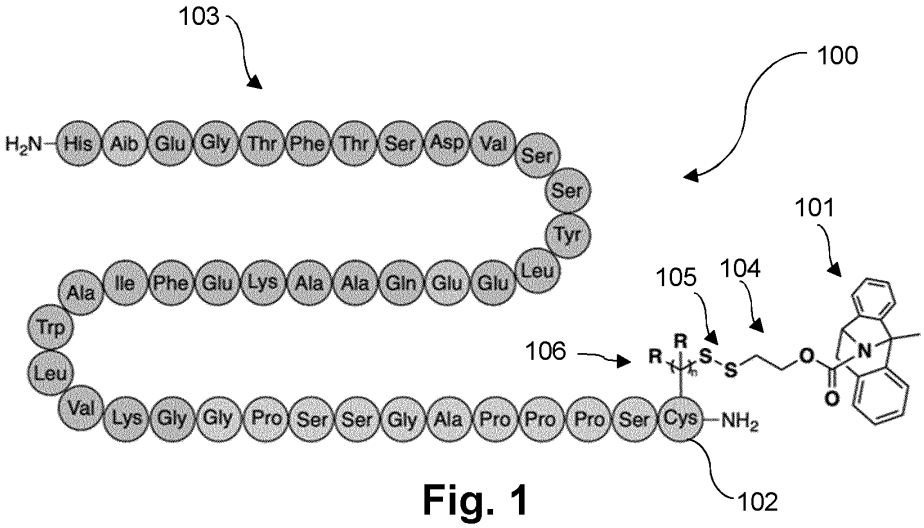

103
100
101
105
104
106
102
H2N
His
Aib
Glu
Gly
Thr
Phe
Thr
Ser
Asp
Val
Ser
Ser
Tyr
Leu
Ala
Ile
Phe
Glu
Lys
Ala
Ala
Gln
Glu
Glu
Trp
Leu
Val
Lys
Gly
Gly
Pro
Ser
Ser
Gly
Ala
Pro
Pro
Pro
Ser
Cys
NH2

Fig. 1

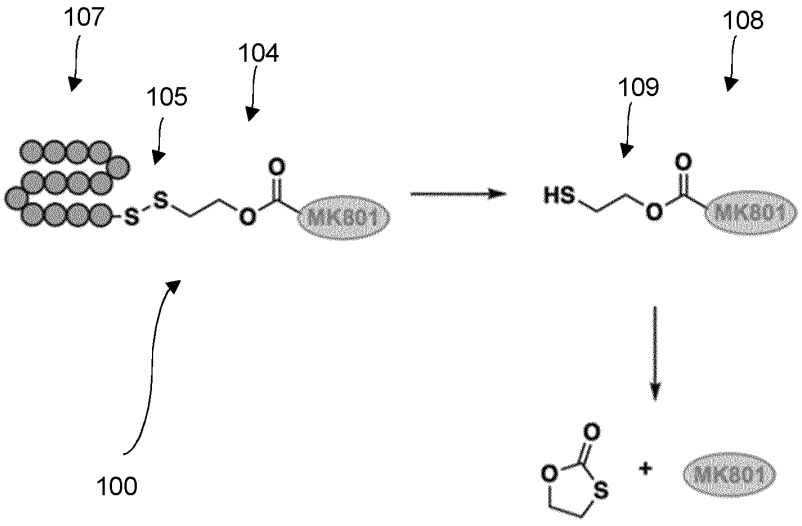

107
104
105
108
109
MK801
HS
MK801
100
MK801

Fig. 2

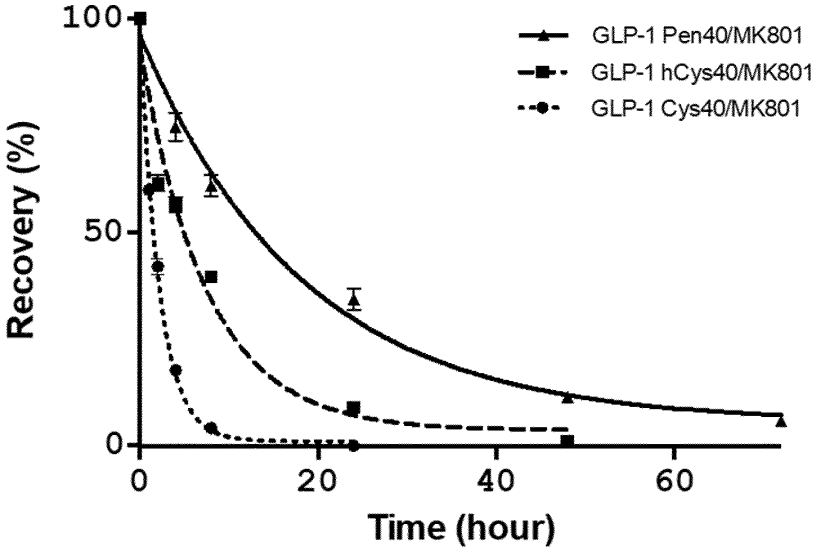

100
50
0
Recovery (%)
0
20
40
60
Time (hour)
GLP-1 Pen40/MK801
GLP-1 hCys40/MK801
GLP-1 Cys40/MK801

Fig. 3

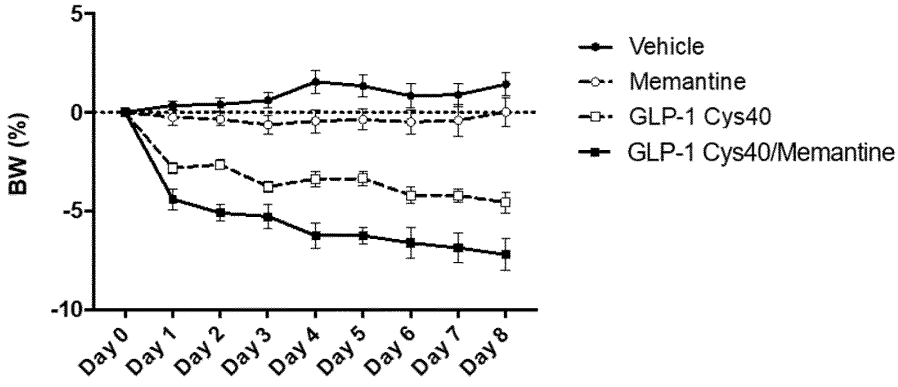

5
0
-5
-10
BW (%)
Day 0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8
Vehicle
Memantine
GLP-1 Cys40
GLP-1 Cys40/Memantine

Fig. 4

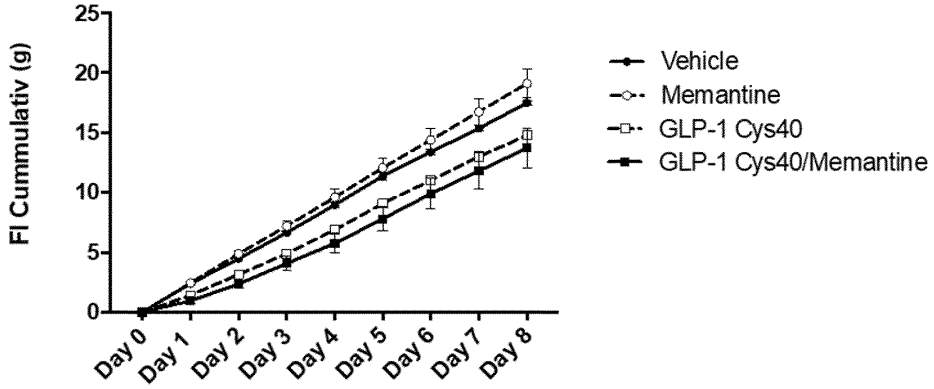

FI Cummulativ (g)
25
20
15
10
5
0
Day 0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8
Vehicle
Memantine
GLP-1 Cys40
GLP-1 Cys40/Memantine

Fig. 5

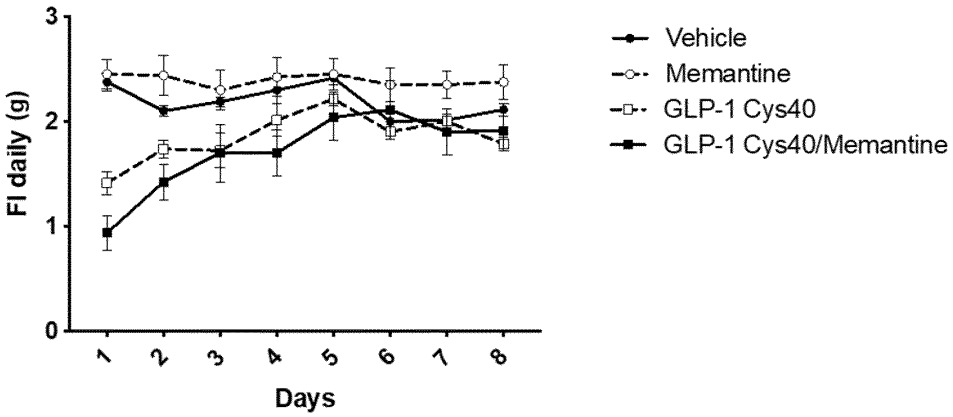

FI daily (g)
3
2
1
0
1
2
3
4
5
6
7
8
Days
Vehicle
Memantine
GLP-1 Cys40
GLP-1 Cys40/Memantine

Fig. 6

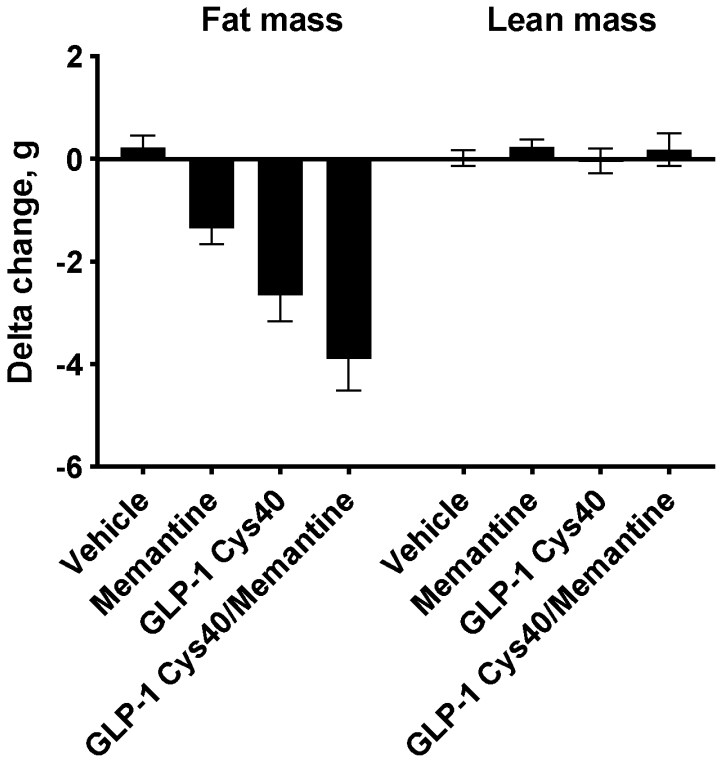

Fat mass
Lean mass
Delta change, g
2
0
-2
-4
-6
Vehicle
Memantine
GLP-1 Cys40
GLP-1 Cys40/Memantine
Vehicle
Memantine
GLP-1 Cys40
GLP-1 Cys40/Memantine

Fig. 7

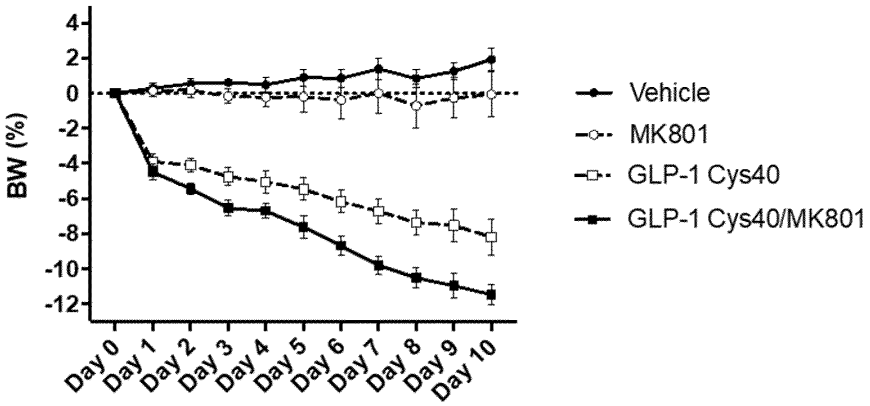

BW (%)
4
2
0
-2
-4
-6
-8
-10
-12
Day 0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8
Day 9
Day 10
Vehicle
MK801
GLP-1 Cys40
GLP-1 Cys40/MK801

Fig. 8

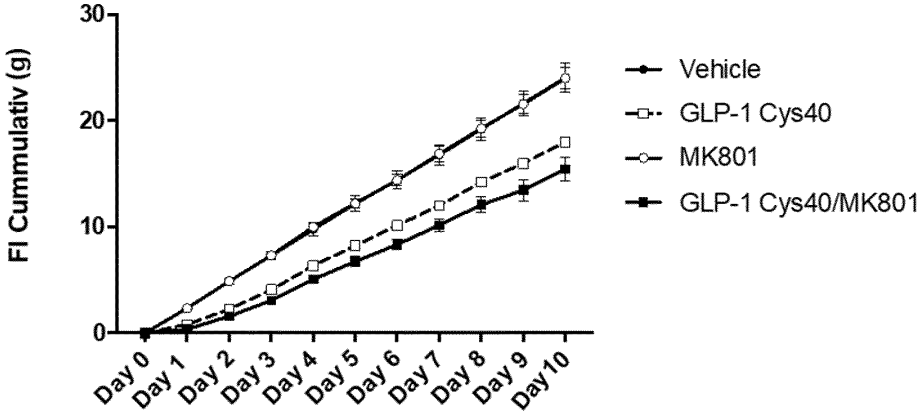

FI Cummulativ (g)
30
20
10
0
Day 0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8
Day 9
Day 10
Vehicle
GLP-1 Cys40
MK801
GLP-1 Cys40/MK801

Fig. 9

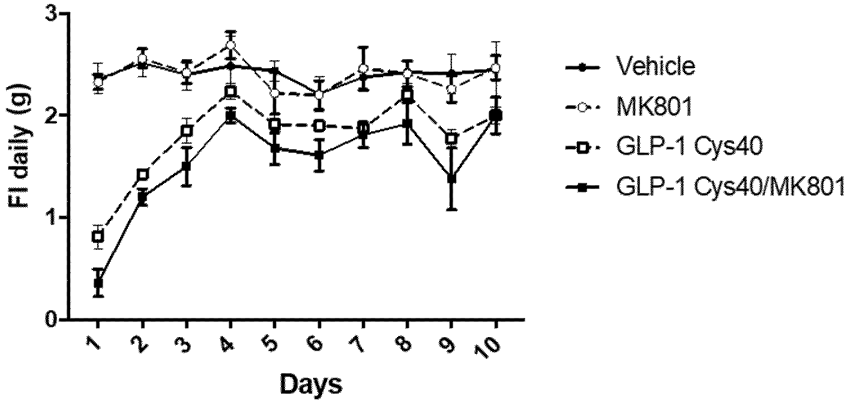

FI daily (g)
3
2
1
0
1
2
3
4
5
6
7
8
9
10
Days
Vehicle
MK801
GLP-1 Cys40
GLP-1 Cys40/MK801

Fig. 10

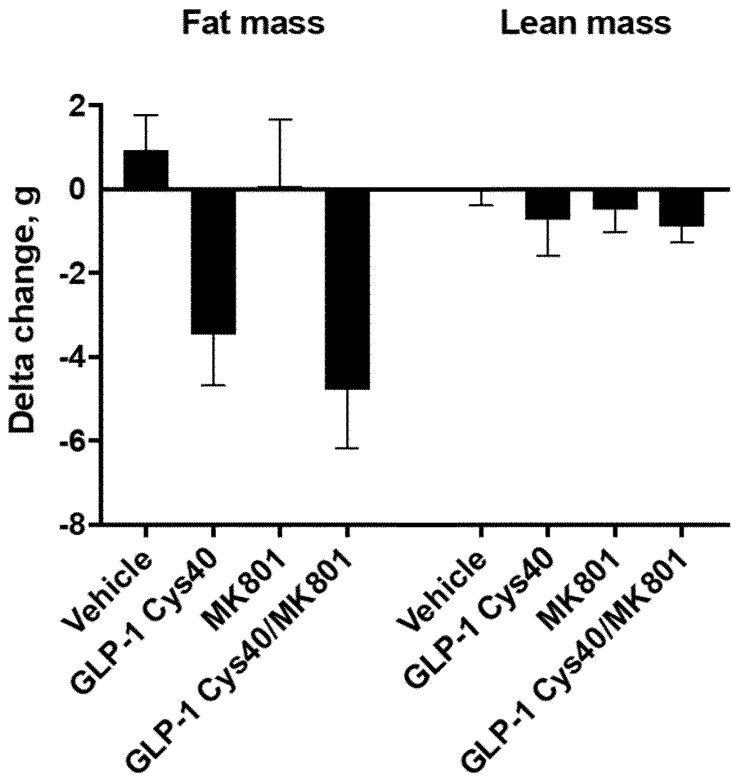

Fat mass
Lean mass
Delta change, g
2
0
-2
-4
-6
-8
Vehicle
GLP-1 Cys40
MK801
GLP-1 Cys40/MK801
Vehicle
GLP-1 Cys40
MK801
GLP-1 Cys40/MK801

Fig. 11

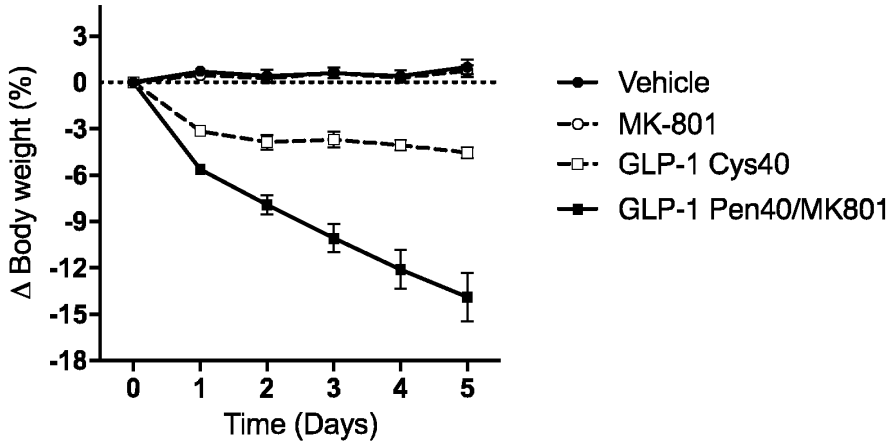

Δ Body weight (%)
3
0
-3
-6
-9
-12
-15
-18
0
1
2
3
4
5
Time (Days)
Vehicle
MK-801
GLP-1 Cys40
GLP-1 Pen40/MK801

Fig. 12

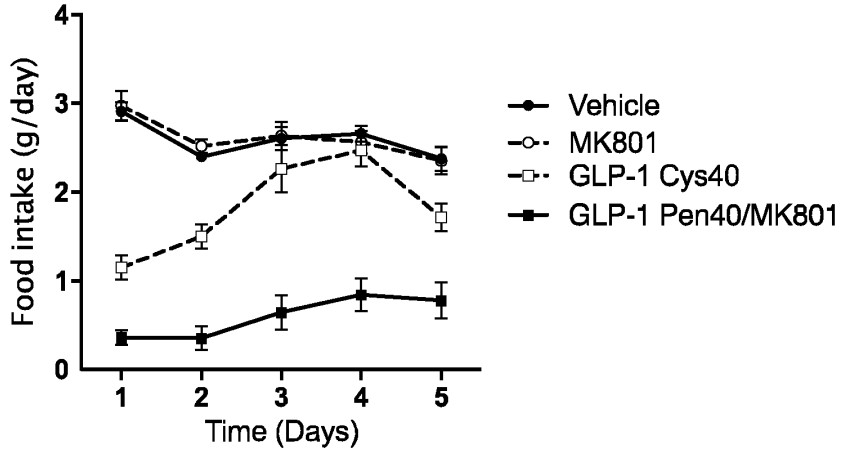

Food intake (g/day)
Time (Days)
Vehicle
MK801
GLP-1 Cys40
GLP-1 Pen40/MK801

Fig. 13

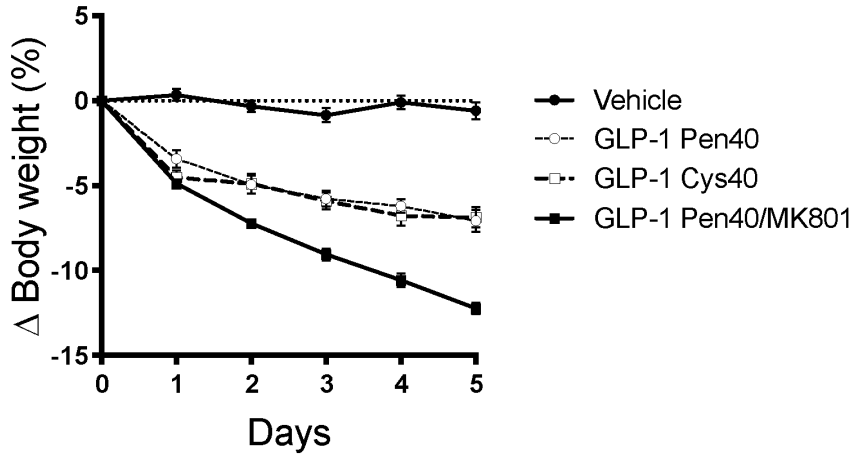

Δ Body weight (%)
Days
Vehicle
GLP-1 Pen40
GLP-1 Cys40
GLP-1 Pen40/MK801

Fig. 14

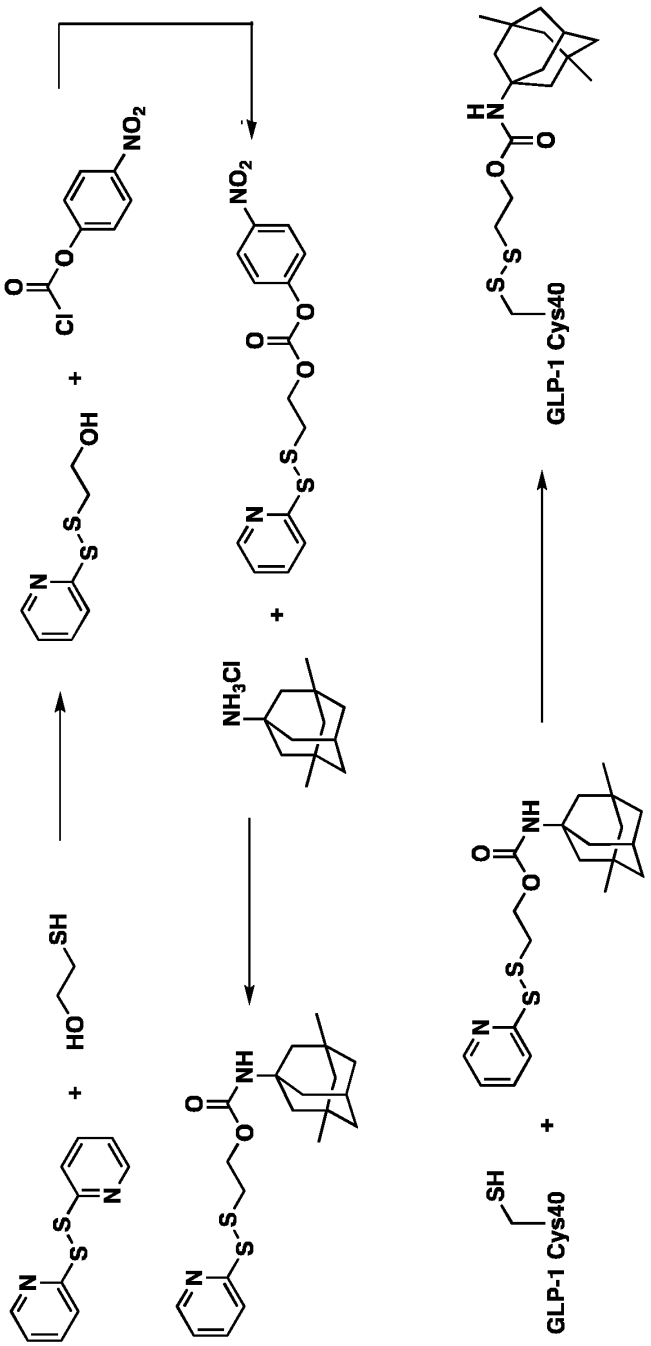


Fig. 15

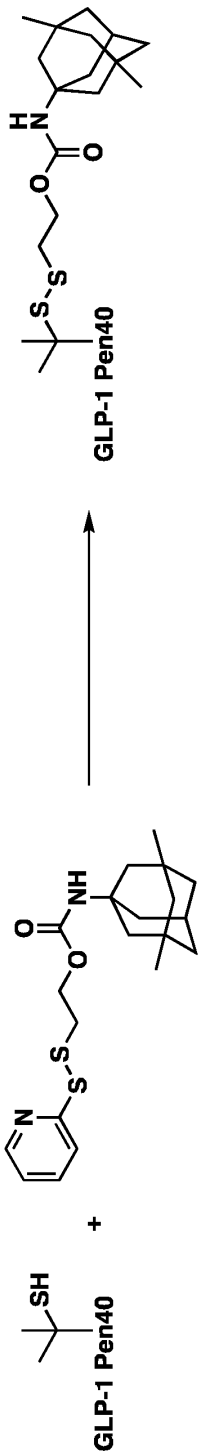


Fig. 16

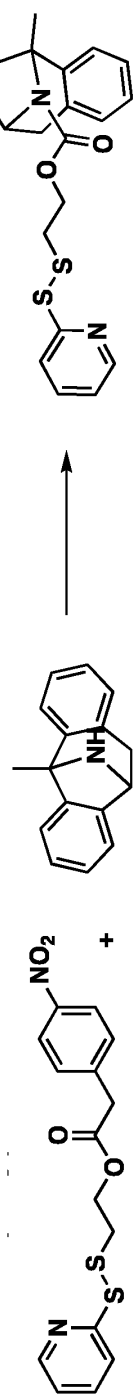


Fig. 17

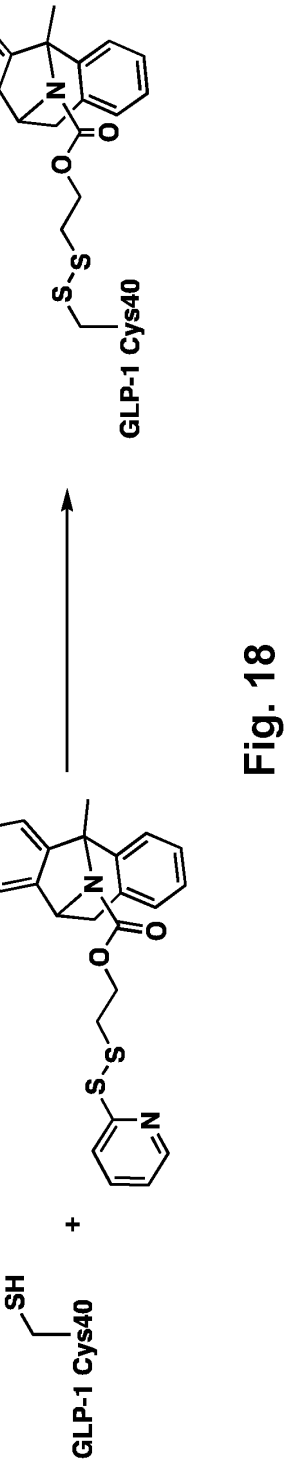


Fig. 18

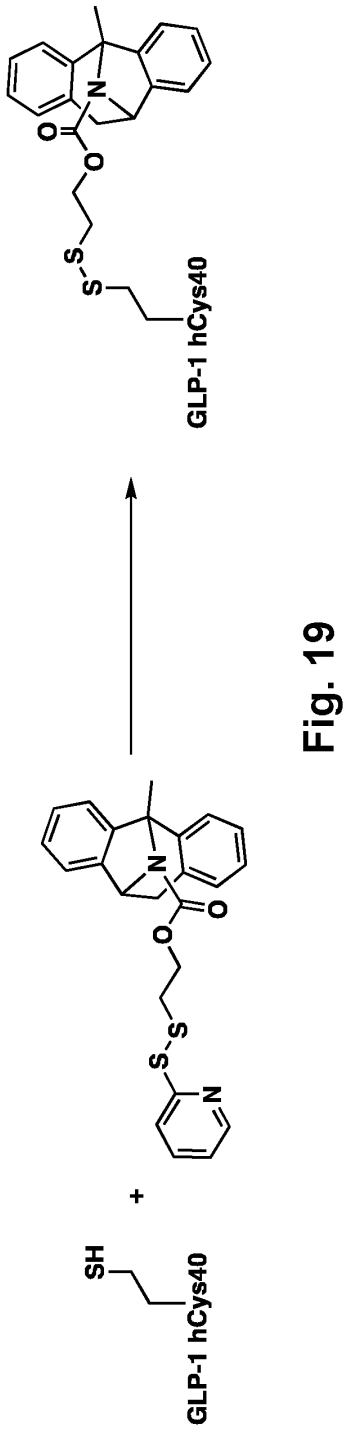


Fig. 19



Fig. 20

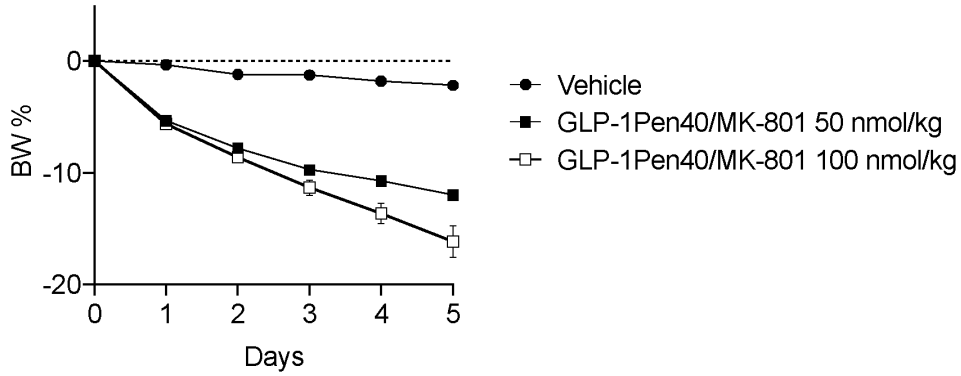


Fig. 21

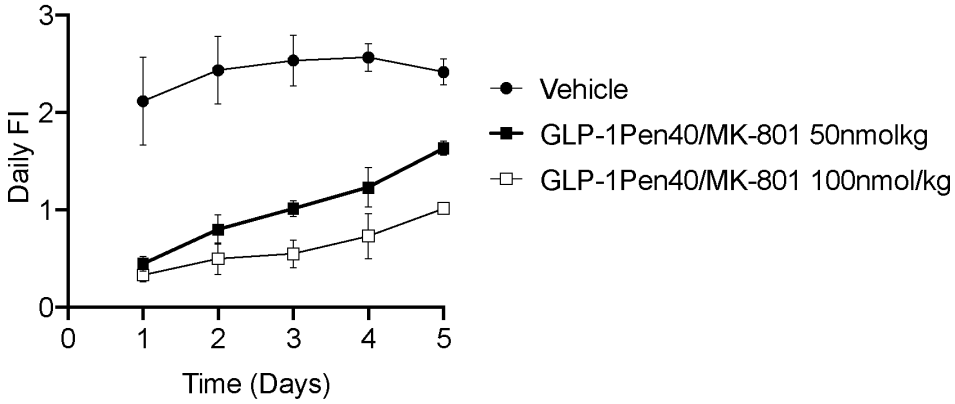


Fig. 22

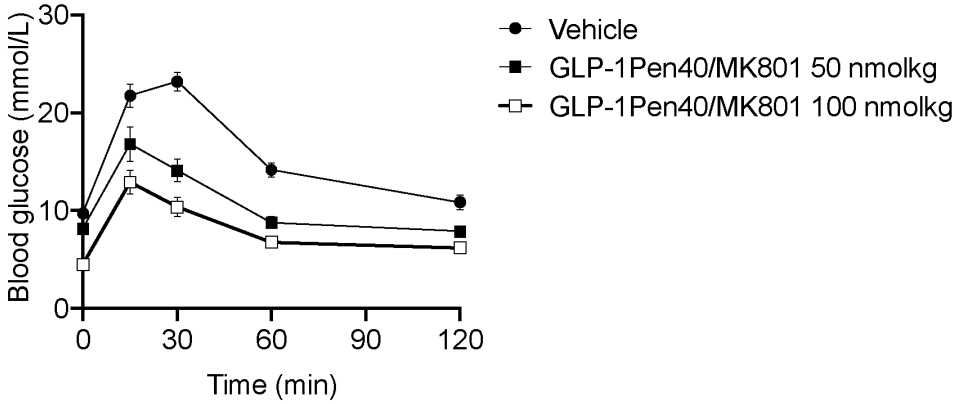


Fig. 23

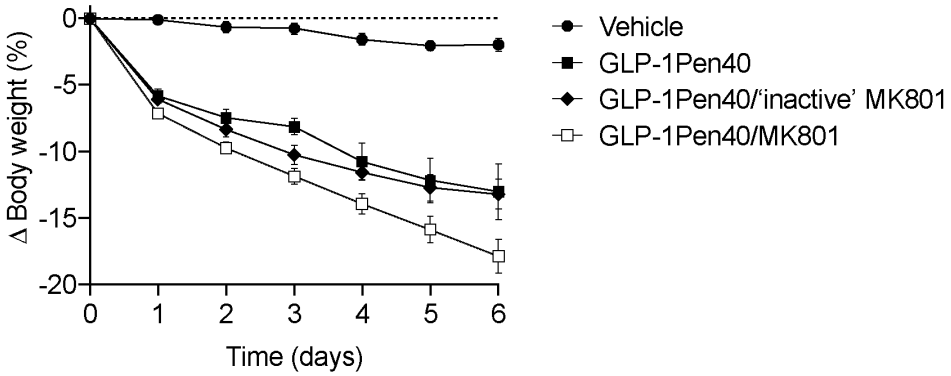


Fig. 24

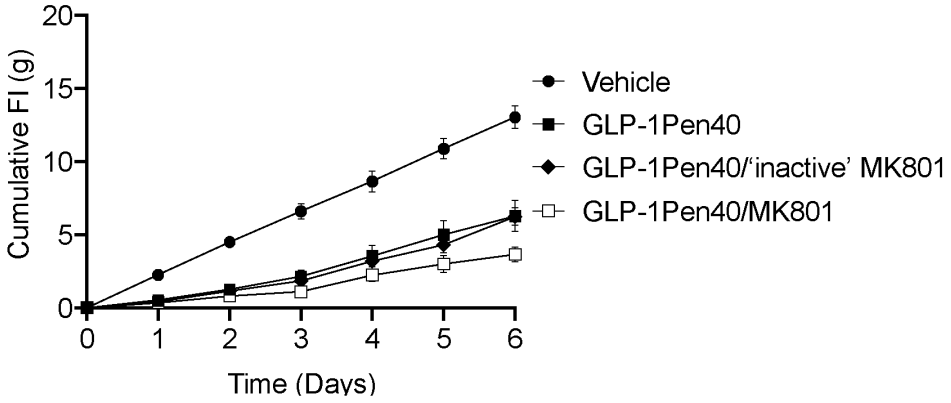


Fig. 25

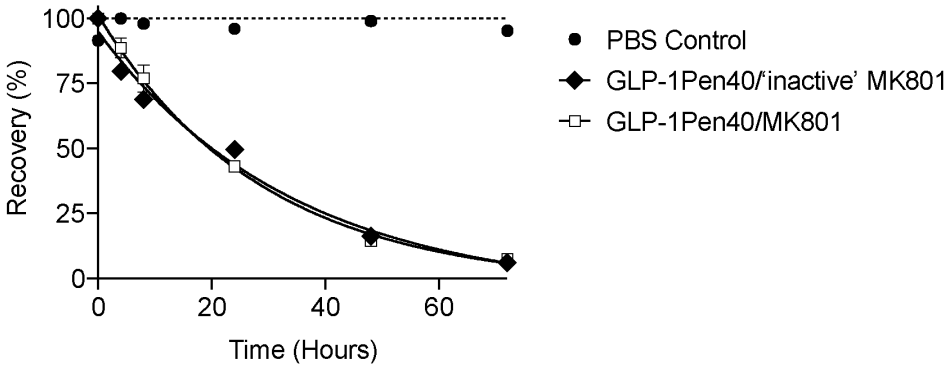


Fig. 26

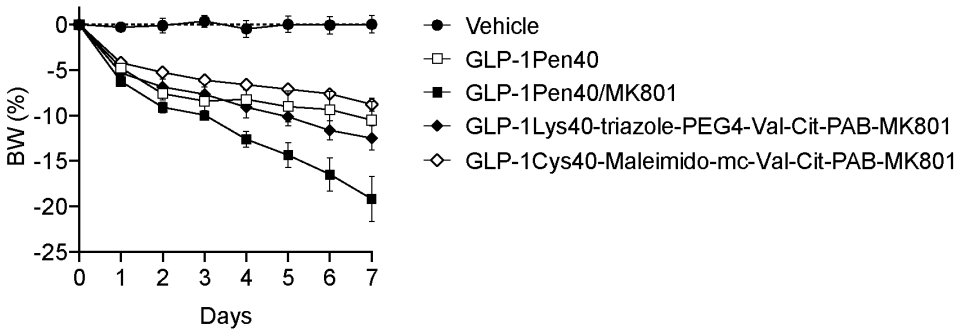

BW (%)
0
-5
-10
-15
-20
-25
0 1 2 3 4 5 6 7
Days
Vehicle
GLP-1Pen40
GLP-1Pen40/MK801
GLP-1Lys40-triazole-PEG4-Val-Cit-PAB-MK801
GLP-1Cys40-Maleimido-mc-Val-Cit-PAB-MK801

Fig. 27

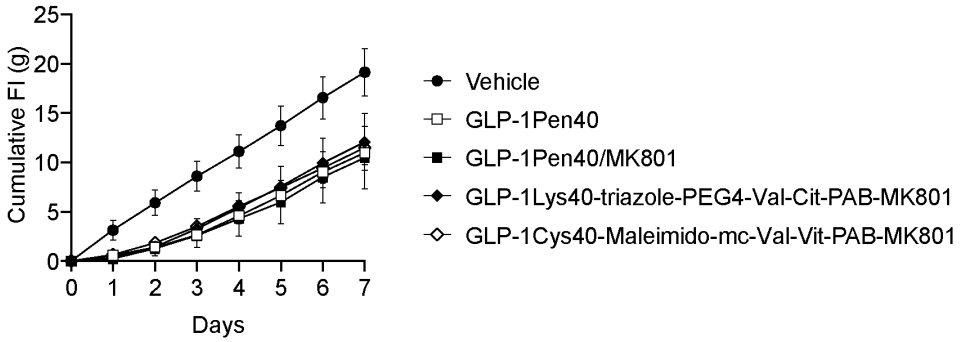

Cumulative FI (g)
25
20
15
10
5
0
0 1 2 3 4 5 6 7
Days
Vehicle
GLP-1Pen40
GLP-1Pen40/MK801
GLP-1Lys40-triazole-PEG4-Val-Cit-PAB-MK801
GLP-1Cys40-Maleimido-mc-Val-Vit-PAB-MK801

Fig. 28

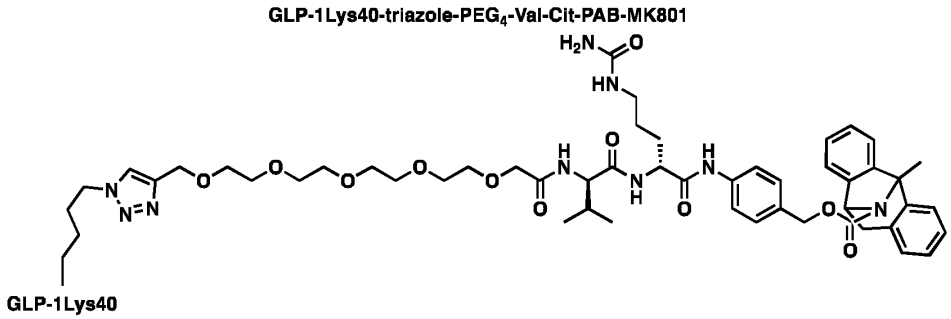

GLP-1Lys40-triazole-PEG4-Val-Cit-PAB-MK801
GLP-1Lys40

Fig. 29

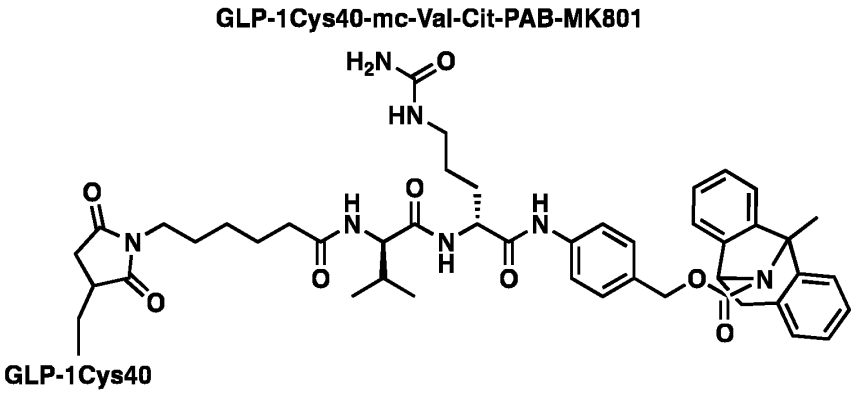

GLP-1Cys40-mc-Val-Cit-PAB-MK801
GLP-1Cys40

Fig. 30

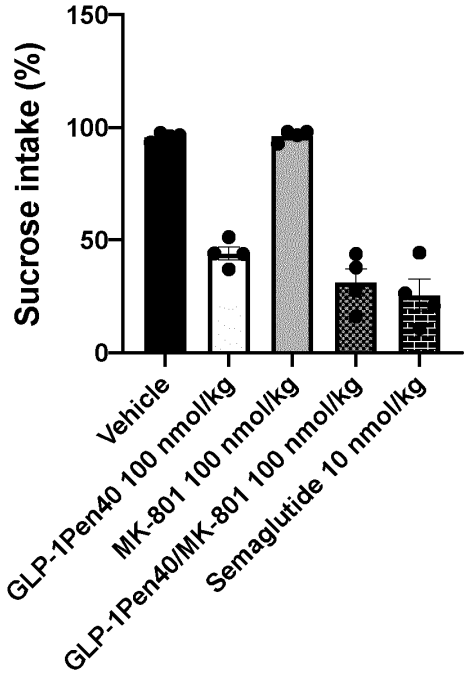

Sucrose intake (%)
150
100
50
0
Vehicle
GLP-1Pen40 100 nmol/kg
MK-801 100 nmol/kg
GLP-1Pen40/MK-801 100 nmol/kg
Semaglutide 10 nmol/kg

Fig. 31

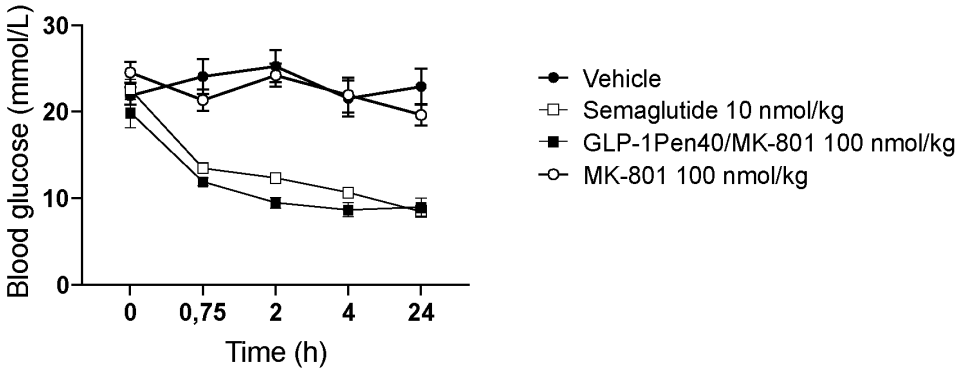

Blood glucose (mmol/L)
30
20
10
0
0
0,75
2
4
24
Time (h)
Vehicle
Semaglutide 10 nmol/kg
GLP-1Pen40/MK-801 100 nmol/kg
MK-801 100 nmol/kg

Fig. 32

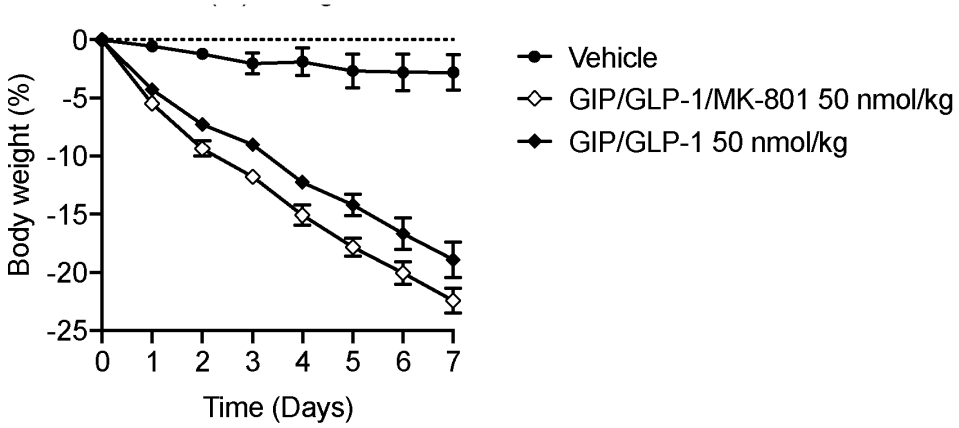


Fig. 33

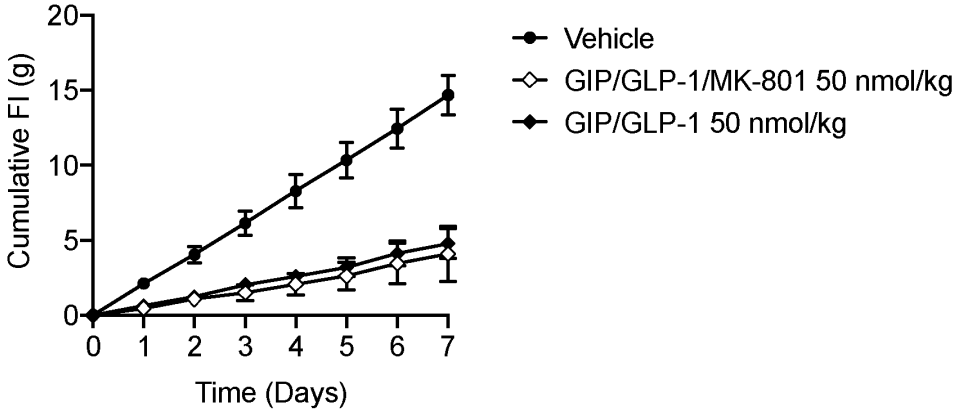


Fig. 34

GLP-1/GIPPen40/MK801 YX_1EGT FTSDY SIYLD KQAAX_1EFVNW LLAGG PSSGA PPPSX_2
GLP-1Pen40/MK801 HX_1EGT FTSDV SSYLE EQAAK EFIAW LVKGG PSSGA PPPSX_2

8 differential amino acids: 80% homology
Without the C_{ex} tail: 71% homology

Fig. 35

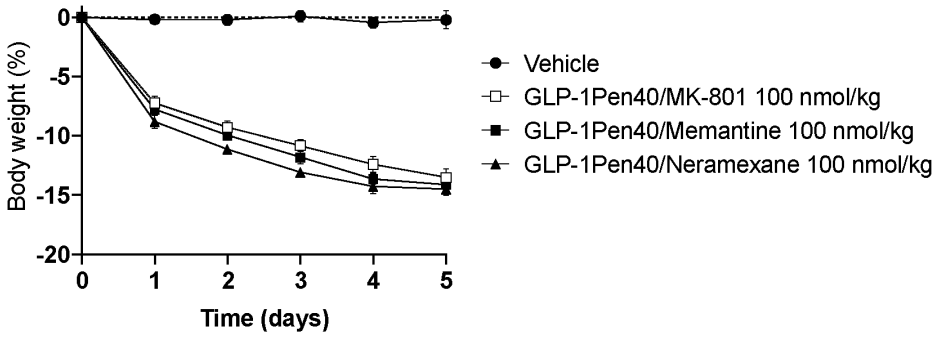


Fig. 36

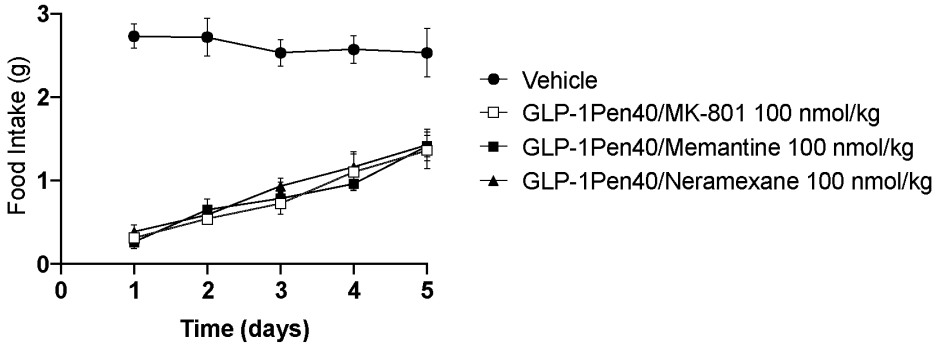


Fig. 37

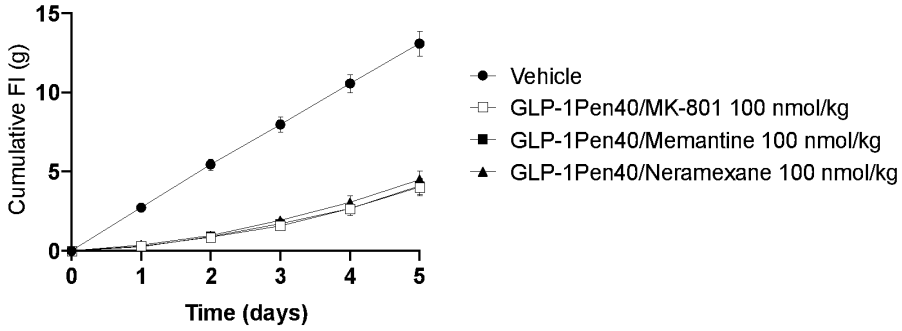


Fig. 38