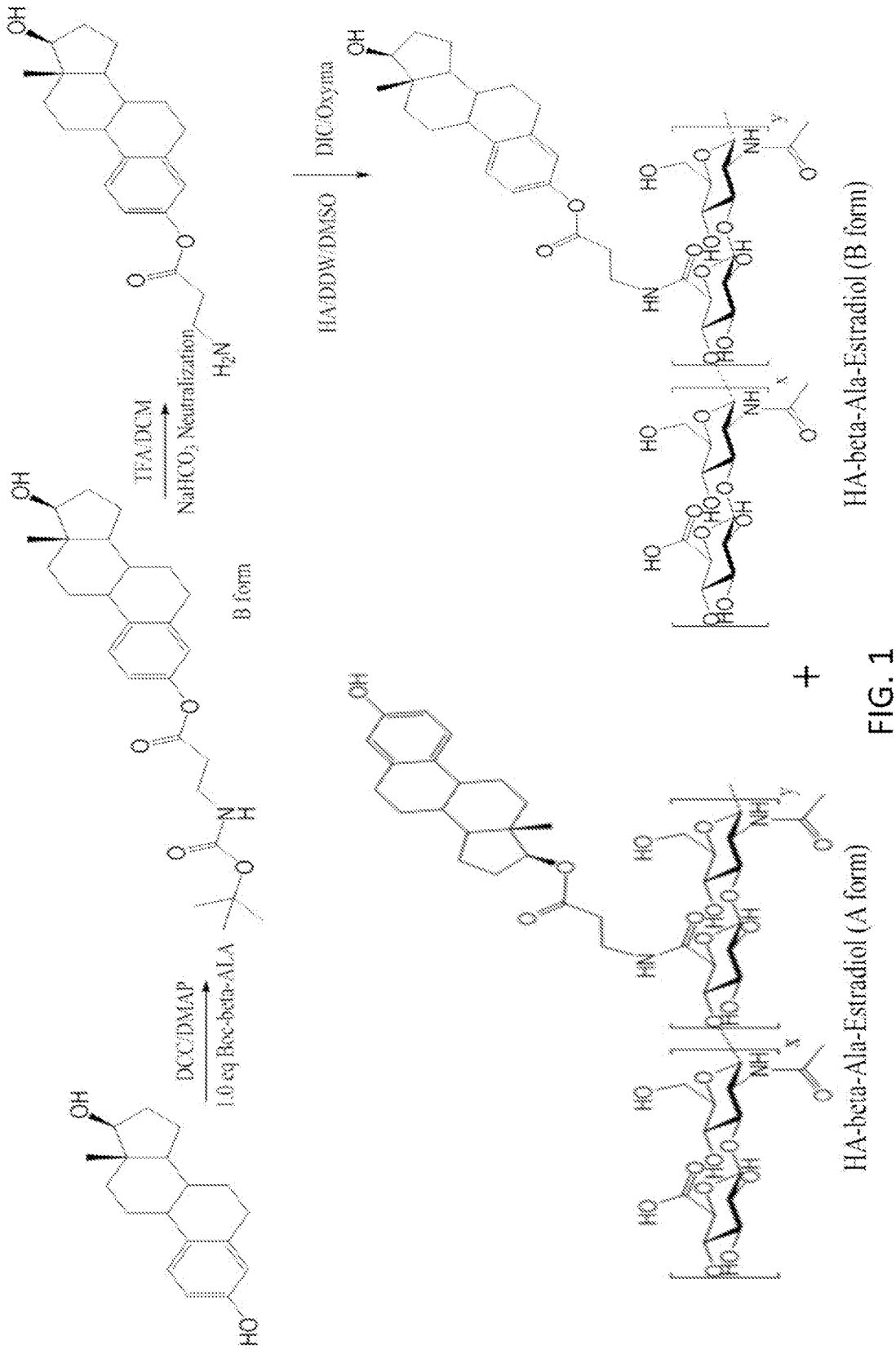

DCC/DMAP
1.0 eq Boc-beta-ALA
TFA/DCM
NaHCO3 Neutralization
B form
HADDW/DMSO
DIC/Oxyma
HA-beta-Ala-Estradiol (A form)
HA-beta-Ala-Estradiol (B form)

FIG. 1

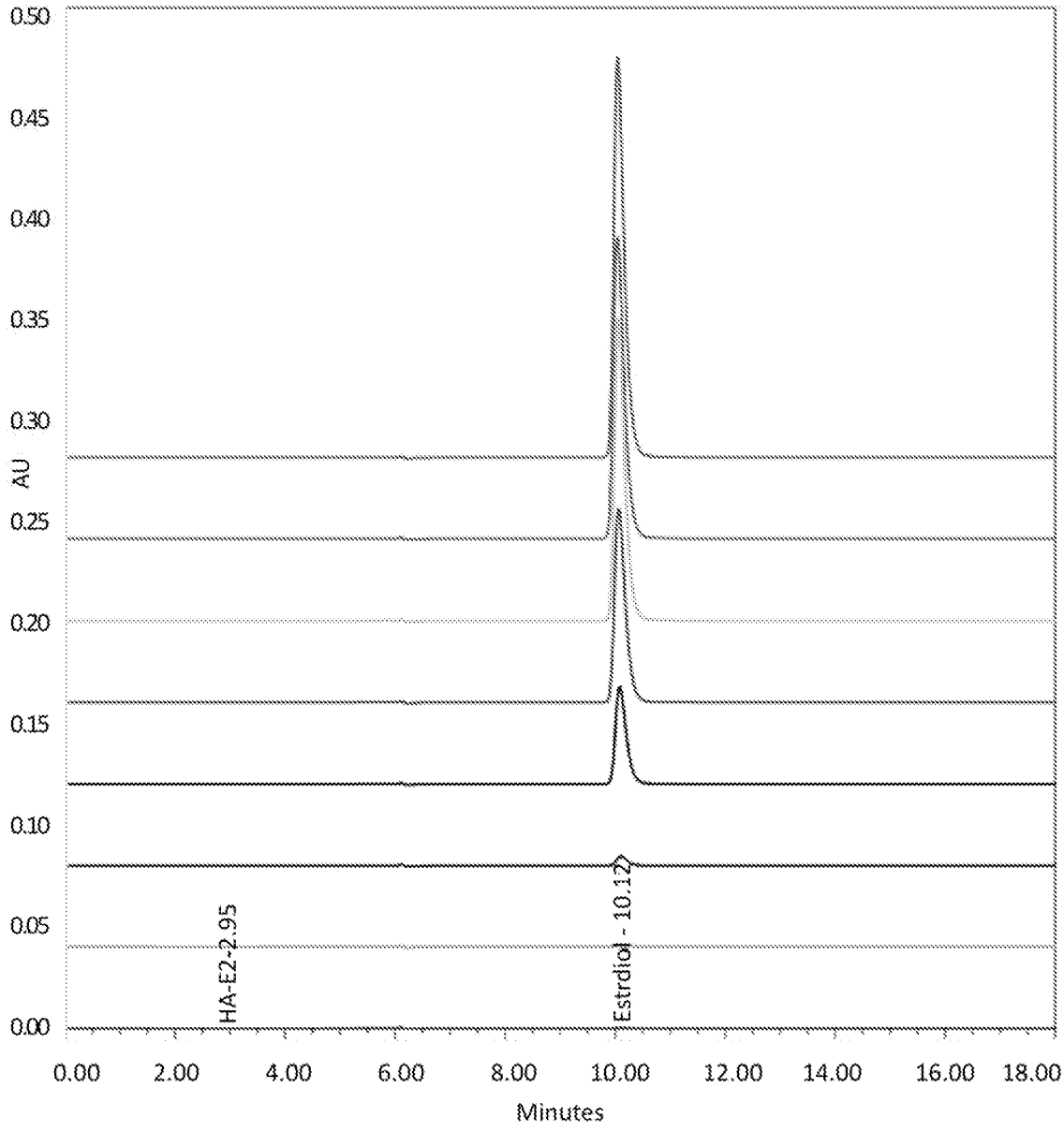

0.50
0.45
0.40
0.35
0.30
AU
0.25
0.20
0.15
0.10
0.05
0.00
HA-E2-2.95
Estrdiol - 10.12
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
Minutes

FIG. 2A

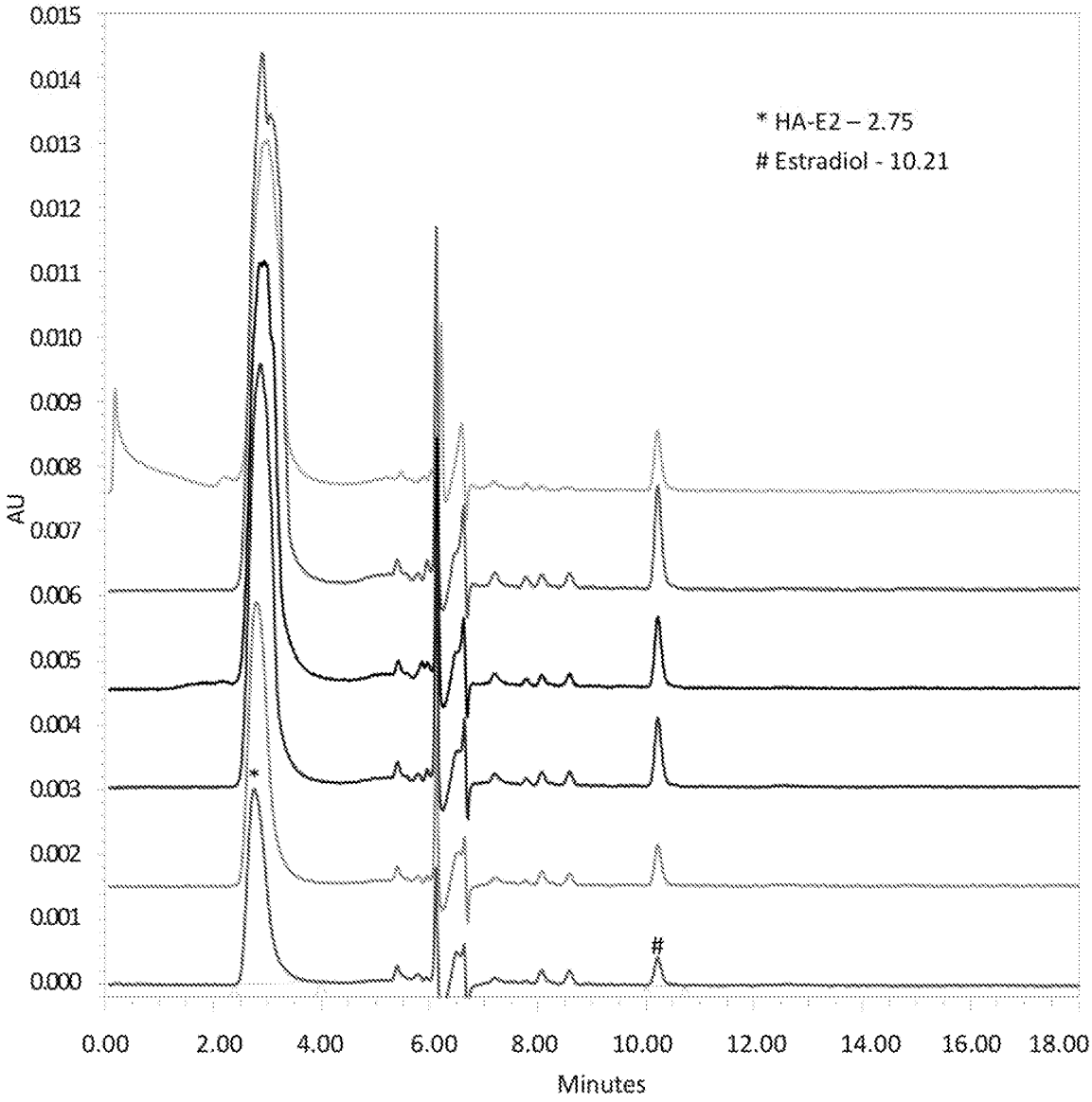

* HA-E2 – 2.75
# Estradiol - 10.21
AU
0.015
0.014
0.013
0.012
0.011
0.010
0.009
0.008
0.007
0.006
0.005
0.004
0.003
0.002
0.001
0.000
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
Minutes

FIG. 2B

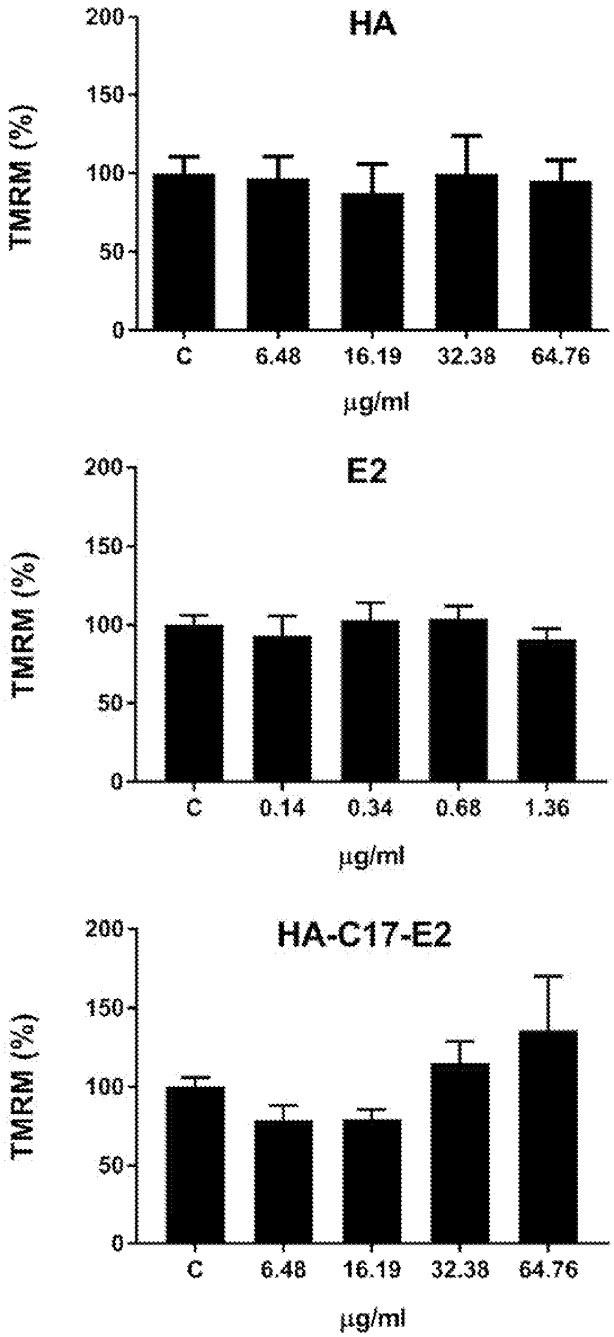

HA
TMRM (%)
200
150
100
50
0
C
6.48
16.19
32.38
64.76
µg/ml
E2
TMRM (%)
200
150
100
50
0
C
0.14
0.34
0.68
1.36
µg/ml
HA-C17-E2
TMRM (%)
200
150
100
50
0
C
6.48
16.19
32.38
64.76
µg/ml

FIG. 3

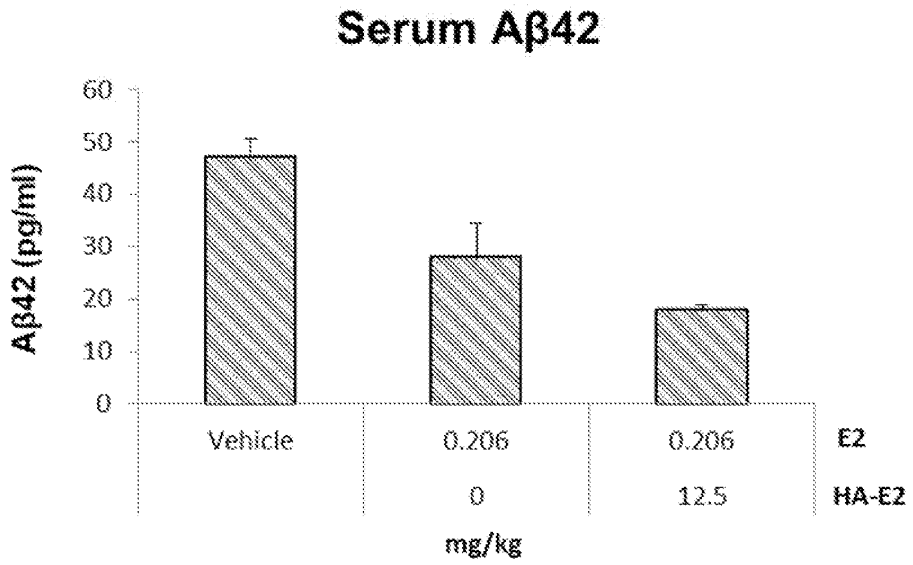

Serum Aβ42
Aβ42 (pg/ml)
60
50
40
30
20
10
0
Vehicle
0.206
0
0.206
12.5
E2
HA-E2
mg/kg

FIG. 4A

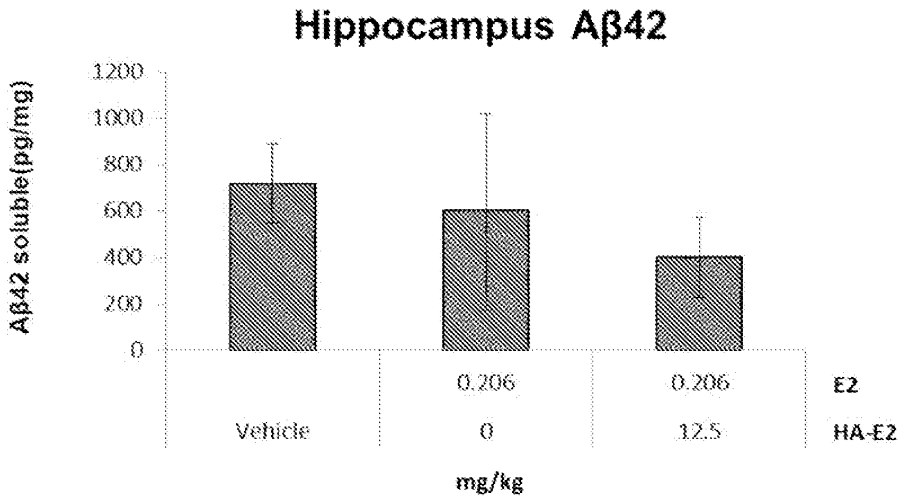

Hippocampus Aβ42
Aβ42 soluble(pg/mg)
1200
1000
800
600
400
200
0
Vehicle
0.206
0
0.206
12.5
E2
HA-E2
mg/kg

FIG. 4B

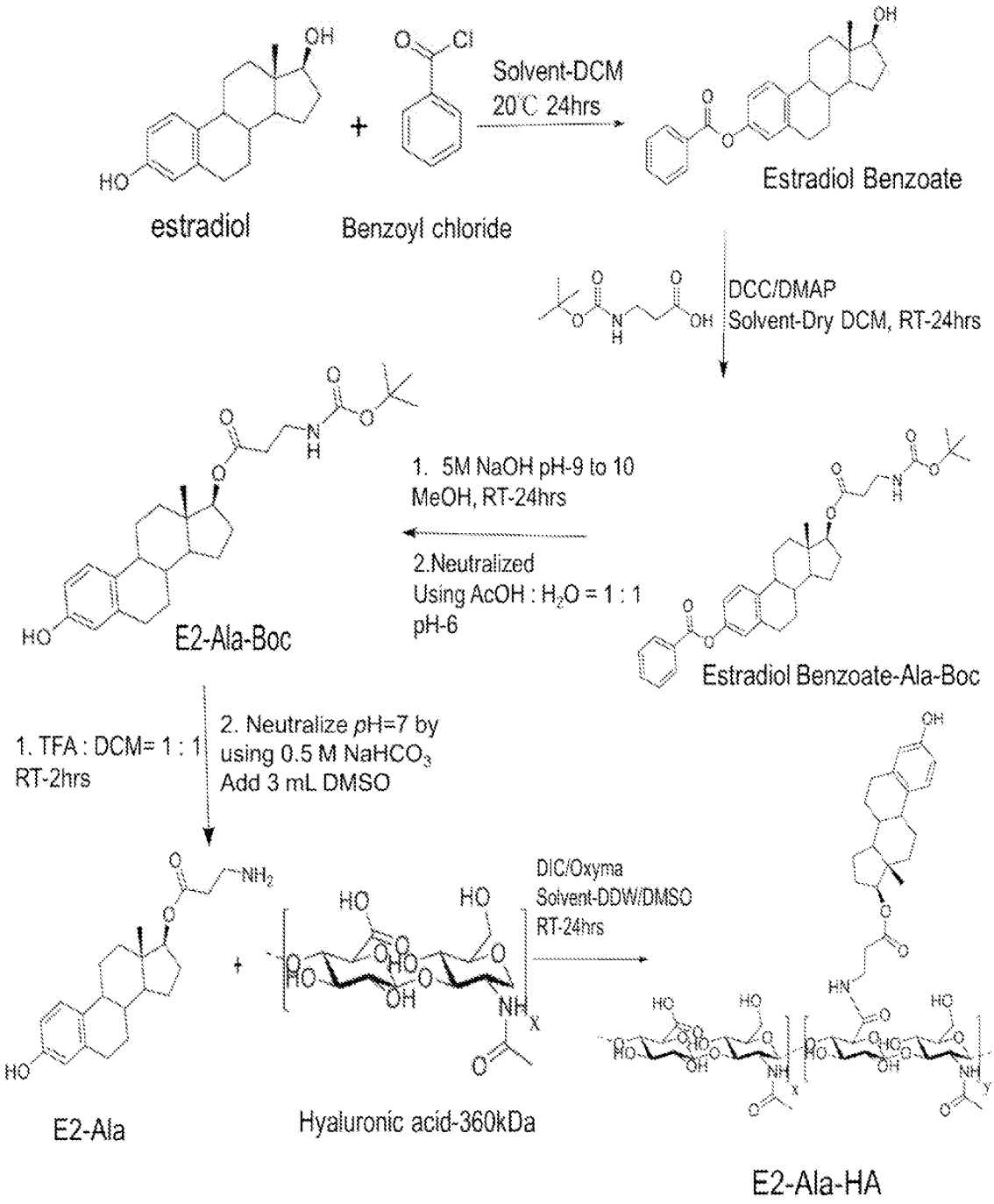

estradiol
Benzoyl chloride
Solvent-DCM
20℃ 24hrs
Estradiol Benzoate
DCC/DMAP
Solvent-Dry DCM, RT-24hrs
1. 5M NaOH pH-9 to 10
MeOH, RT-24hrs
2.Neutralized
Using AcOH : H2O = 1 : 1
pH-6
E2-Ala-Boc
Estradiol Benzoate-Ala-Boc
1. TFA : DCM= 1 : 1
RT-2hrs
2. Neutralize pH=7 by
using 0.5 M NaHCO3
Add 3 mL DMSO
DIC/Oxyma
Solvent-DDW/DMSO
RT-24hrs
E2-Ala
Hyaluronic acid-360kDa
E2-Ala-HA

FIG. 5

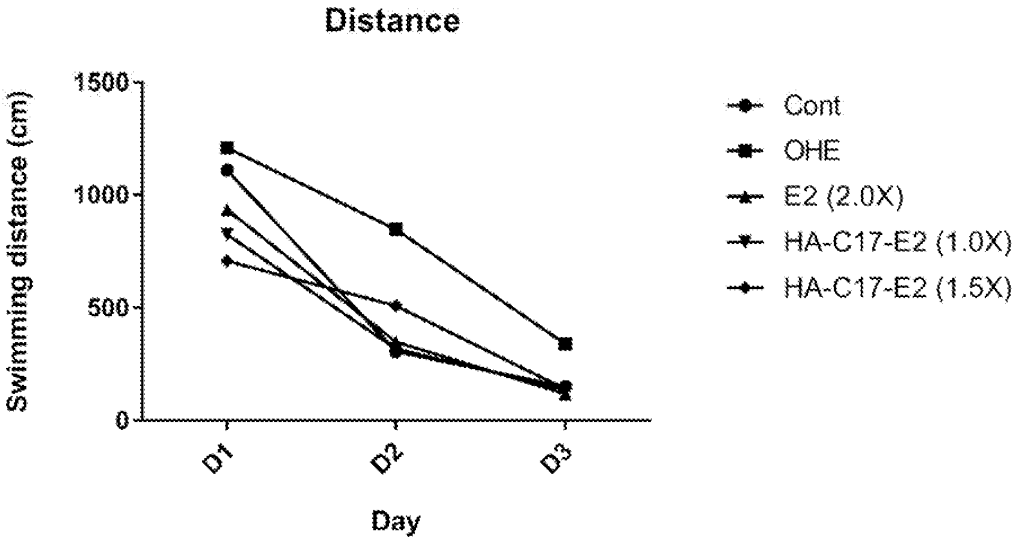

Distance
Swimming distance (cm)
1500
1000
500
0
D1
D2
D3
Day
Cont
OHE
E2 (2.0X)
HA-C17-E2 (1.0X)
HA-C17-E2 (1.5X)

FIG. 6A

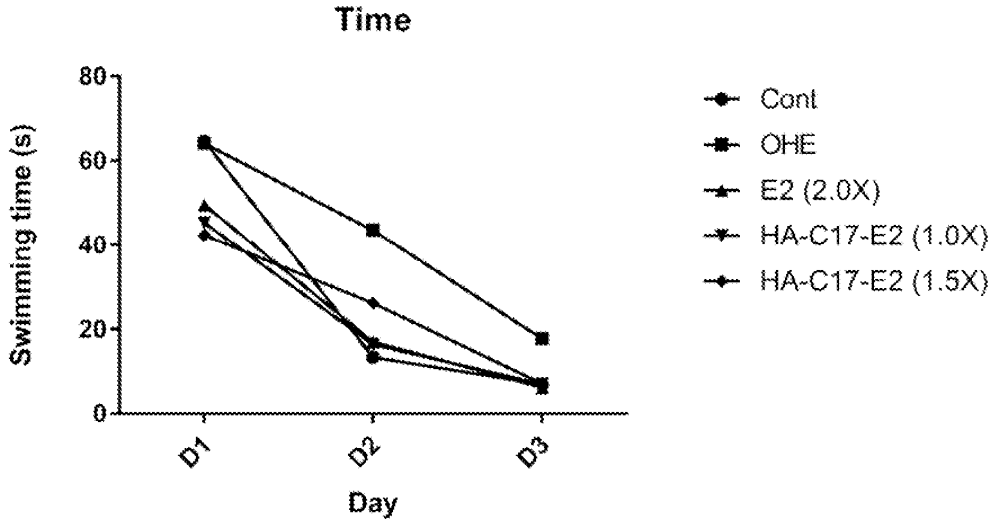

Time
Swimming time (s)
80
60
40
20
0
D1
D2
D3
Day
Cont
OHE
E2 (2.0X)
HA-C17-E2 (1.0X)
HA-C17-E2 (1.5X)

FIG. 6B

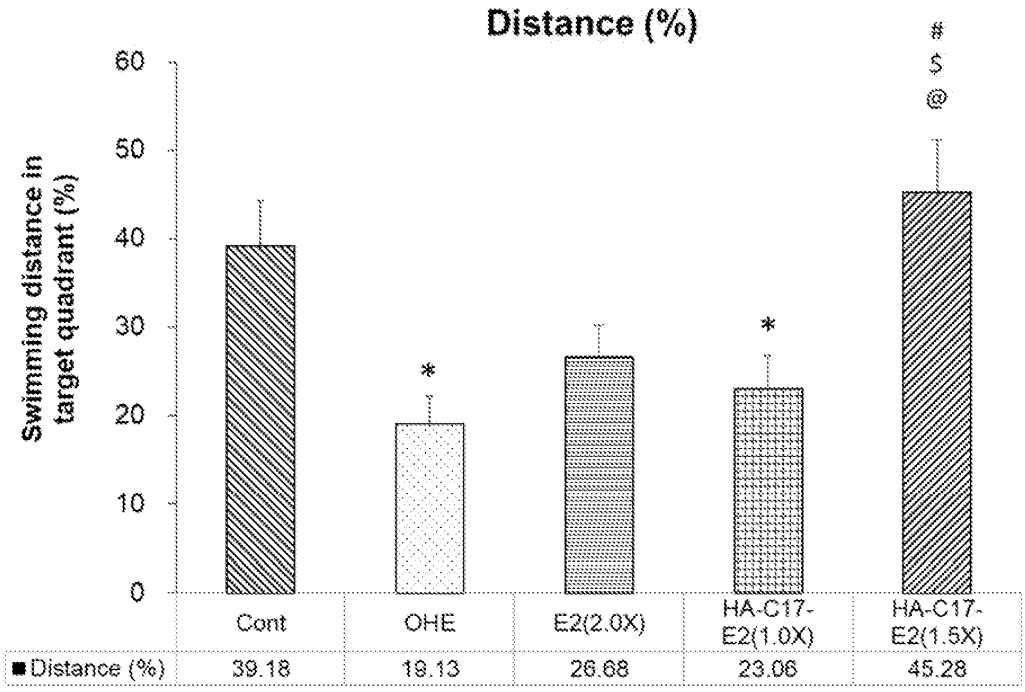

Distance (%)
Swimming distance in target quadrant (%)
60
50
40
30
20
10
0
*
*
#
$
@
Cont
OHE
E2(2.0X)
HA-C17-E2(1.0X)
HA-C17-E2(1.5X)
Distance (%)
39.18
19.13
26.68
23.06
45.28

FIG. 7A

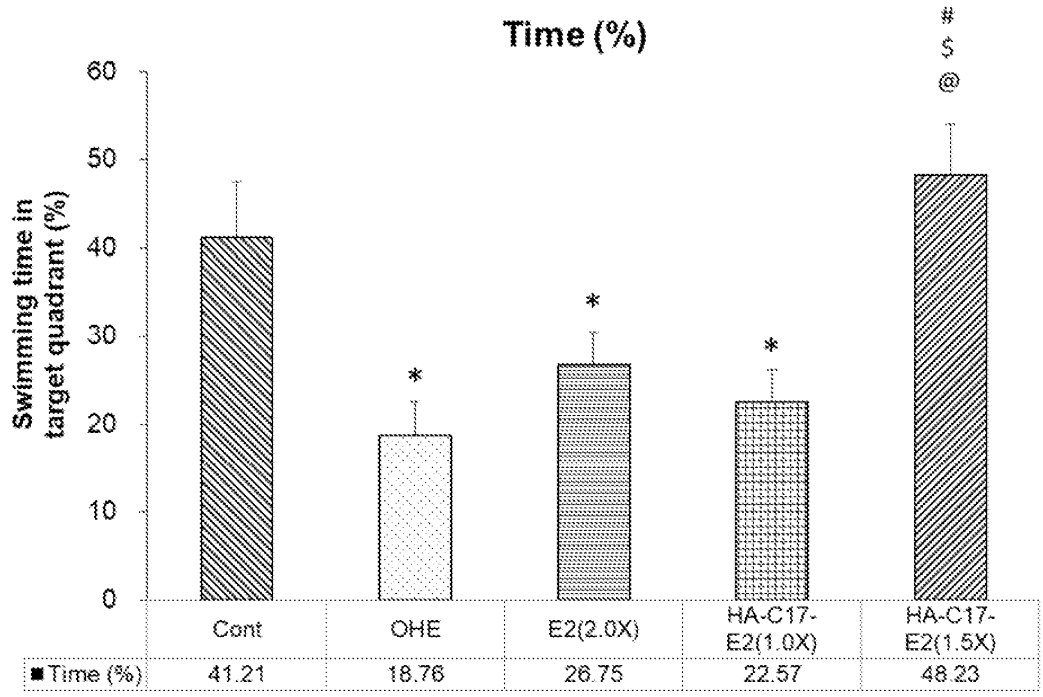

Time (%)
Swimming time in target quadrant (%)
60
50
40
30
20
10
0
*
*
*
#
$
@
Cont
OHE
E2(2.0X)
HA-C17-E2(1.0X)
HA-C17-E2(1.5X)
Time (%)
41.21
18.76
26.75
22.57
48.23

FIG. 7B

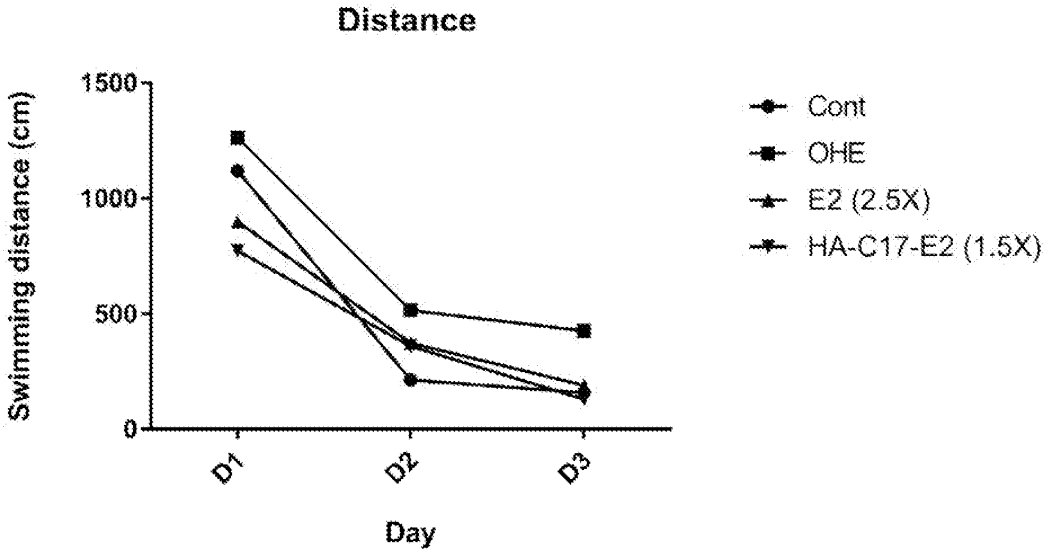

Distance
Swimming distance (cm)
1500
1000
500
0
D1
D2
D3
Day
Cont
OHE
E2 (2.5X)
HA-C17-E2 (1.5X)

FIG. 8A

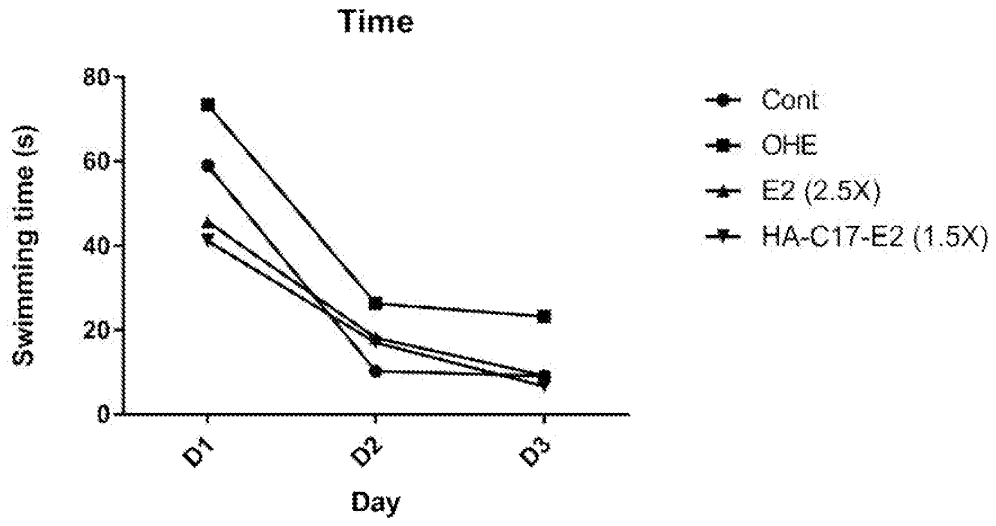

Time
Swimming time (s)
80
60
40
20
0
D1
D2
D3
Day
Cont
OHE
E2 (2.5X)
HA-C17-E2 (1.5X)

FIG. 8B

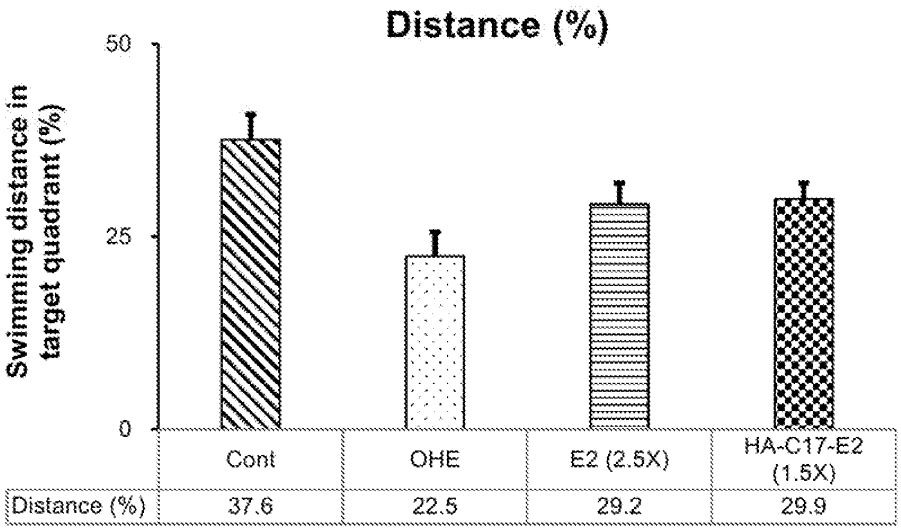

Distance (%)
Swimming distance in target quadrant (%)
50
25
0
Cont
OHE
E2 (2.5X)
HA-C17-E2 (1.5X)
Distance (%)
37.6
22.5
29.2
29.9

FIG. 9A

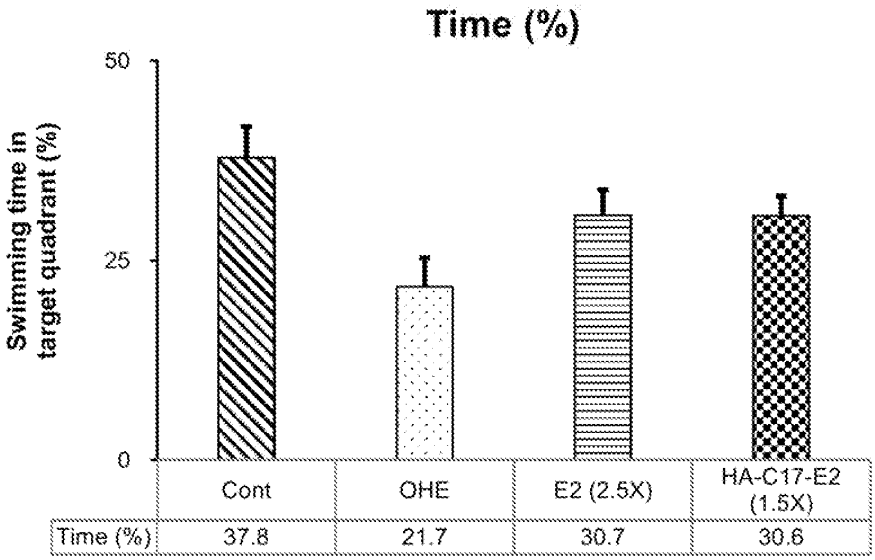

Time (%)
Swimming time in target quadrant (%)
50
25
0
Cont
OHE
E2 (2.5X)
HA-C17-E2 (1.5X)
Time (%)
37.8
21.7
30.7
30.6

FIG. 9B

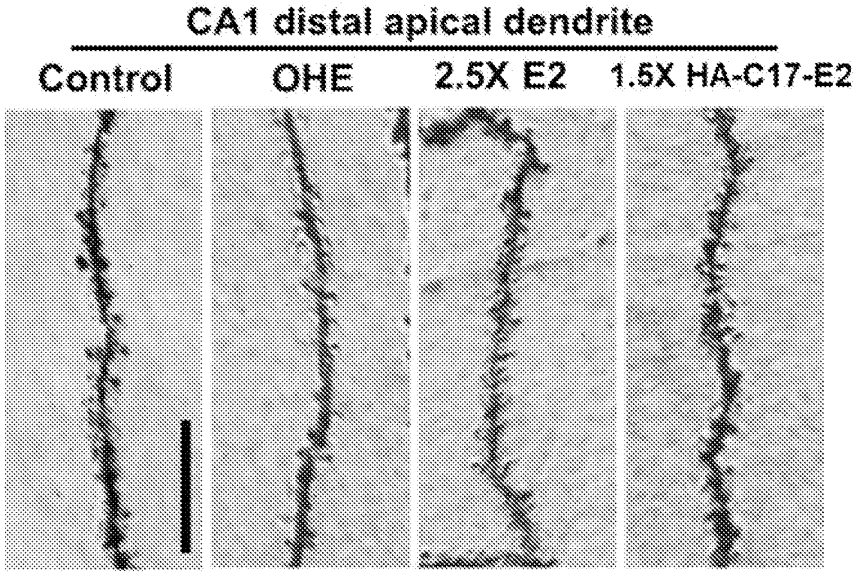


FIG. 10A

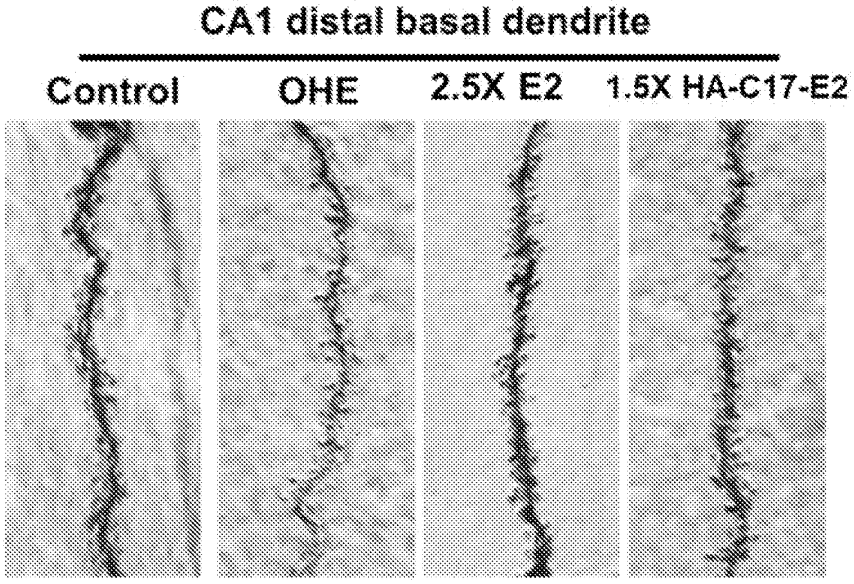


FIG. 10B

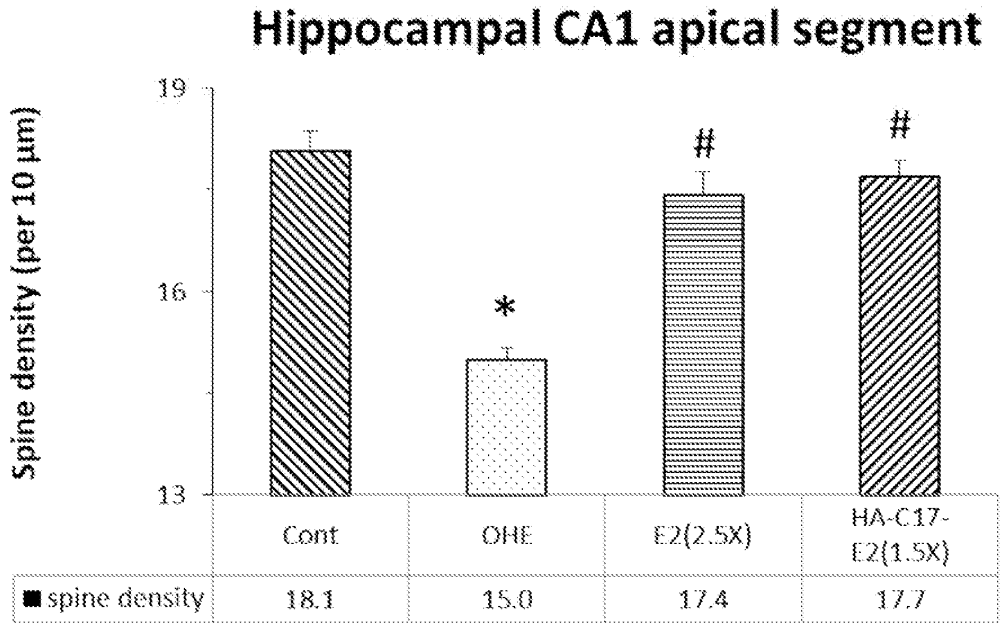


FIG. 11A

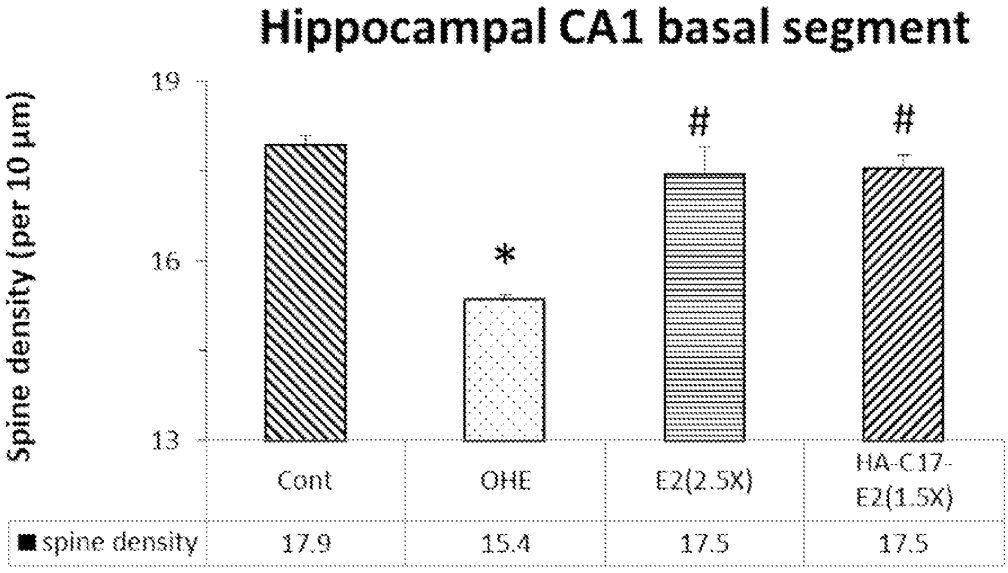


FIG. 11B

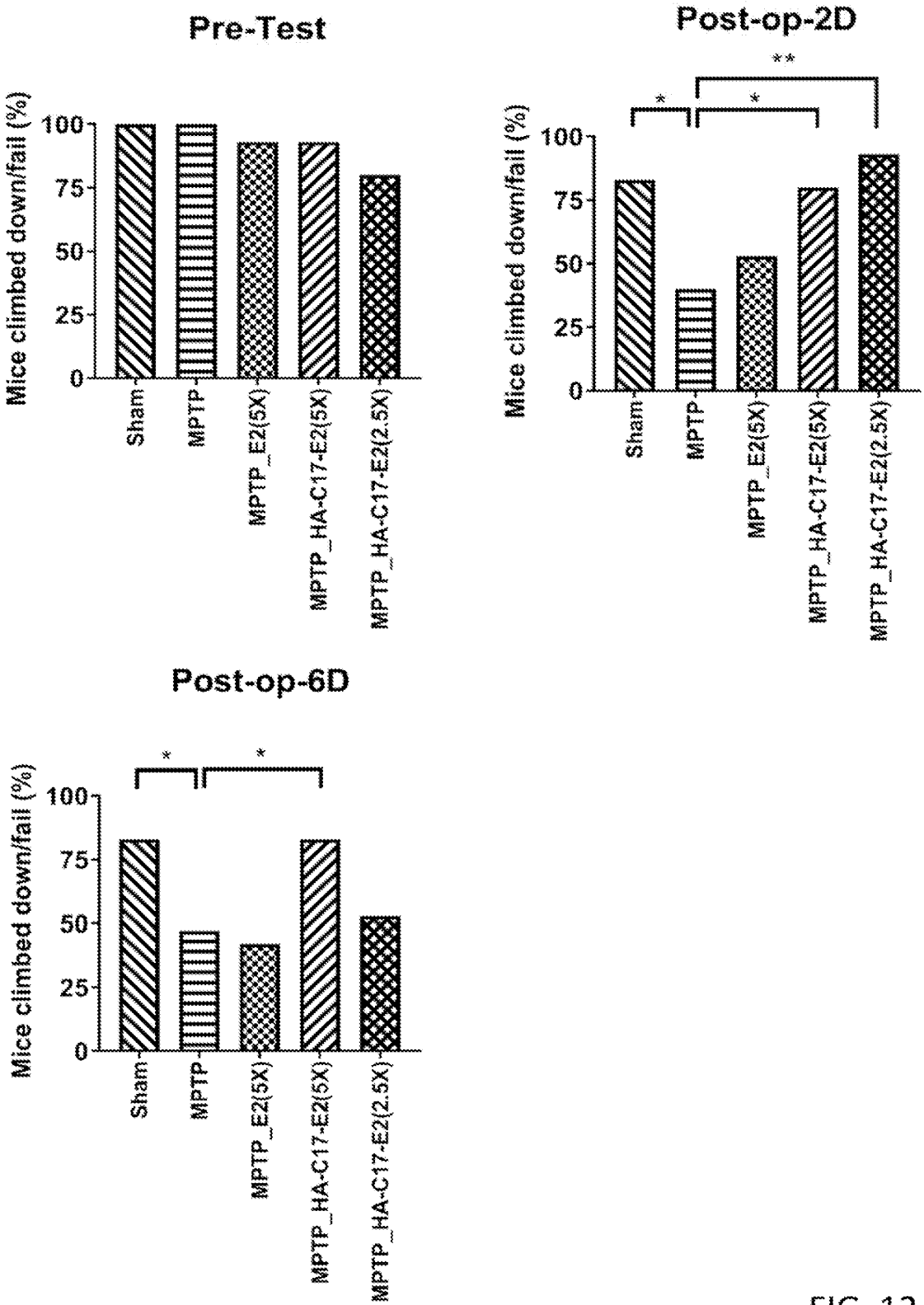

Pre-Test
Mice climbed down/fail (%)
100
75
50
25
0
Sham
MPTP
MPTP_E2(5X)
MPTP_HA-C17-E2(5X)
MPTP_HA-C17-E2(2.5X)
Post-op-2D
**
*
*
Mice climbed down/fail (%)
100
75
50
25
0
Sham
MPTP
MPTP_E2(5X)
MPTP_HA-C17-E2(5X)
MPTP_HA-C17-E2(2.5X)
Post-op-6D
*
*
Mice climbed down/fail (%)
100
75
50
25
0
Sham
MPTP
MPTP_E2(5X)
MPTP_HA-C17-E2(5X)
MPTP_HA-C17-E2(2.5X)

FIG. 12