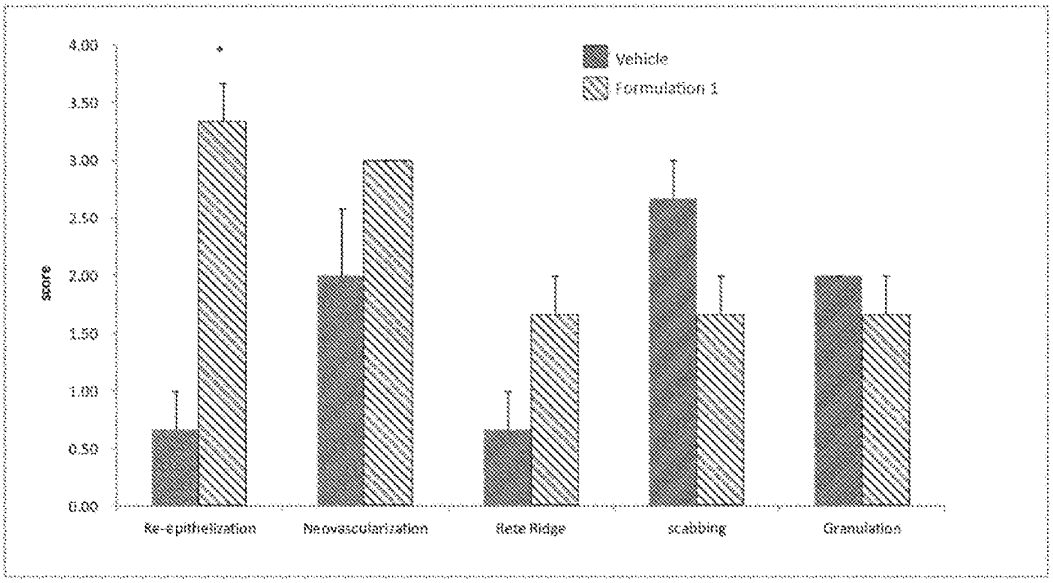

4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
score
Vehicle
Formulation 1
Re-epithelization
Neovascularization
Rete Ridge
scabbing
Granulation

FIG. 1

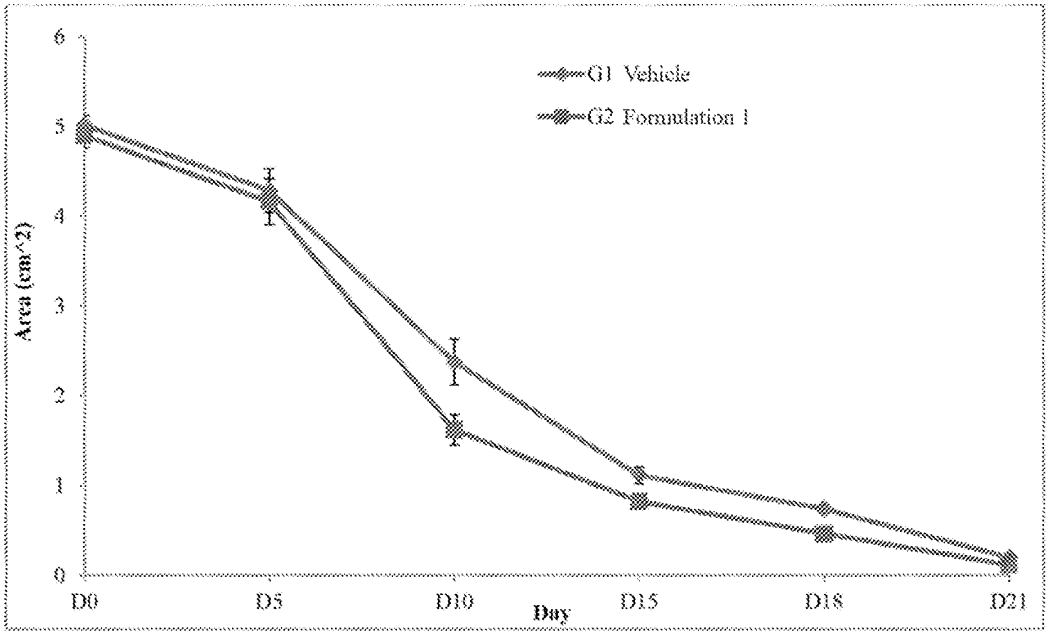

6
5
4
3
2
1
0
Area (cm^2)
G1 Vehicle
G2 Formulation 1
D0
D5
D10
D15
D18
D21
Day

FIG. 2

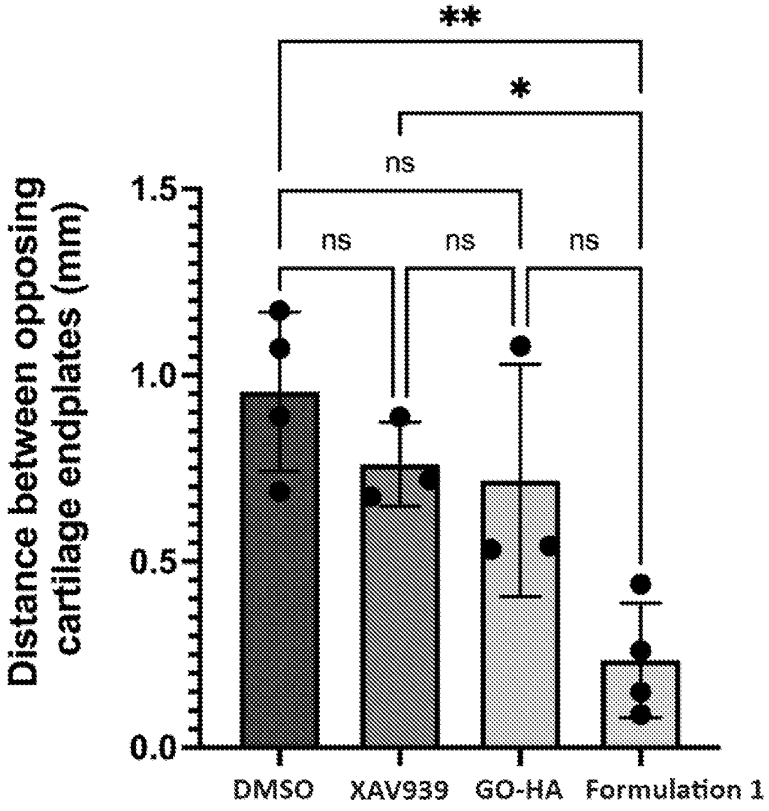

**
*
ns
ns
ns
ns
Distance between opposing cartilage endplates (mm)
1.5
1.0
0.5
0.0
DMSO
XAV939
GO-HA
Formulation 1

FIG. 3

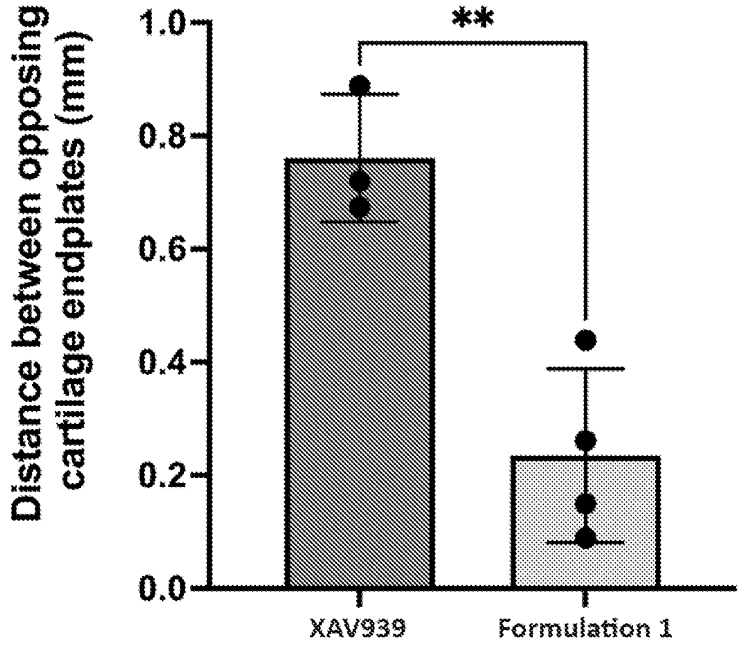

Distance between opposing cartilage endplates (mm)
1.0
0.8
0.6
0.4
0.2
0.0
**
XAV939
Formulation 1

FIG. 4

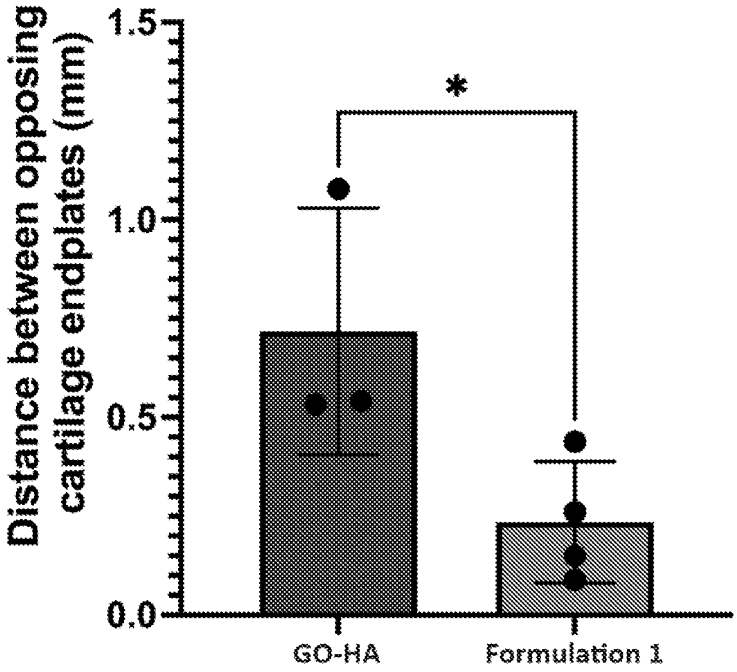

Distance between opposing cartilage endplates (mm)
1.5
1.0
0.5
0.0
*
GO-HA
Formulation 1

FIG. 5

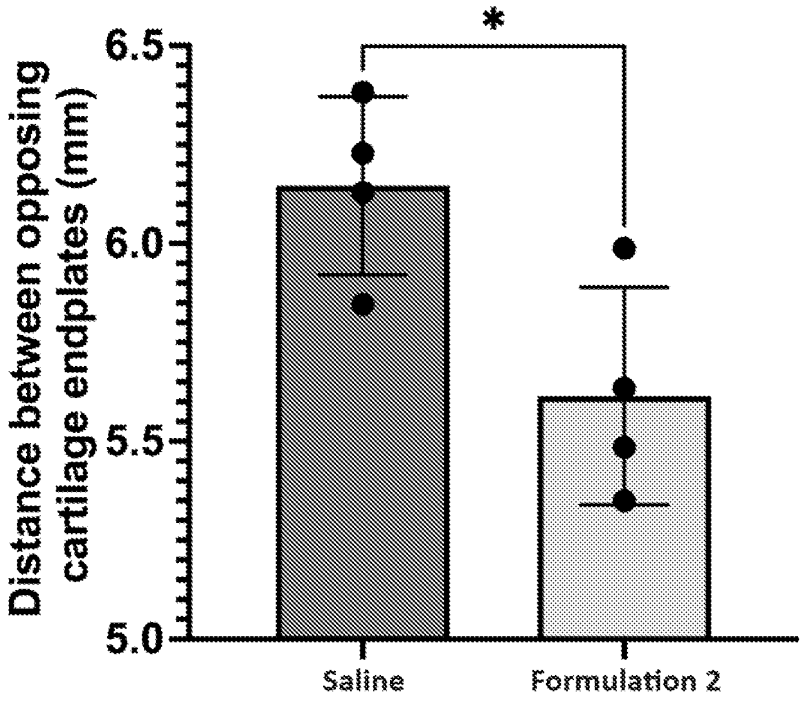

*
Distance between opposing cartilage endplates (mm)
6.5
6.0
5.5
5.0
Saline
Formulation 2

FIG. 6

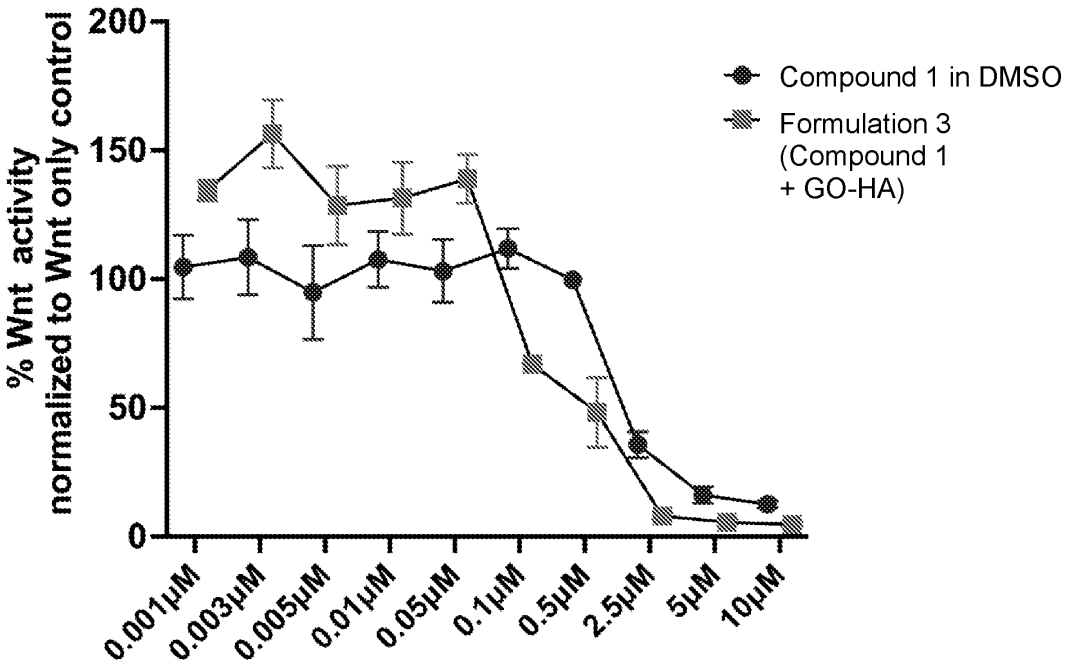

% Wnt activity
normalized to Wnt only control
200
150
100
50
0
0.001μM
0.003μM
0.005μM
0.01μM
0.05μM
0.1μM
0.5μM
2.5μM
5μM
10μM
Compound 1 in DMSO
Formulation 3
(Compound 1
+ GO-HA)

FIG. 7

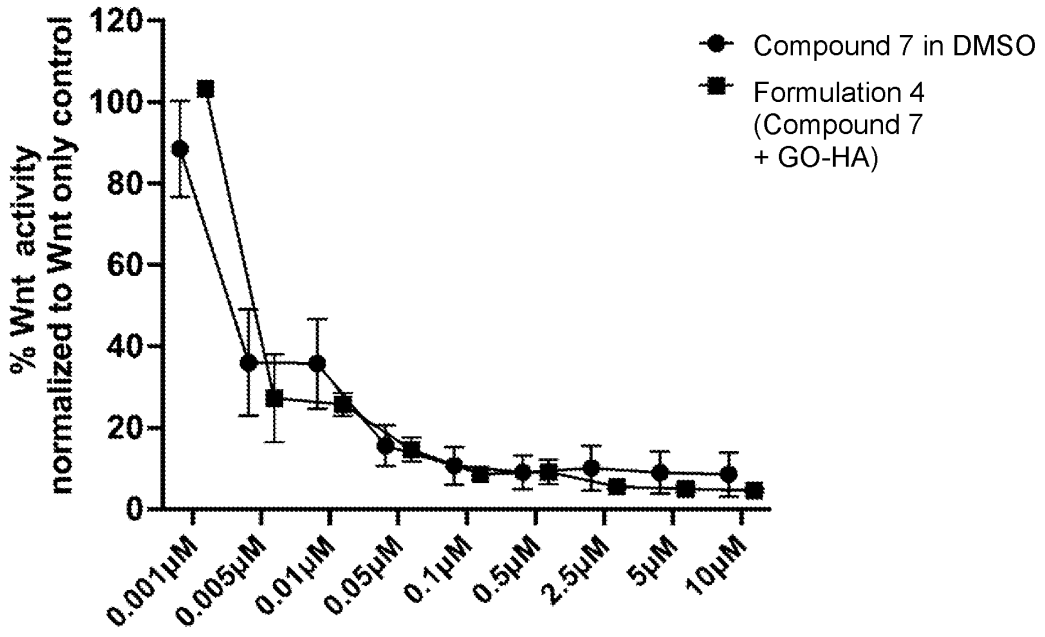

% Wnt activity
normalized to Wnt only control
120
100
80
60
40
20
0
0.001μM
0.005μM
0.01μM
0.05μM
0.1μM
0.5μM
2.5μM
5μM
10μM
Compound 7 in DMSO
Formulation 4
(Compound 7
+ GO-HA)

FIG. 8

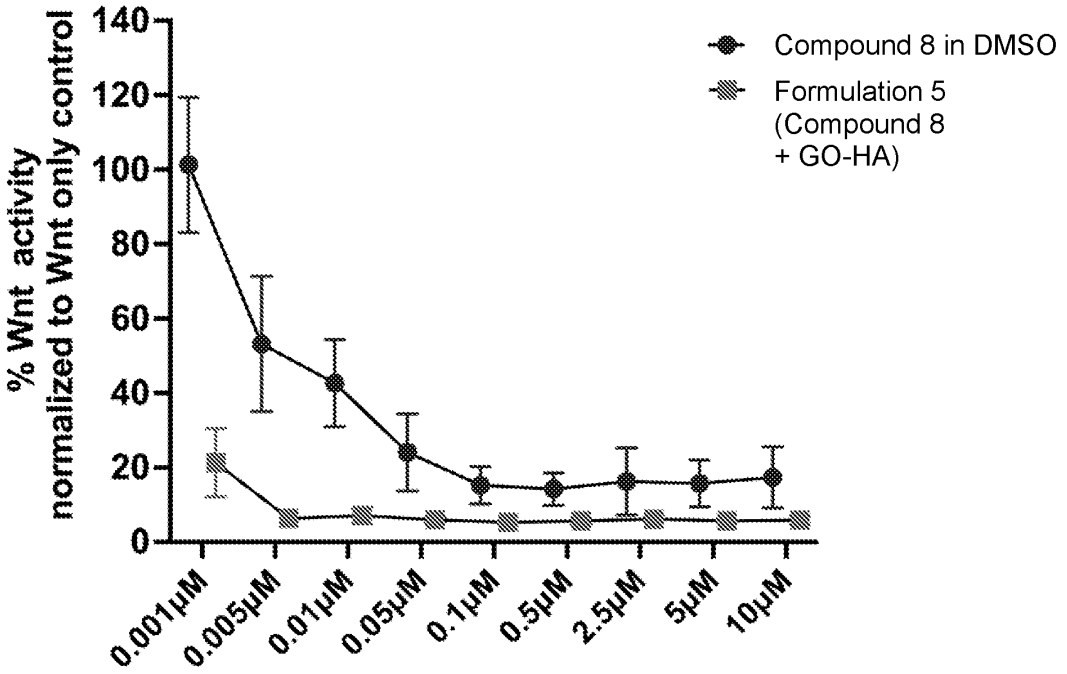

% Wnt activity
normalized to Wnt only control
140
120
100
80
60
40
20
0
0.001μM
0.005μM
0.01μM
0.05μM
0.1μM
0.5μM
2.5μM
5μM
10μM
Compound 8 in DMSO
Formulation 5
(Compound 8
+ GO-HA)

FIG. 9

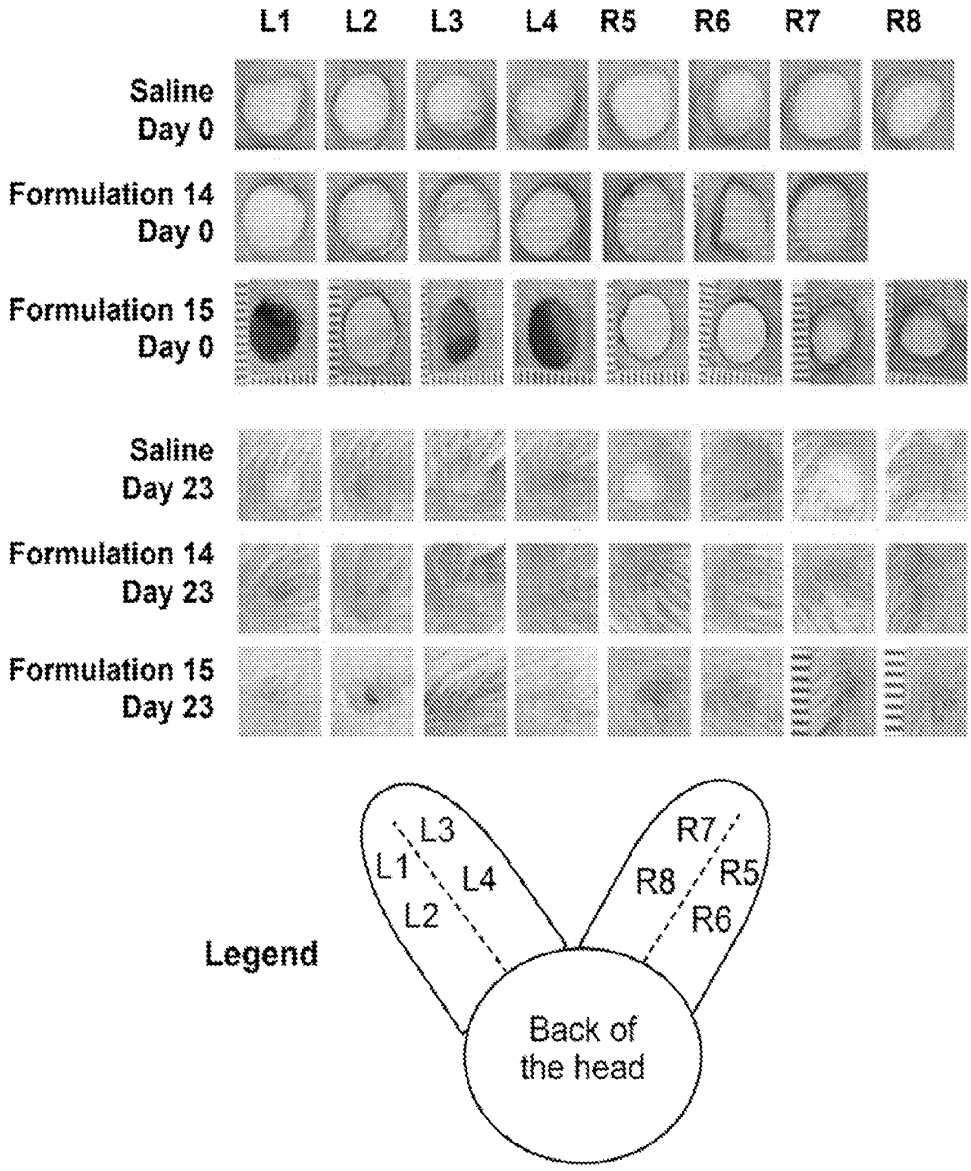

L1
L2
L3
L4
R5
R6
R7
R8
Saline Day 0
Formulation 14 Day 0
Formulation 15 Day 0
Saline Day 23
Formulation 14 Day 23
Formulation 15 Day 23
Legend
L3
L1
L4
L2
R7
R8
R5
R6
Back of the head

FIG. 10

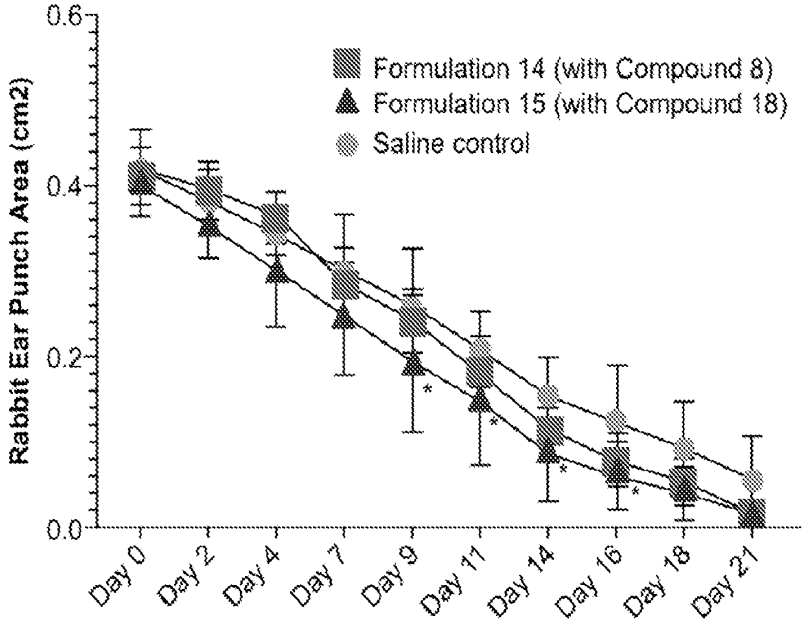


FIG. 11A

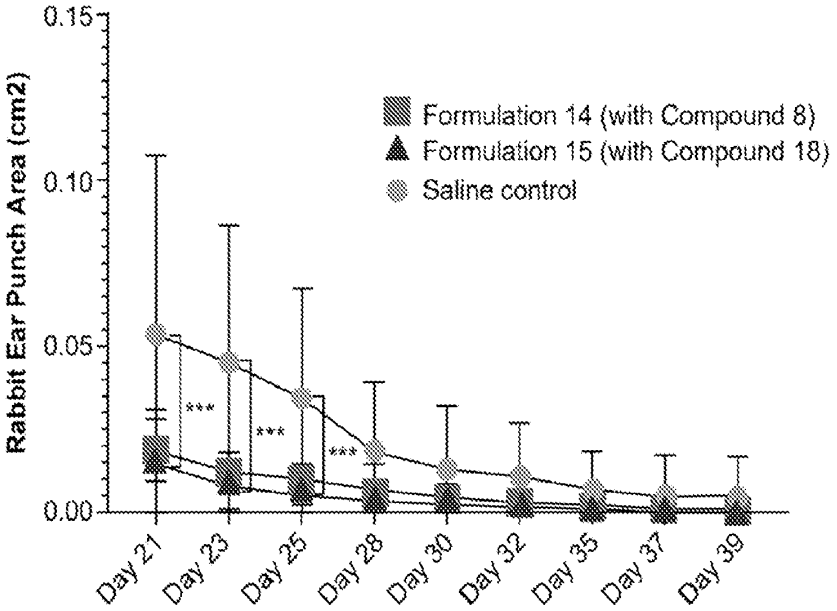


FIG. 11B

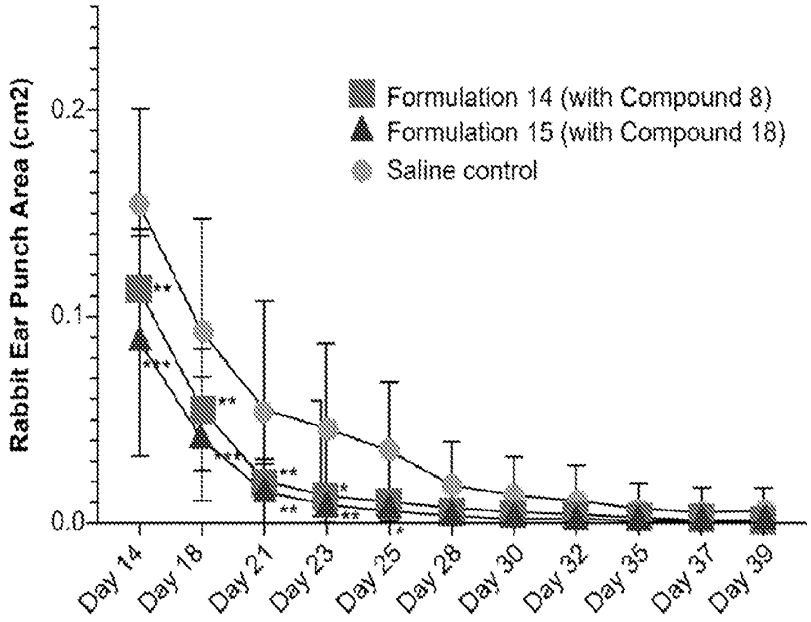

Rabbit Ear Punch Area (cm2)
0.2
0.1
0.0
Formulation 14 (with Compound 8)
Formulation 15 (with Compound 18)
Saline control
Day 14
Day 18
Day 21
Day 23
Day 25
Day 28
Day 30
Day 32
Day 35
Day 37
Day 39

FIG. 12

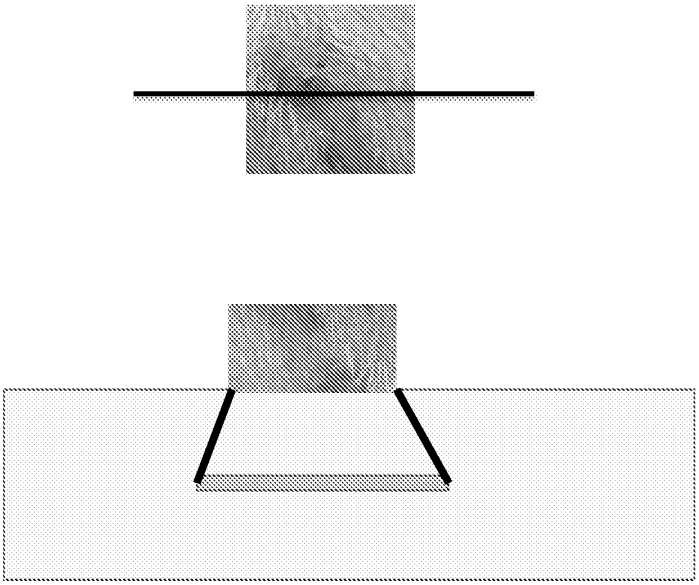


FIG. 13

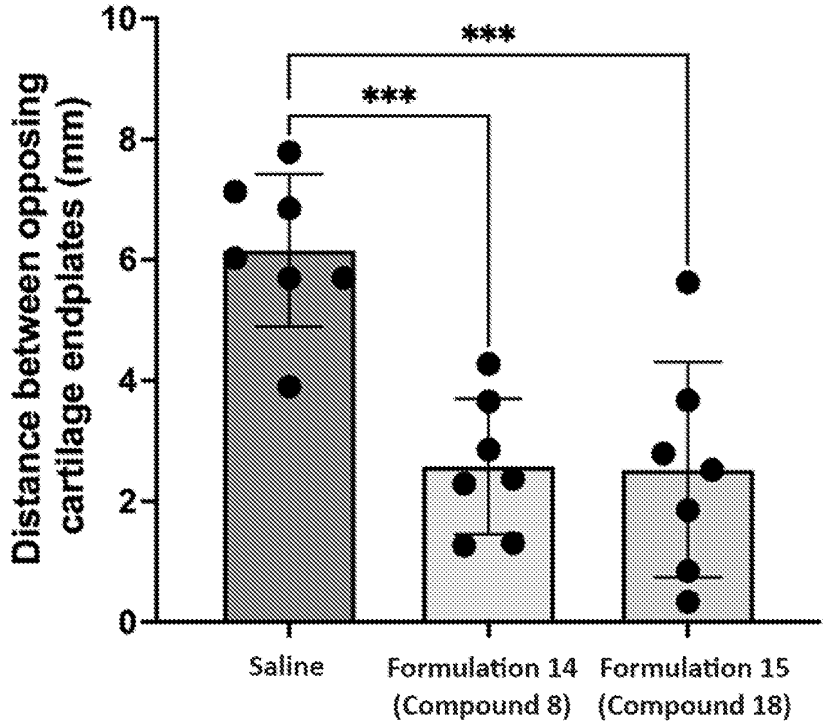
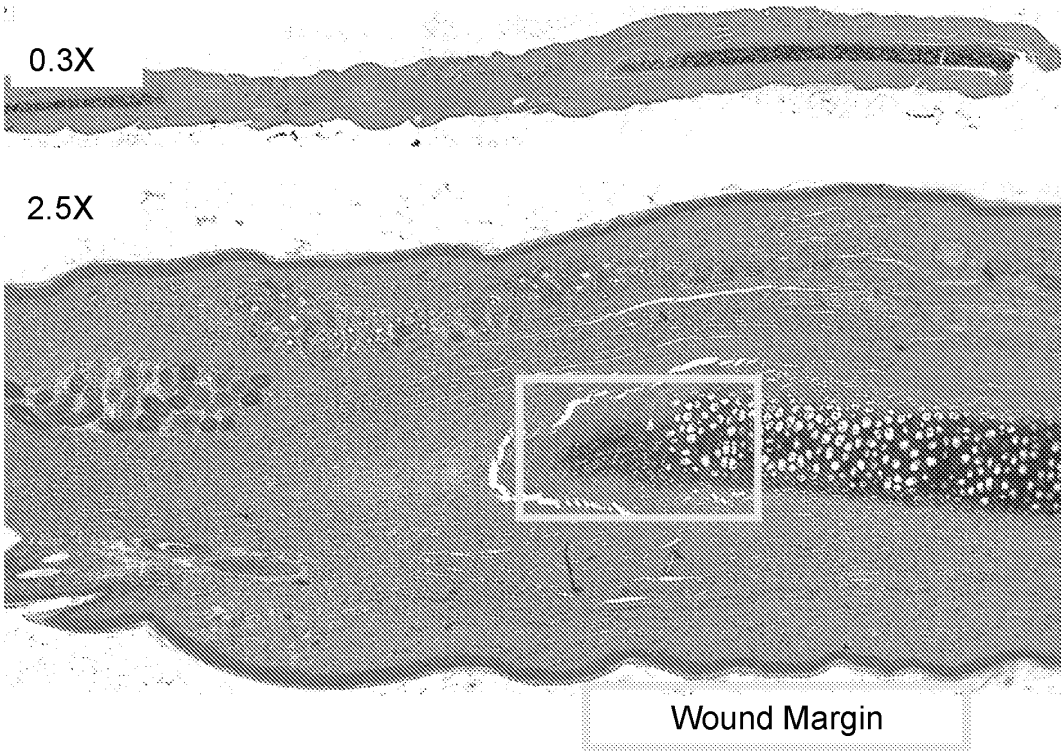

Distance between opposing cartilage endplates (mm)
10
8
6
4
2
0
***
***
Saline
Formulation 14 (Compound 8)
Formulation 15 (Compound 18)

FIG. 14


0.3X
2.5X
Wound Margin

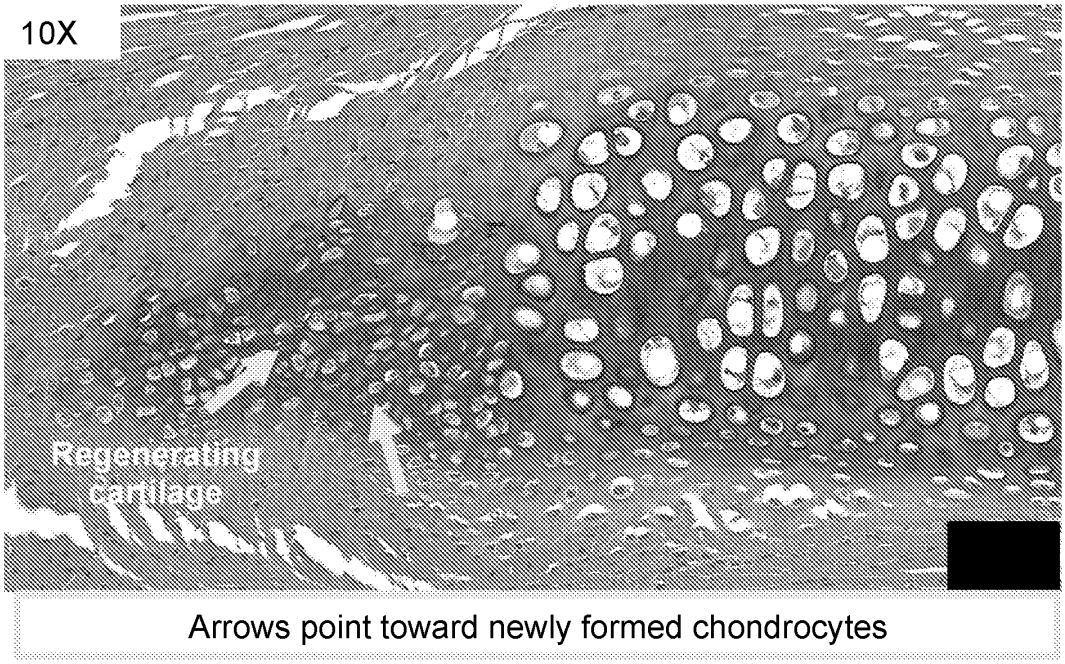

10X
Regenerating cartilage
Arrows point toward newly formed chondrocytes

FIG. 15

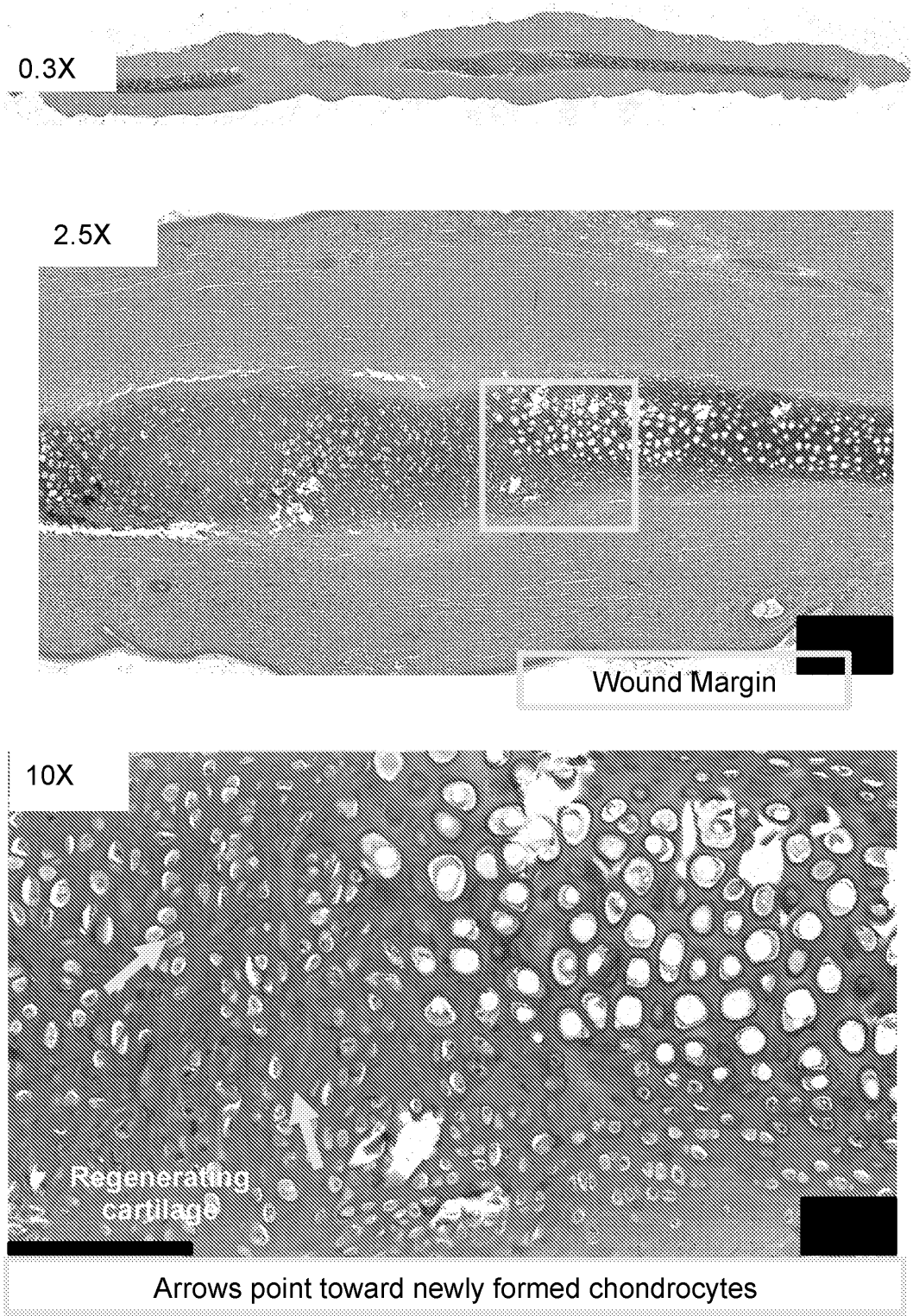

0.3X
2.5X
Wound Margin
10X
Regenerating cartilage
Arrows point toward newly formed chondrocytes

FIG. 16

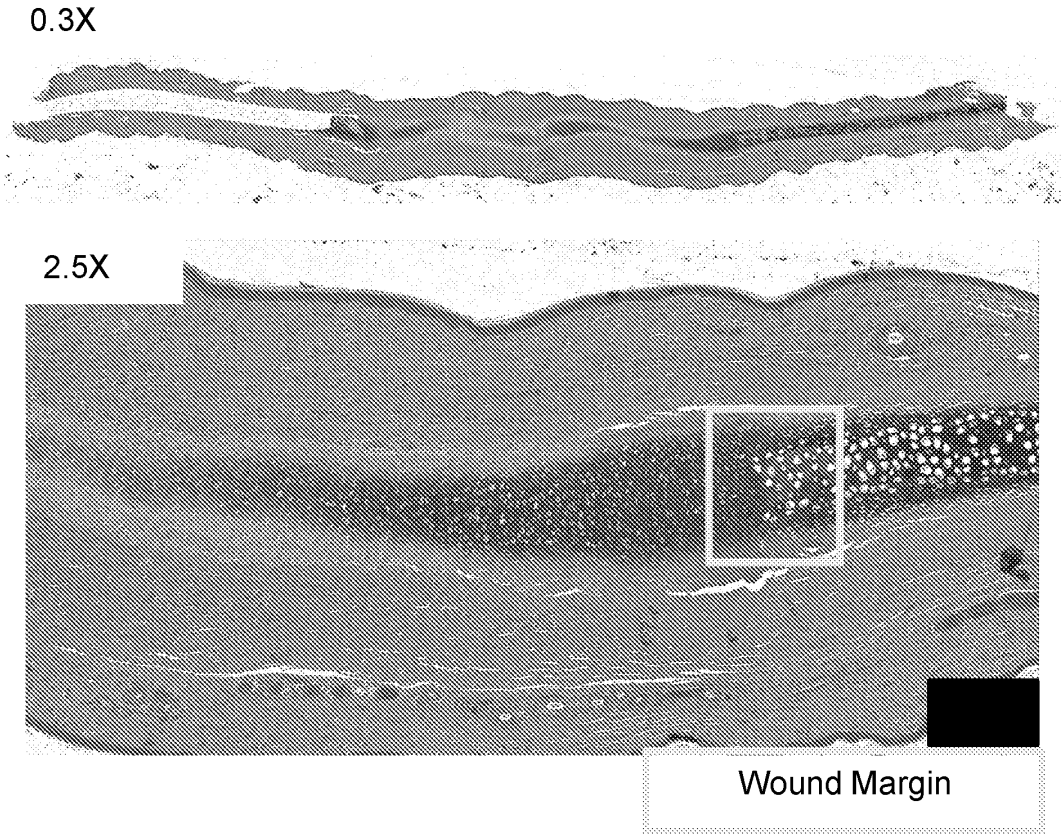

0.3X
2.5X
Wound Margin
10X
Regenerating cartilage
Arrows point towards newly formed chondrocytes

FIG. 17

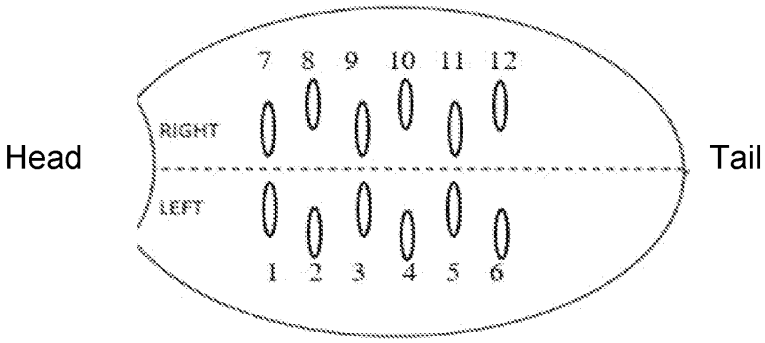


FIG. 18

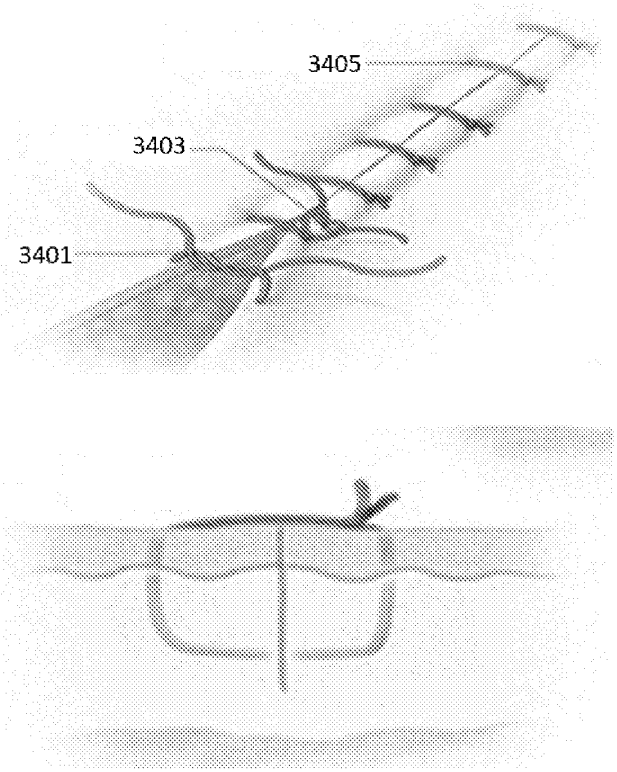


FIG. 19

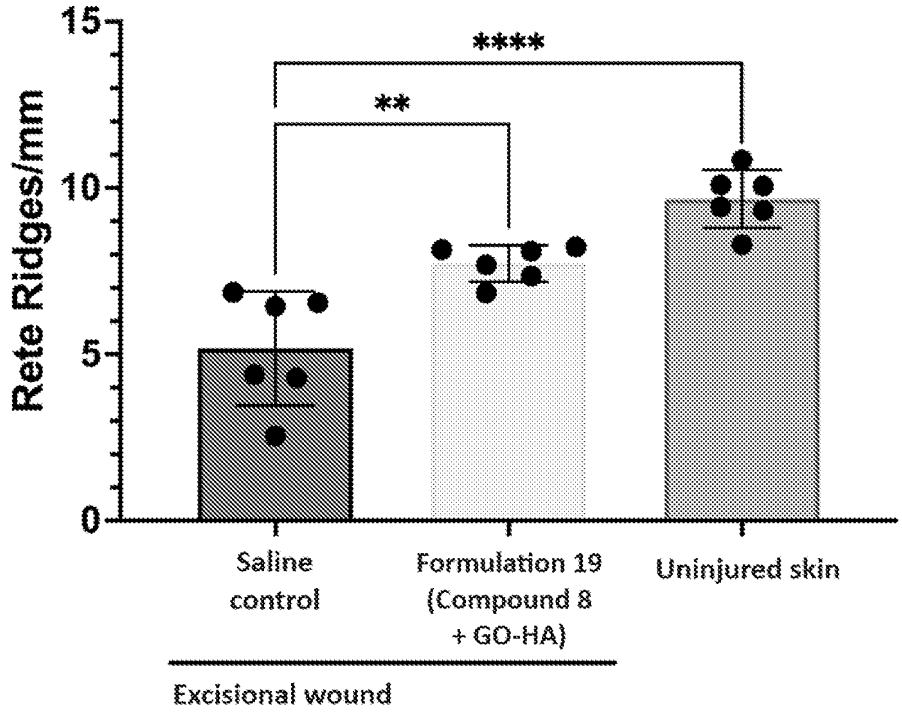

15
10
5
0
Rete Ridges/mm
****
**
Saline control
Formulation 19 (Compound 8 + GO-HA)
Uninjured skin
Excisional wound

FIG. 20A

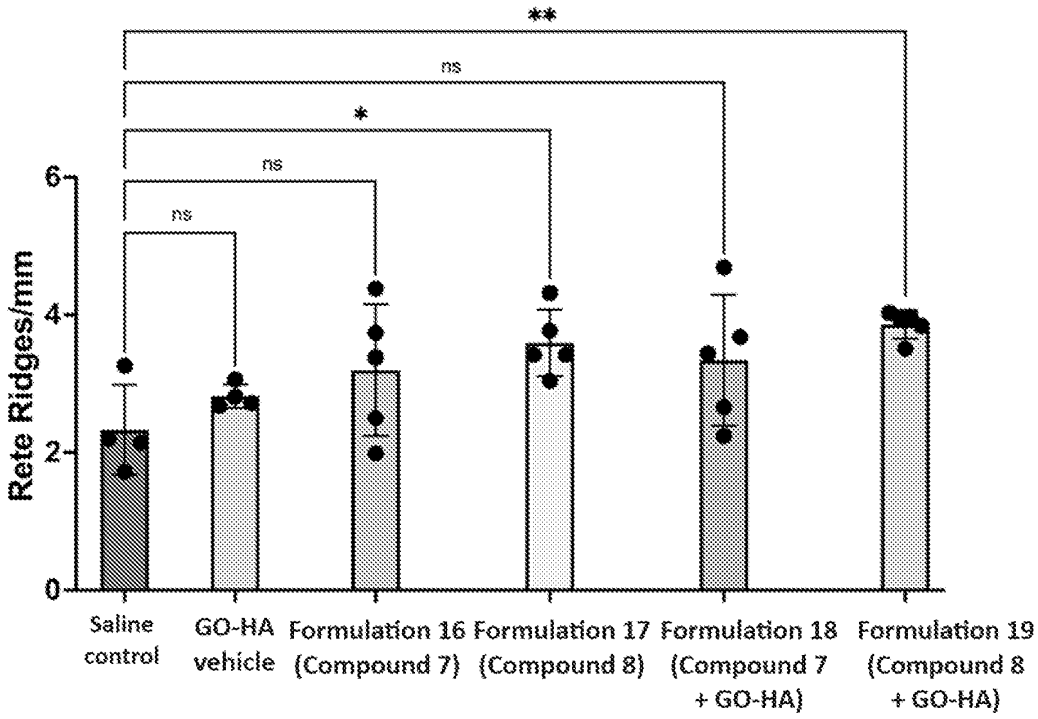

**
ns
*
ns
ns
Rete Ridges/mm
6
4
2
0
Saline control
GO-HA vehicle
Formulation 16 (Compound 7)
Formulation 17 (Compound 8)
Formulation 18 (Compound 7 + GO-HA)
Formulation 19 (Compound 8 + GO-HA)

FIG. 20B

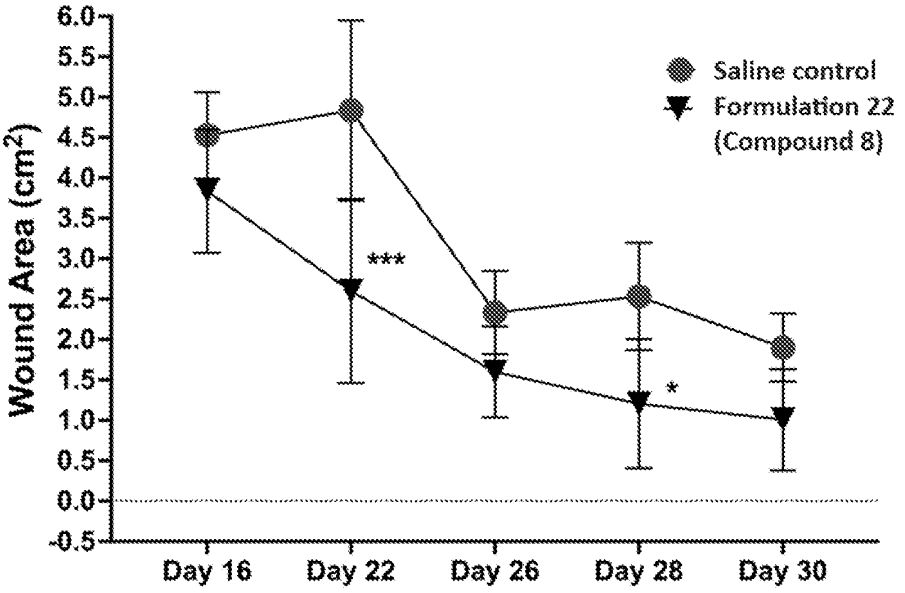

Wound Area (cm²)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
Day 16
Day 22
Day 26
Day 28
Day 30
Saline control
Formulation 22
(Compound 8)
***
*

FIG. 21

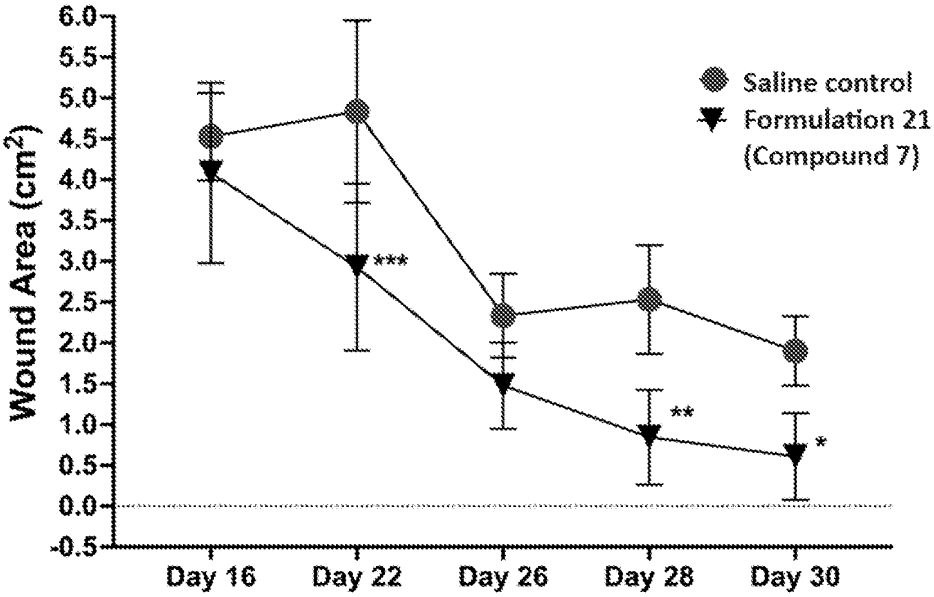

Wound Area (cm²)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
Day 16
Day 22
Day 26
Day 28
Day 30
Saline control
Formulation 21
(Compound 7)
***
**
*

FIG. 22

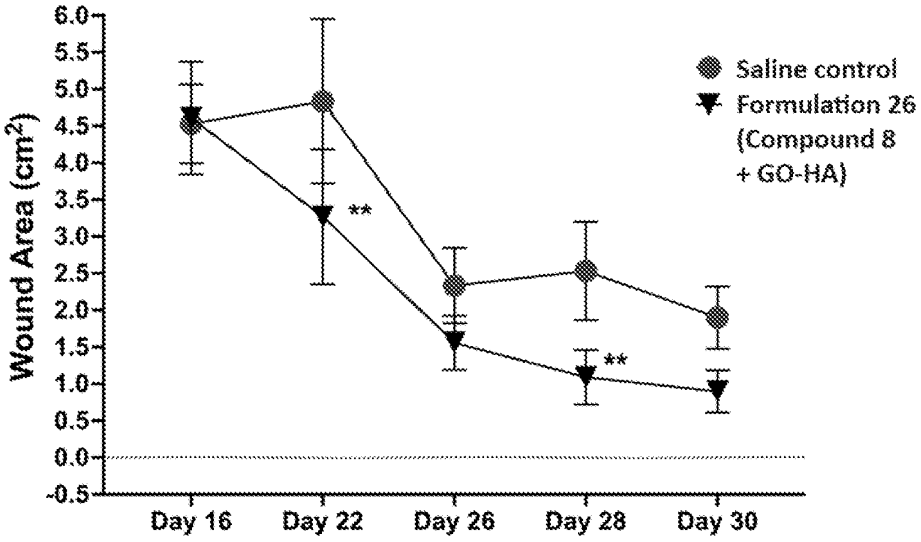

Wound Area (cm²)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
Day 16
Day 22
Day 26
Day 28
Day 30
**
**
Saline control
Formulation 26
(Compound 8
+ GO-HA)

FIG. 23

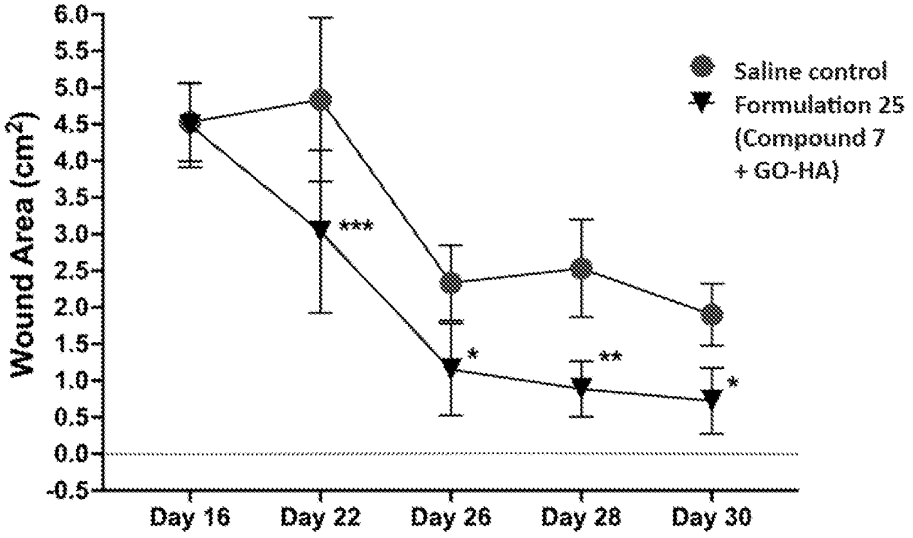

Wound Area (cm²)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
Day 16
Day 22
Day 26
Day 28
Day 30
***
*
**
*
Saline control
Formulation 25
(Compound 7
+ GO-HA)

FIG. 24

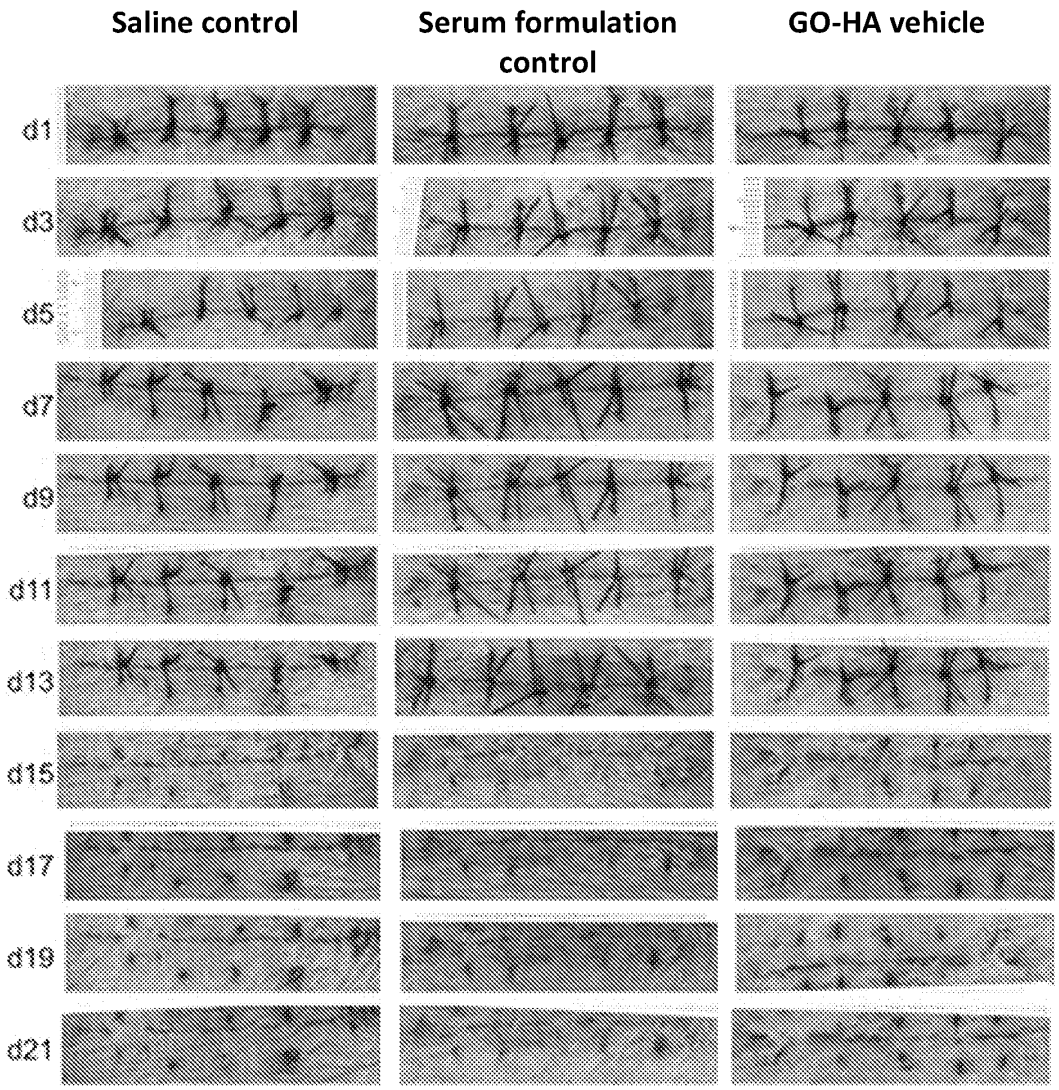

Saline control
Serum formulation control
GO-HA vehicle
d1
d3
d5
d7
d9
d11
d13
d15
d17
d19
d21

FIG. 25

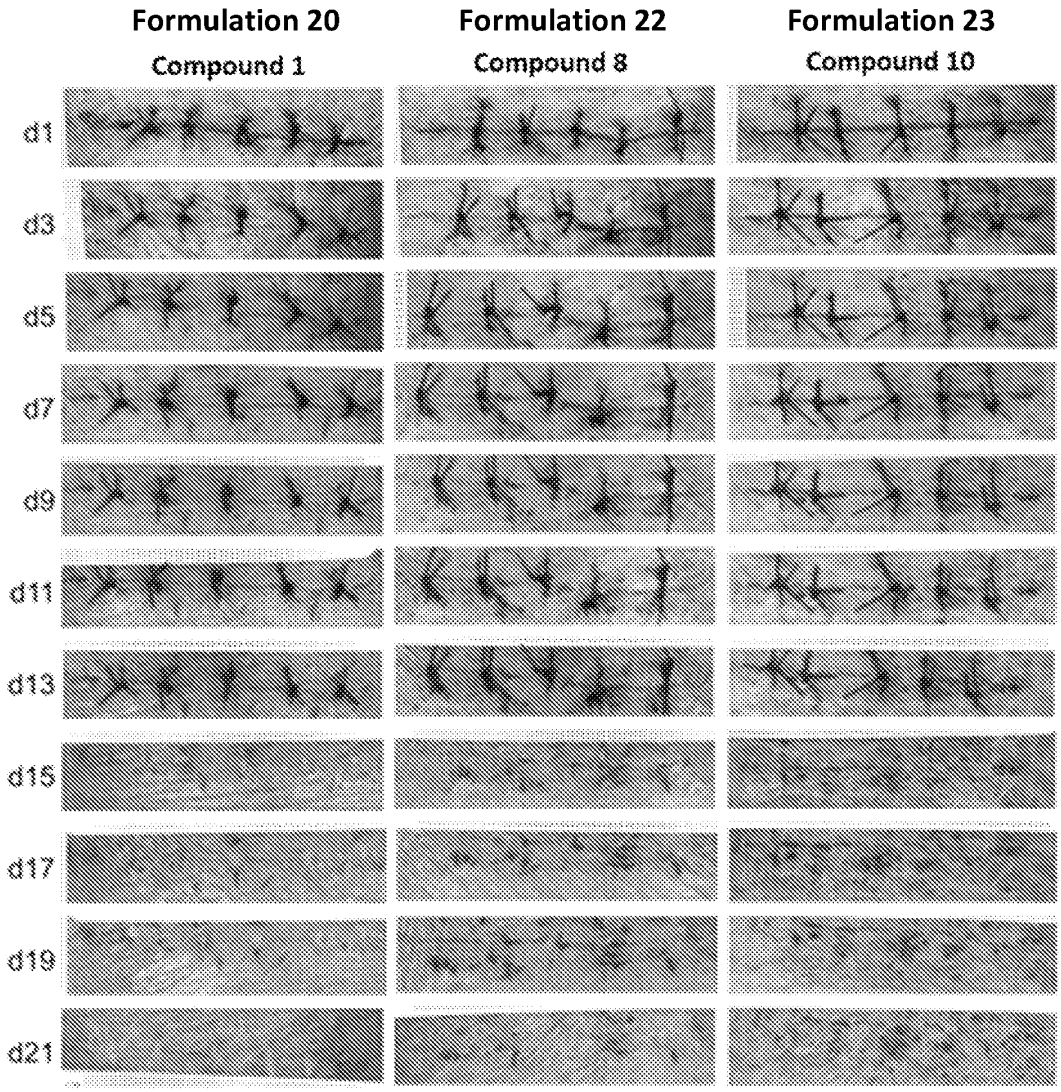

Formulation 20
Compound 1
Formulation 22
Compound 8
Formulation 23
Compound 10
d1
d3
d5
d7
d9
d11
d13
d15
d17
d19
d21

FIG. 26

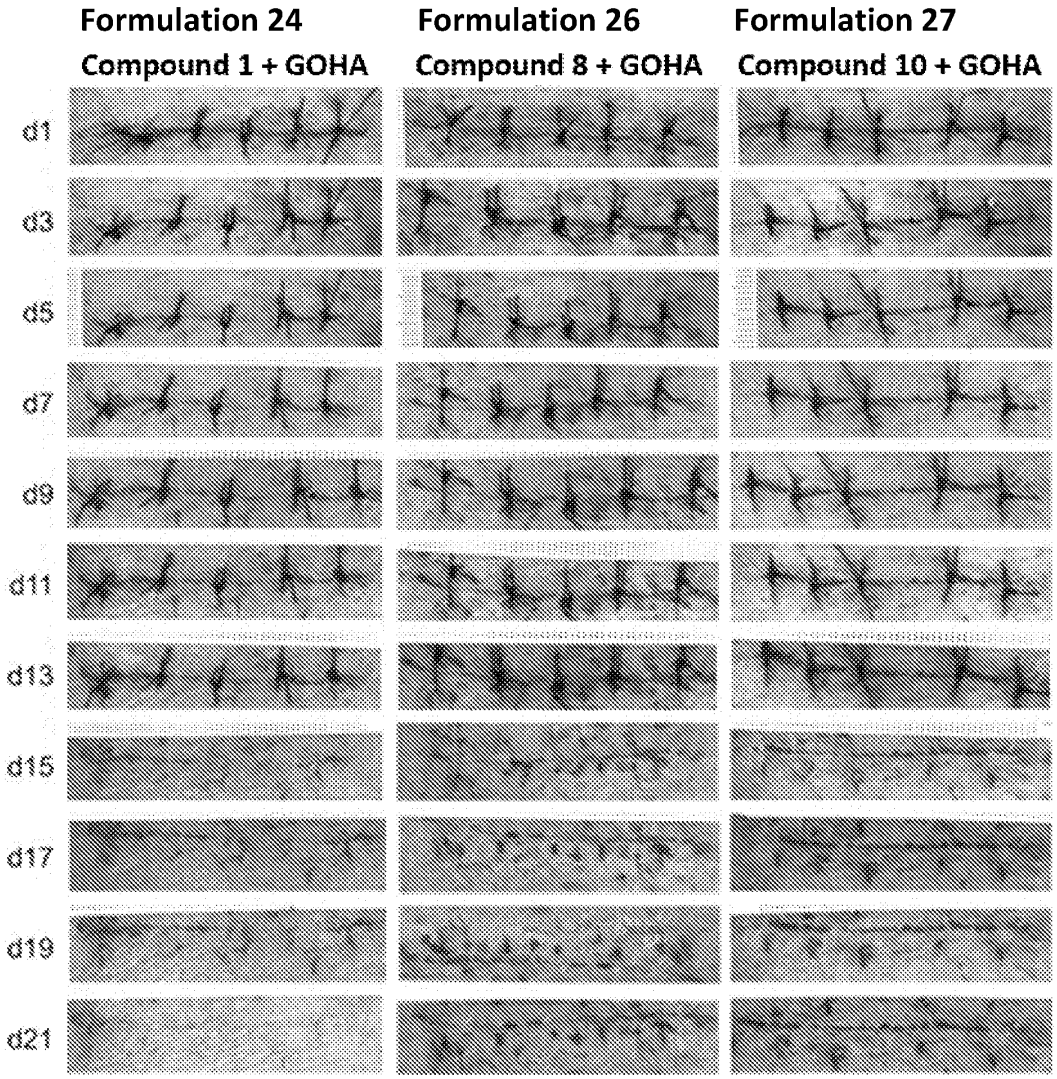

Formulation 24
Compound 1 + GOHA
Formulation 26
Compound 8 + GOHA
Formulation 27
Compound 10 + GOHA
d1
d3
d5
d7
d9
d11
d13
d15
d17
d19
d21

FIG. 27

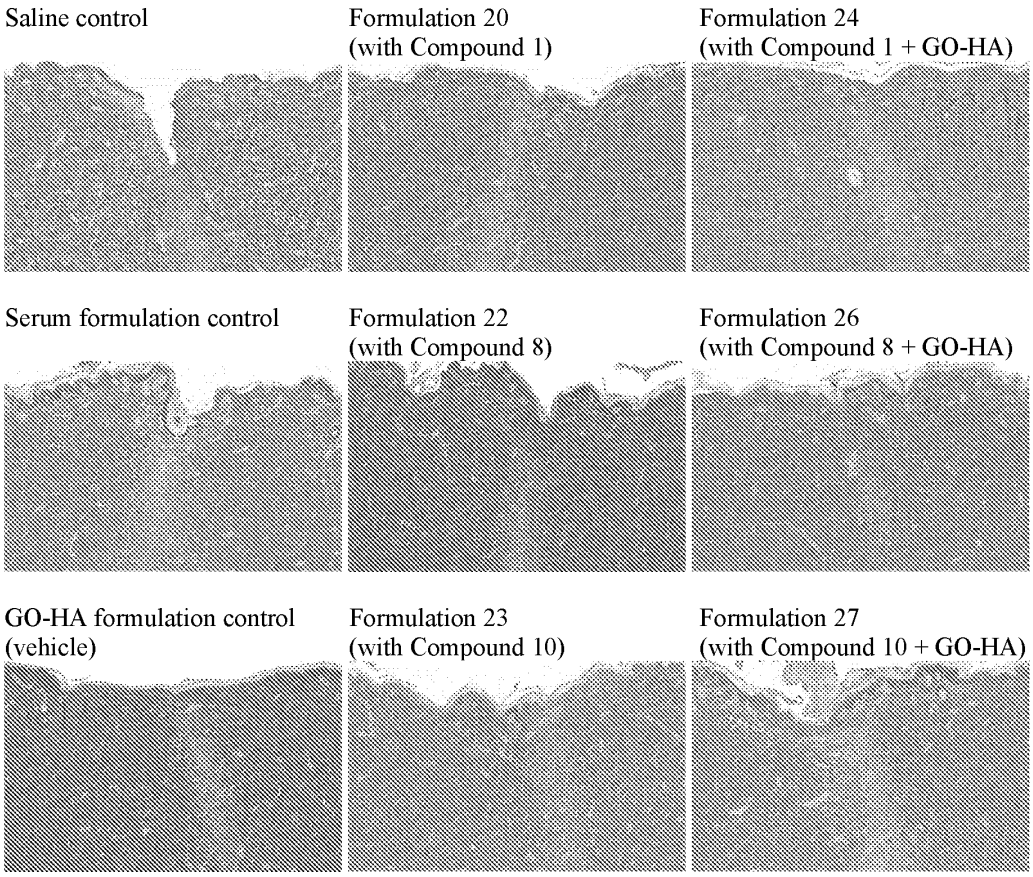

Saline control
Formulation 20
(with Compound 1)
Formulation 24
(with Compound 1 + GO-HA)
Serum formulation control
Formulation 22
(with Compound 8)
Formulation 26
(with Compound 8 + GO-HA)
GO-HA formulation control
(vehicle)
Formulation 23
(with Compound 10)
Formulation 27
(with Compound 10 + GO-HA)

FIG. 28

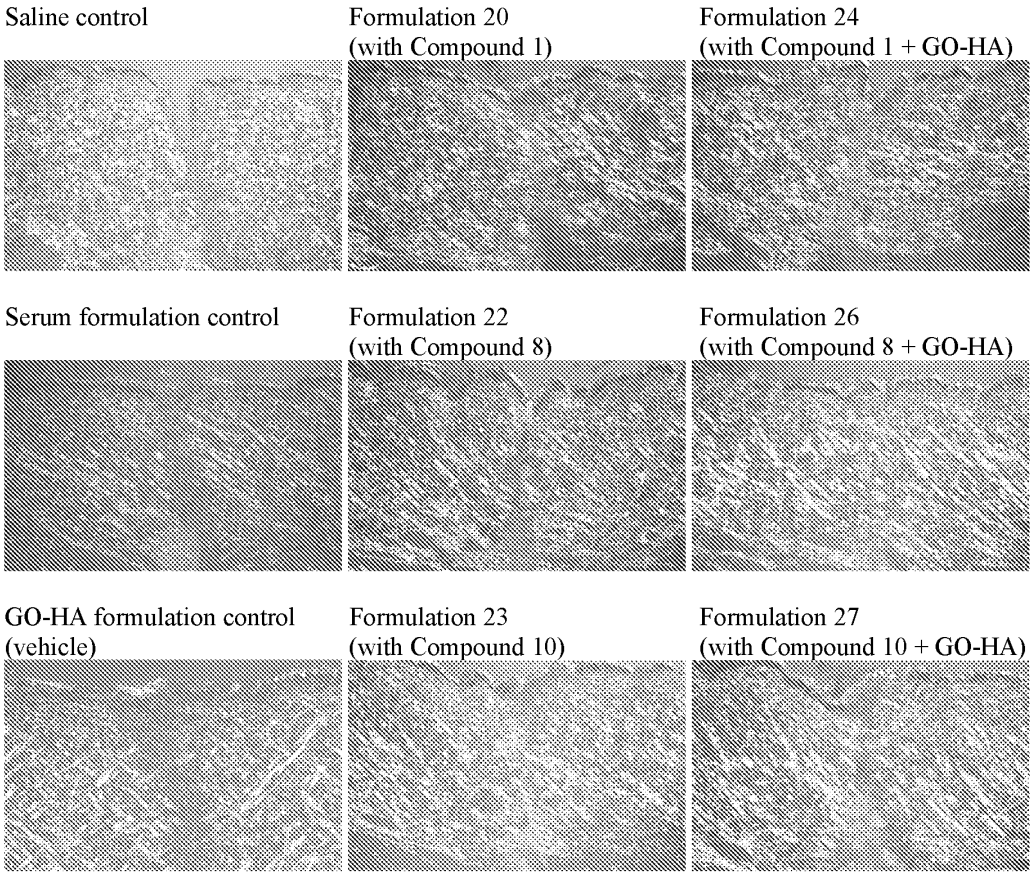
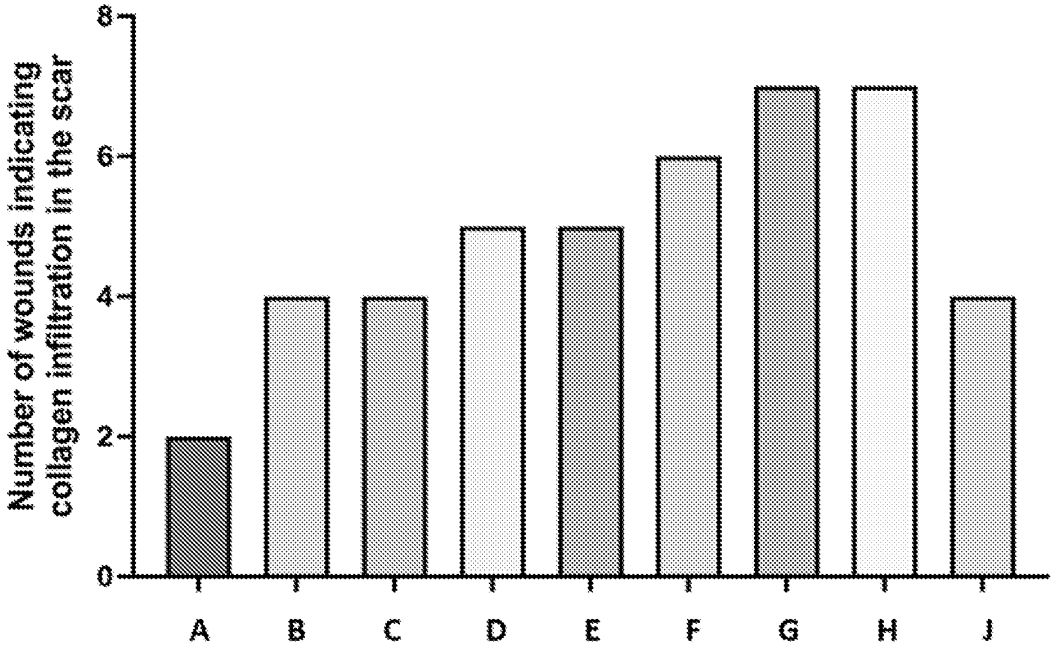

Saline control
Formulation 20
(with Compound 1)
Formulation 24
(with Compound 1 + GO-HA)
Serum formulation control
Formulation 22
(with Compound 8)
Formulation 26
(with Compound 8 + GO-HA)
GO-HA formulation control
(vehicle)
Formulation 23
(with Compound 10)
Formulation 27
(with Compound 10 + GO-HA)

FIG. 29



A - Saline control
B - Serum formulation control
C - GO-HA vehicle
D - Formulation 20 (with Compound 1)
E - Formulation 24 (with Compound 1 + GO-HA)
F - Formulation 22 (with Compound 8)
G - Formulation 26 (with Compound 8 + GO-HA)
H - Formulation 23 (with Compound 10)
J - Formulation 27 (with Compound 10 + GO-HA)

FIG. 30

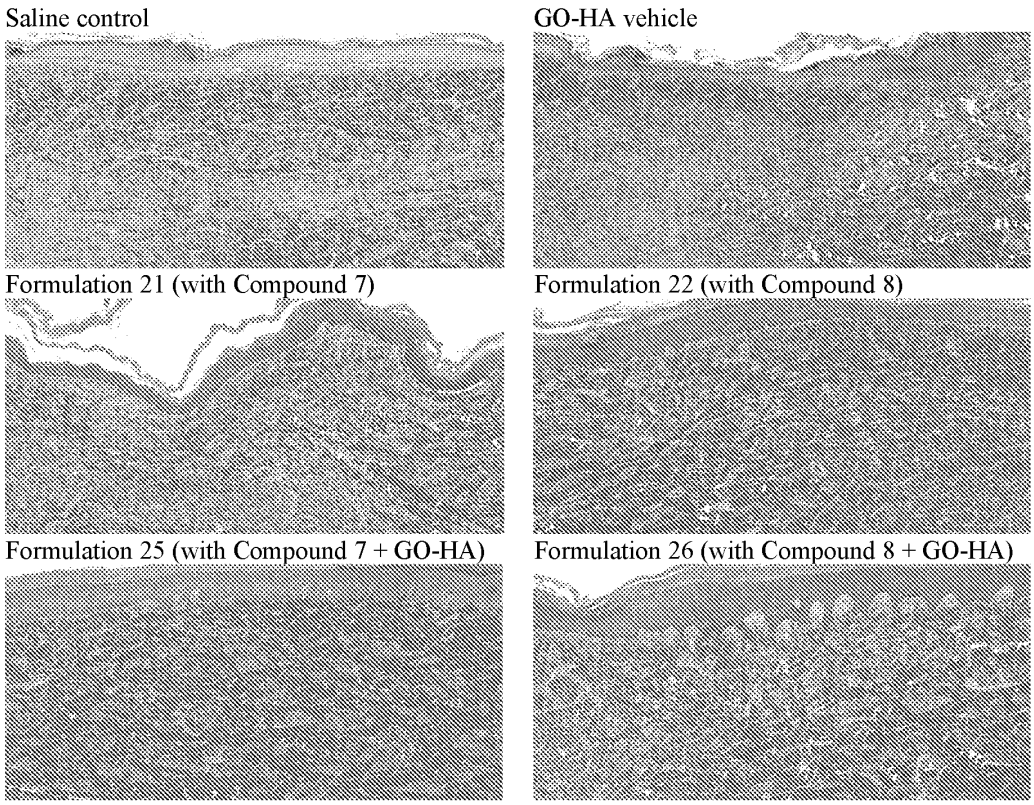

Saline control
GO-HA vehicle
Formulation 21 (with Compound 7)
Formulation 22 (with Compound 8)
Formulation 25 (with Compound 7 + GO-HA)
Formulation 26 (with Compound 8 + GO-HA)
Center of the Wound

FIG. 31

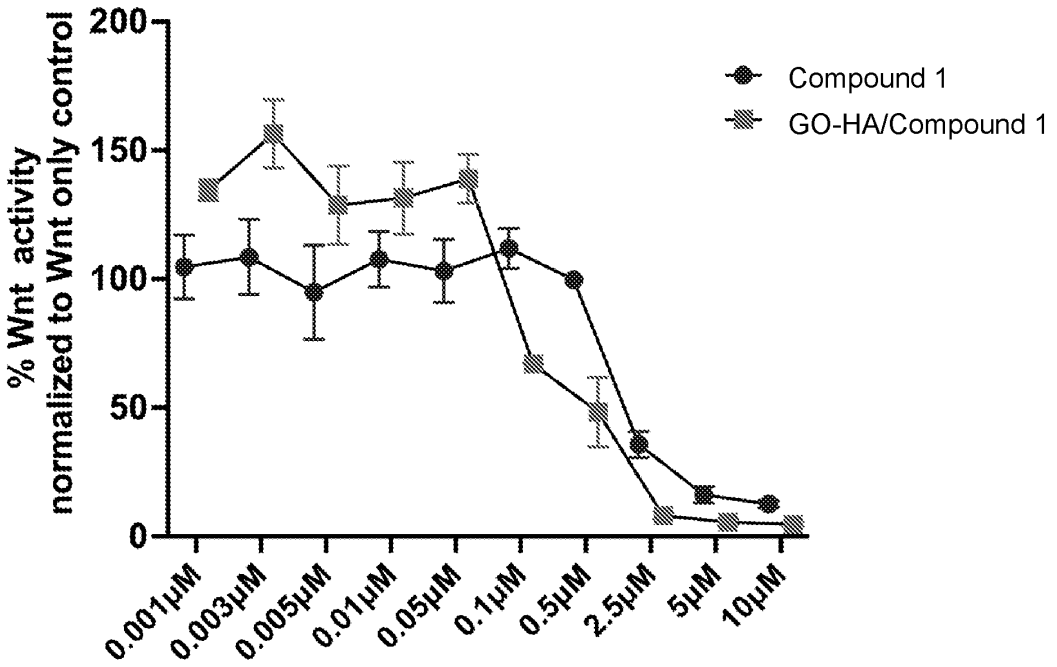

% Wnt activity
normalized to Wnt only control
200
150
100
50
0
0.001μM
0.003μM
0.005μM
0.01μM
0.05μM
0.1μM
0.5μM
2.5μM
5μM
10μM
Compound 1
GO-HA/Compound 1

FIG. 32

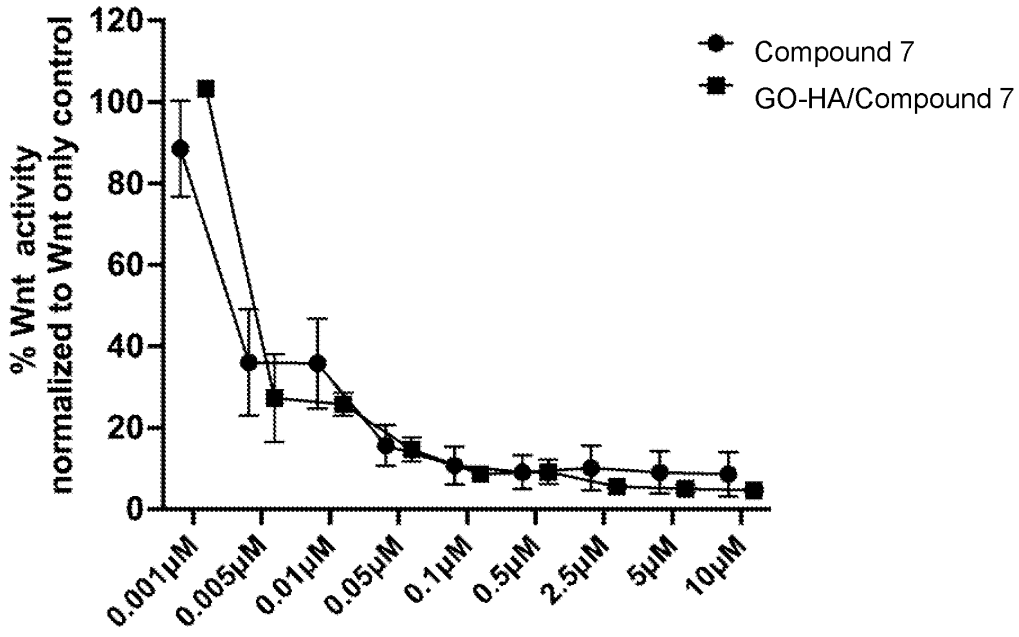

% Wnt activity
normalized to Wnt only control
120
100
80
60
40
20
0
0.001μM
0.005μM
0.01μM
0.05μM
0.1μM
0.5μM
2.5μM
5μM
10μM
Compound 7
GO-HA/Compound 7

FIG. 33

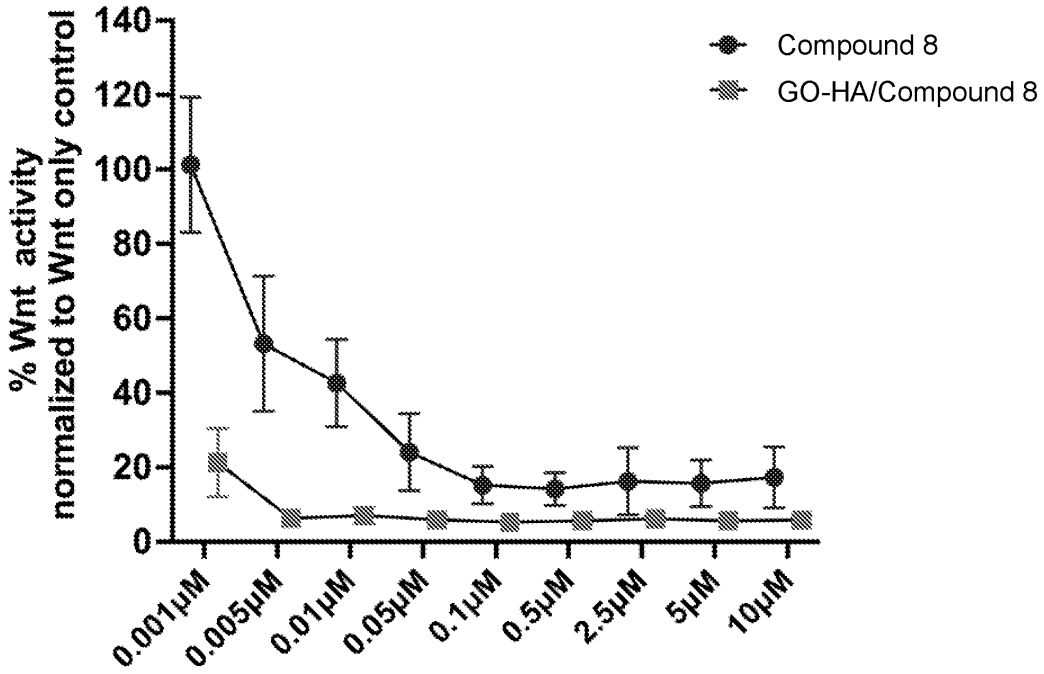

% Wnt activity
normalized to Wnt only control
140
120
100
80
60
40
20
0
0.001μM
0.005μM
0.01μM
0.05μM
0.1μM
0.5μM
2.5μM
5μM
10μM
Compound 8
GO-HA/Compound 8

FIG. 34