FIG. 1

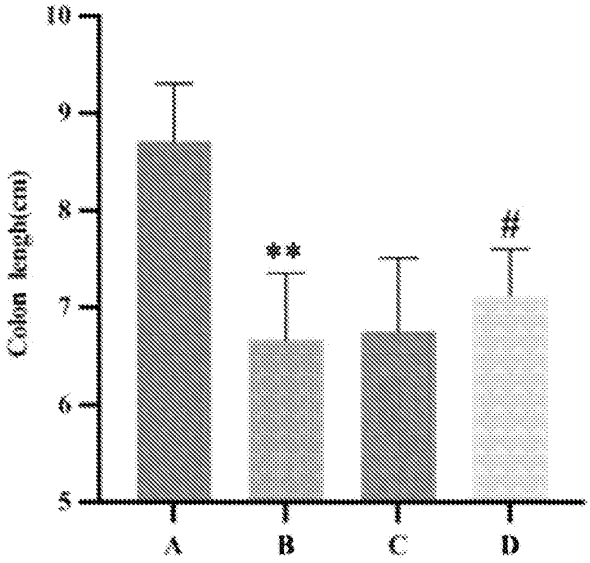


FIG. 2

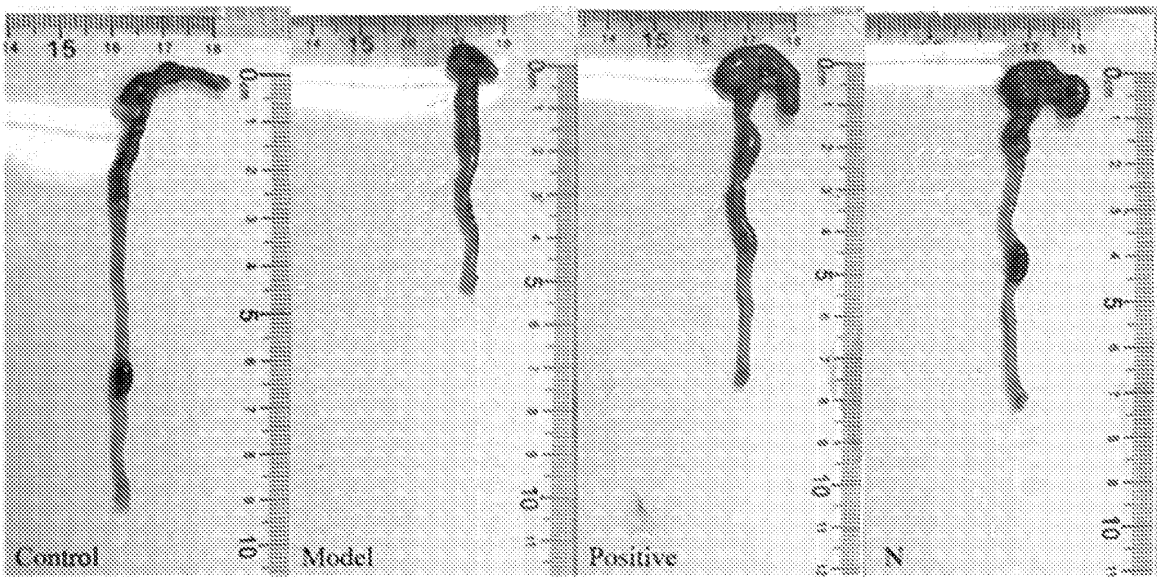


FIG. 3

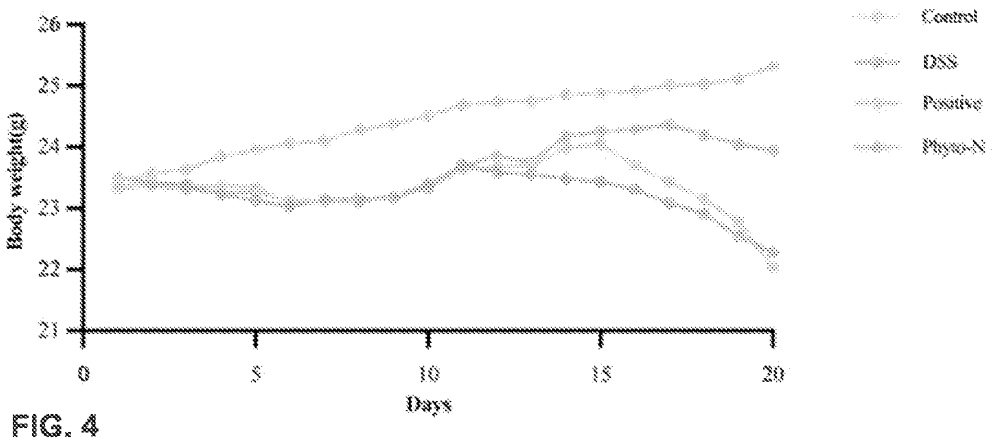

Body weight(g)
26
25
24
23
22
21
0
5
10
15
20
Days
Control
DSS
Positive
Phyto-N

FIG. 4

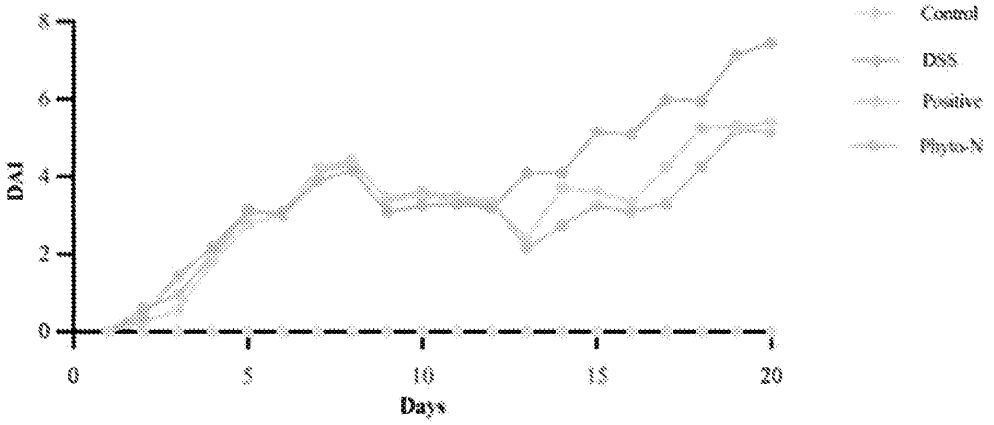

DAI
8
6
4
2
0
0
5
10
15
20
Days
Control
DSS
Positive
Phyto-N

FIG. 5

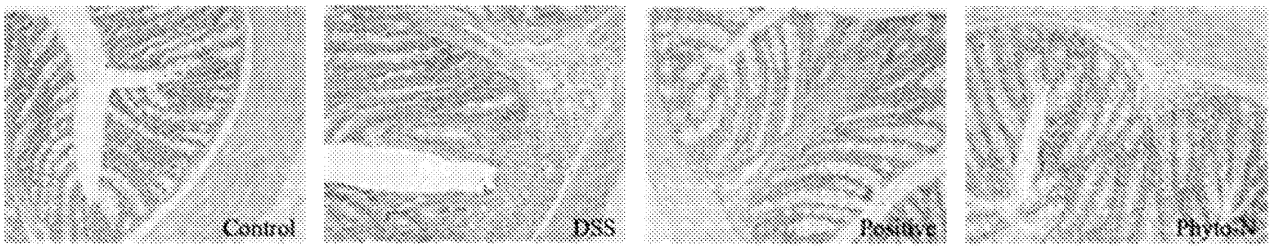


FIG. 6

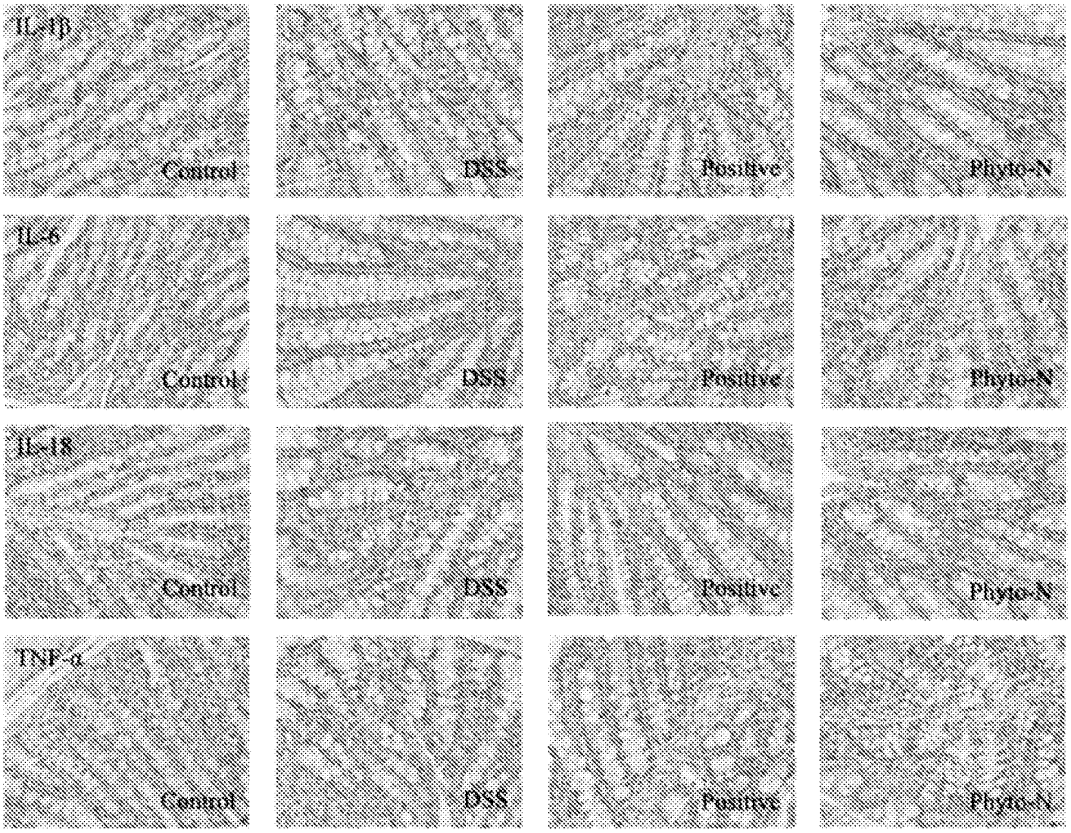

IL-1β
Control
DSS
Positive
Phyto-N
IL-6
Control
DSS
Positive
Phyto-N
IL-18
Control
DSS
Positive
Phyto-N
TNF-α
Control
DSS
Positive
Phyto-N

FIG. 7A

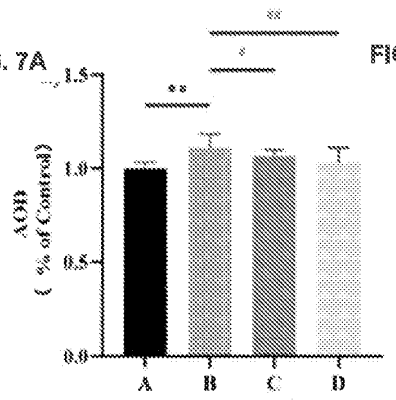


FIG. 7B

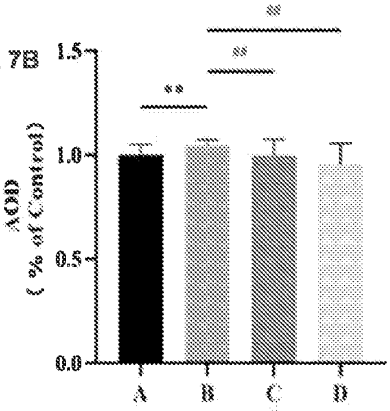


FIG. 7C

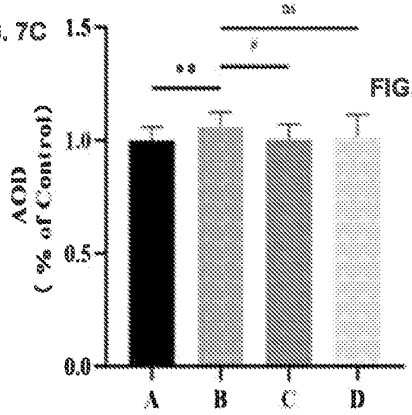


FIG. 7D

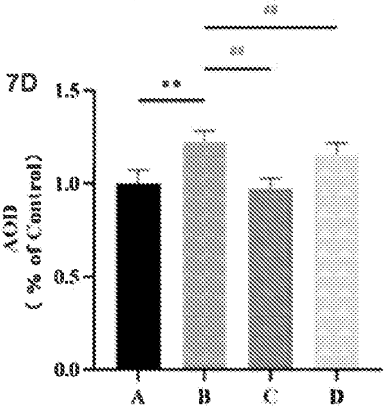


FIG. 8

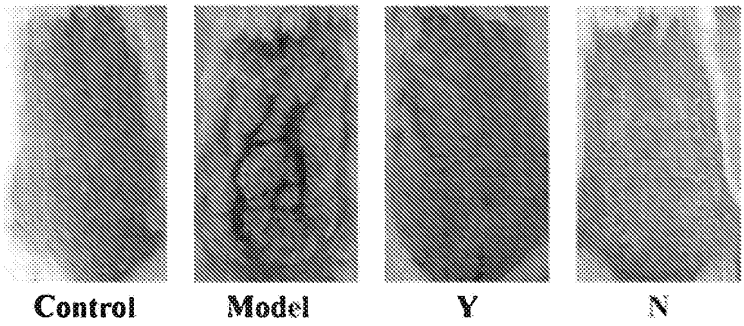


FIG. 9A

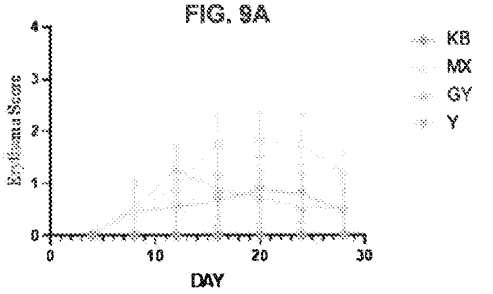


FIG. 9B

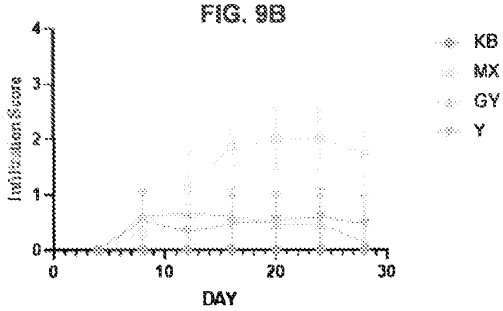


FIG. 9C

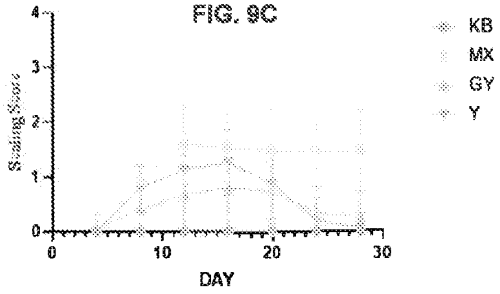


FIG. 9D

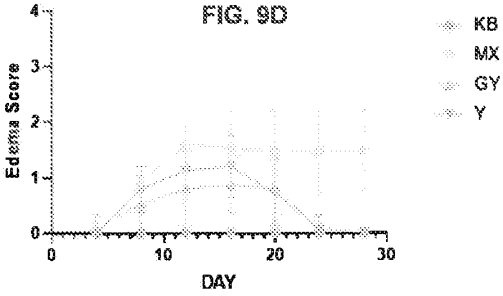


FIG. 9E

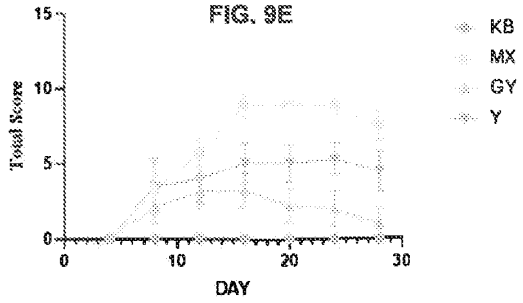


FIG. 10

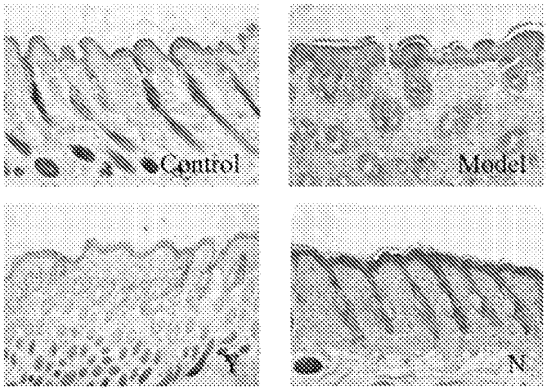


FIG. 11

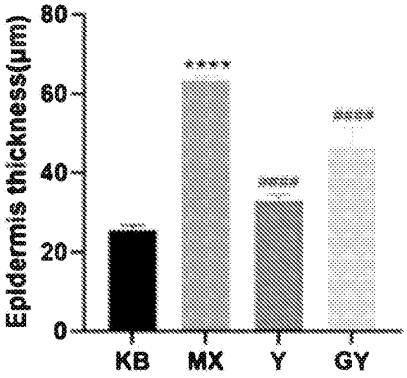


FIG. 12

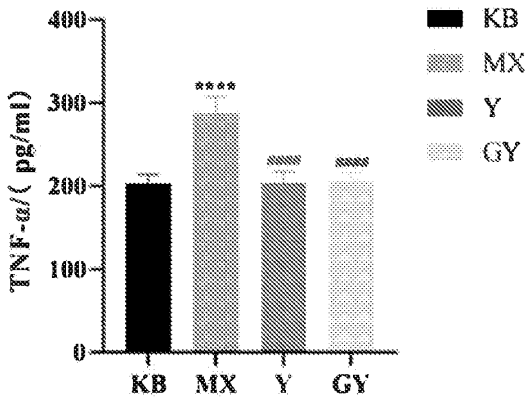


FIG. 13



FIG. 14A

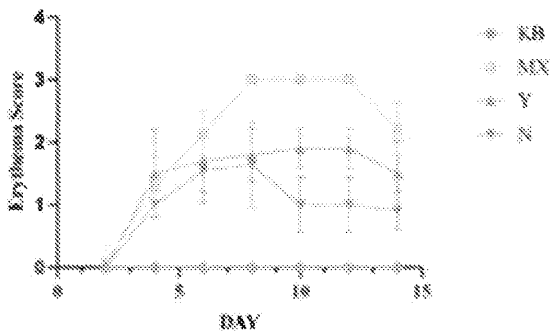


FIG. 14B

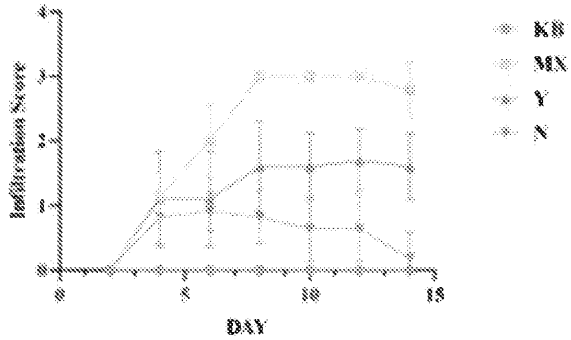


FIG. 14C

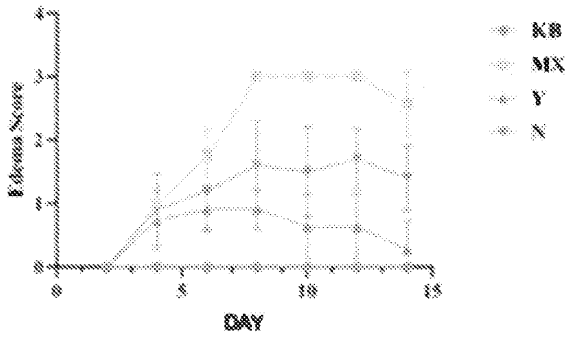


FIG. 14D

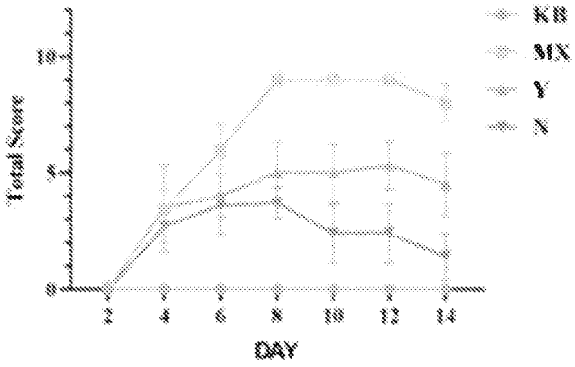


FIG. 15

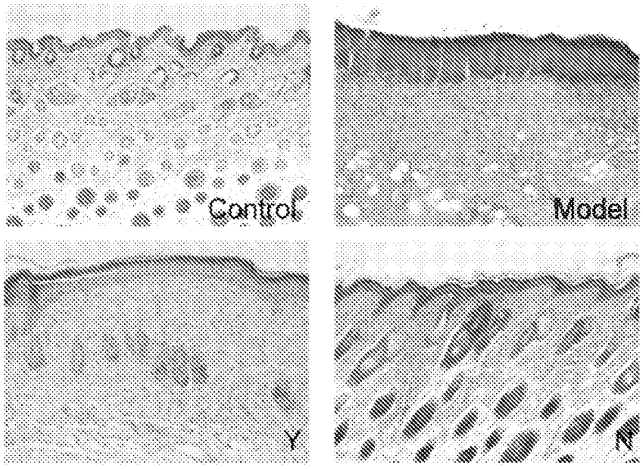


FIG. 16

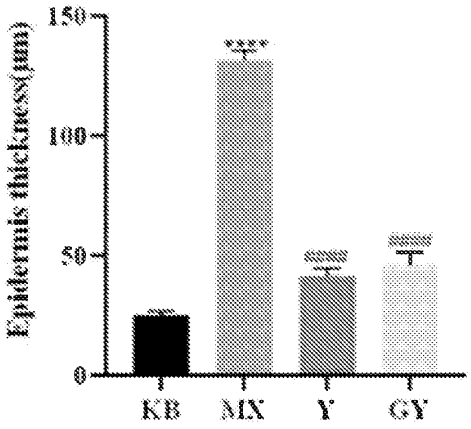


FIG. 17

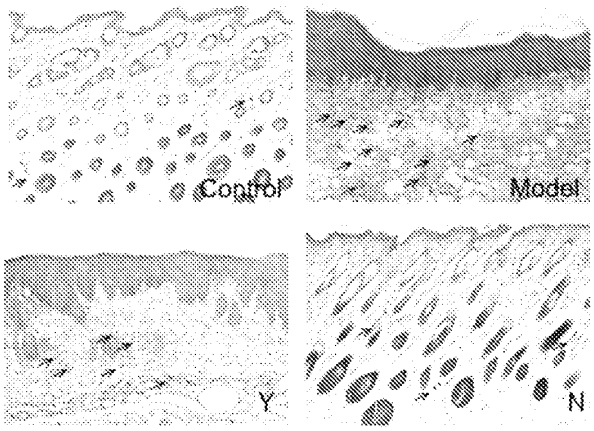


FIG. 18

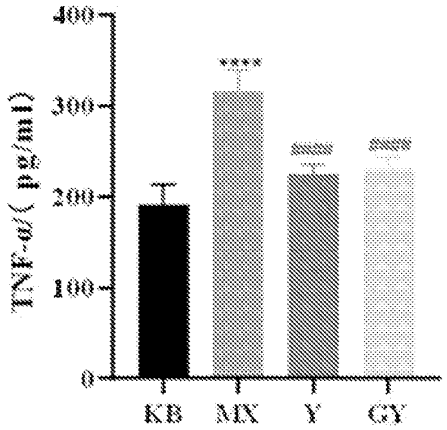


FIG. 19

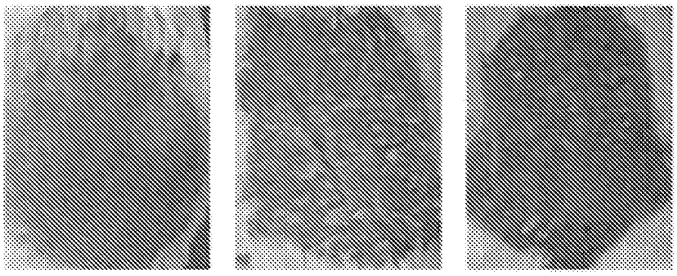


FIG. 20A

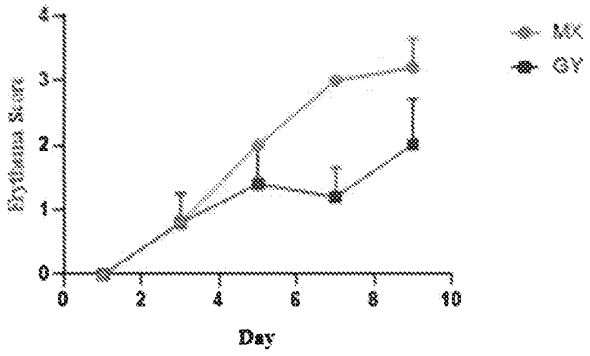


FIG. 20B

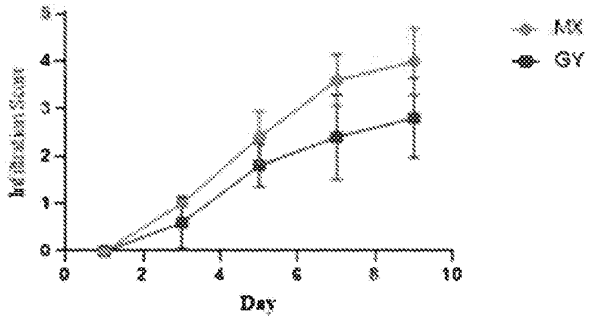


FIG. 20C

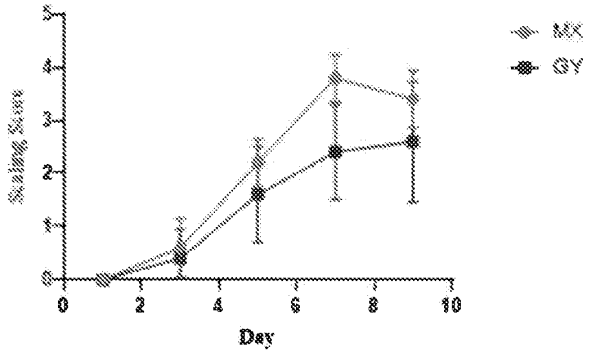


FIG. 20D

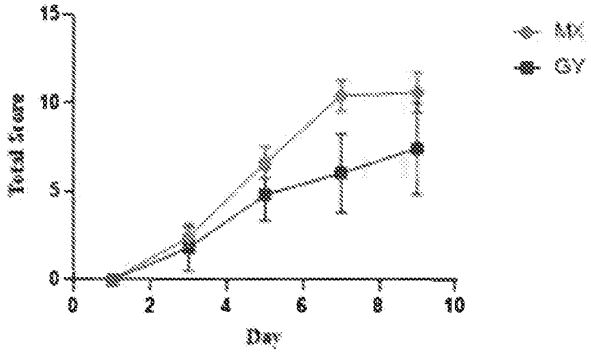


FIG. 21

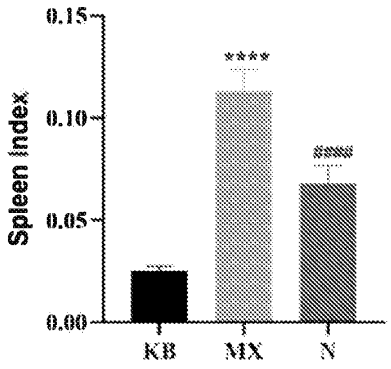


FIG. 22

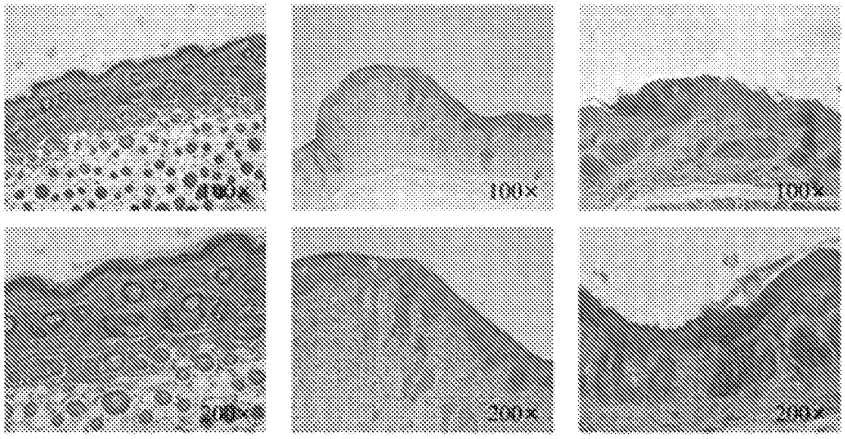


FIG. 23

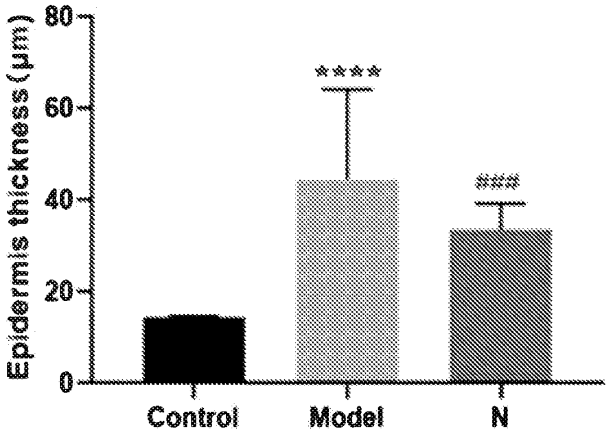


FIG. 24A

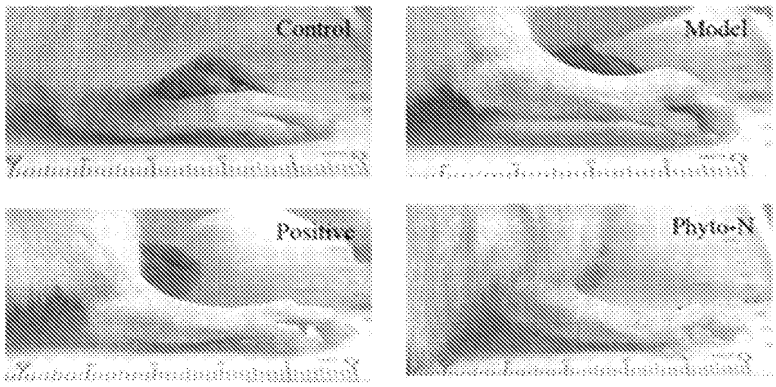


FIG. 24B

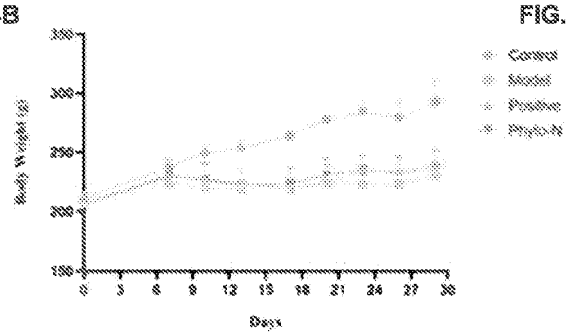


FIG. 24C

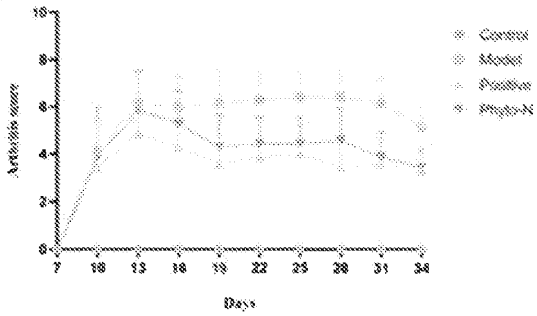


FIG. 25A

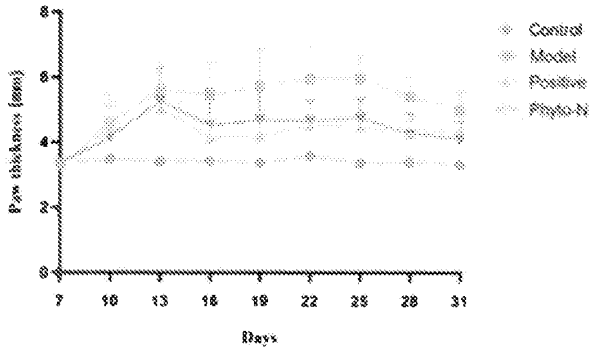


FIG. 25B

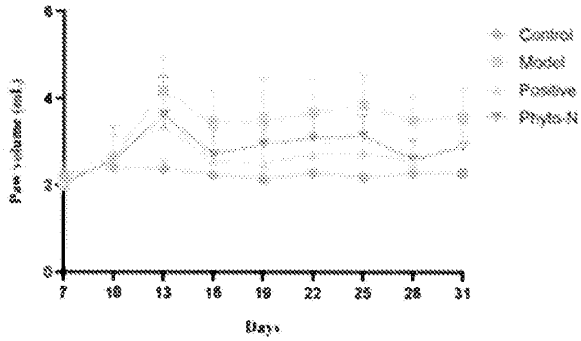


FIG. 26

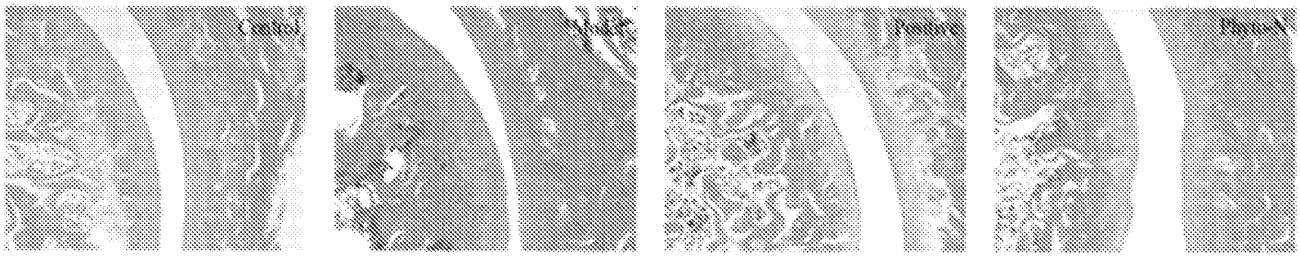


FIG. 27A

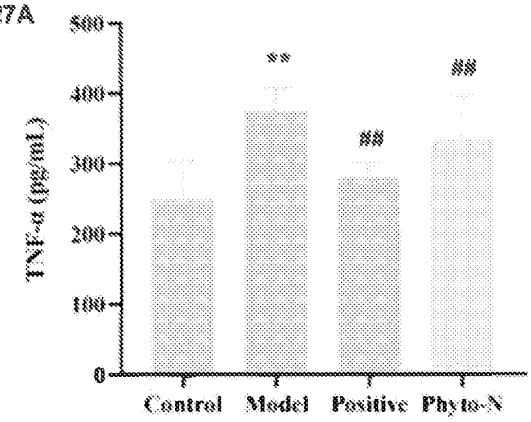


FIG. 27B

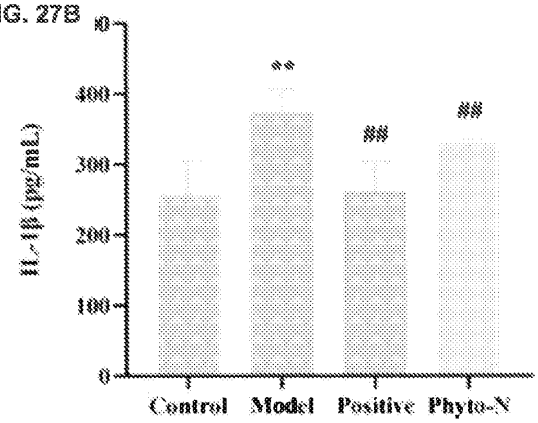


FIG. 28

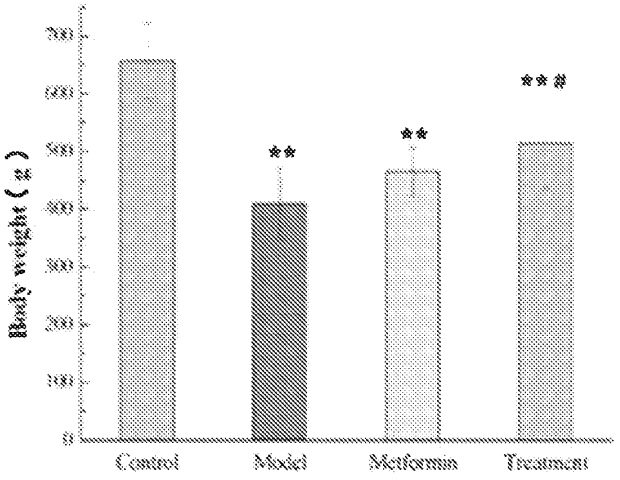

Body weight (g)
0
100
200
300
400
500
600
700
**
**
***#
Control
Model
Metformin
Treatment

FIG. 29

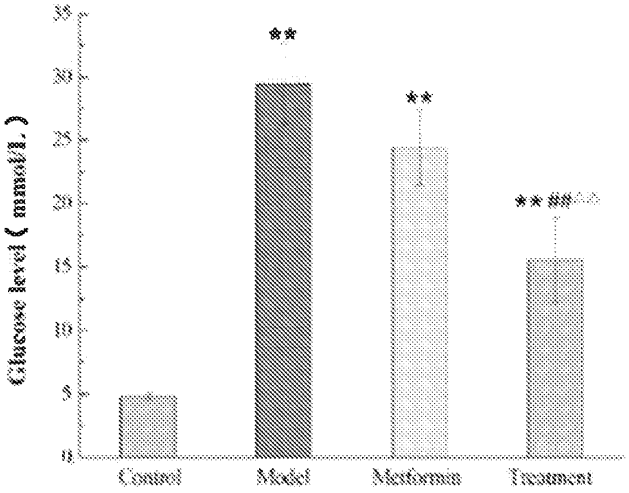

Glucose level (mmol/L)
0
5
10
15
20
25
30
35
**
**
**##△△
Control
Model
Metformin
Treatment

FIG. 30

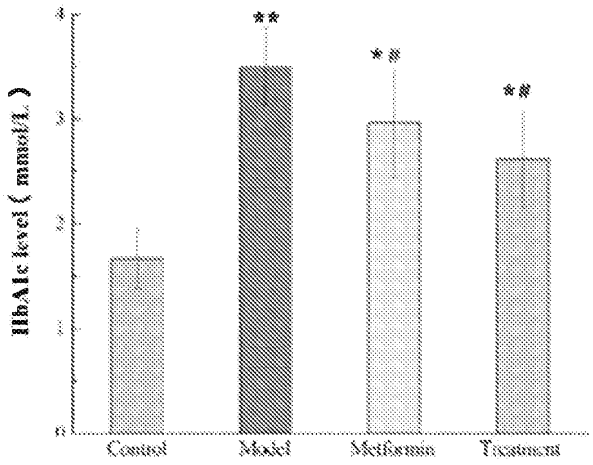

HbA1c level (mmol/L)
**
**#
**#
Control
Model
Metformin
Treatment

FIG. 31

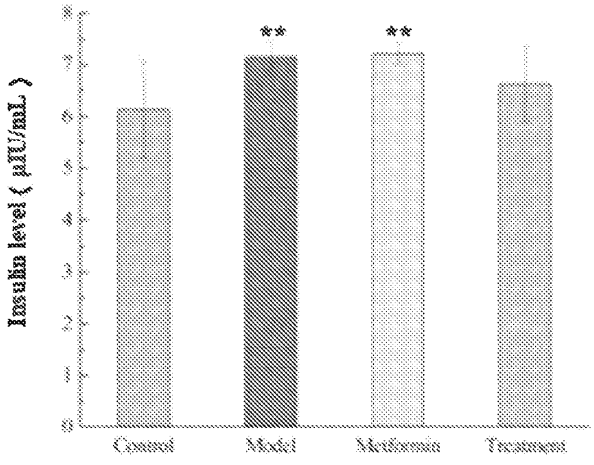

Insulin level (μIU/mL)
**
**
Control
Model
Metformin
Treatment

FIG. 32A

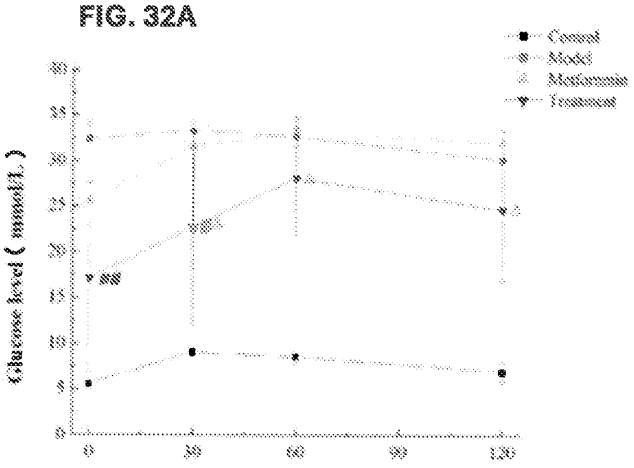


FIG. 32B

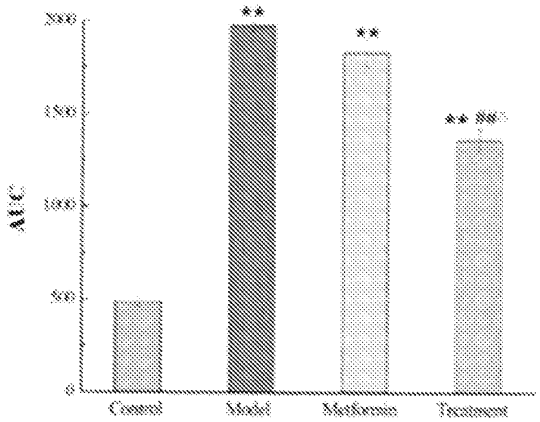


FIG. 33A

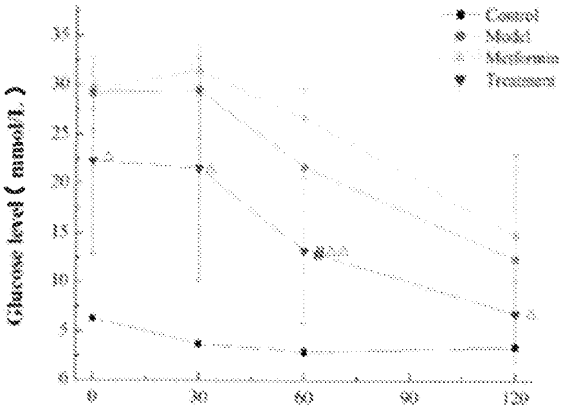


FIG. 33B

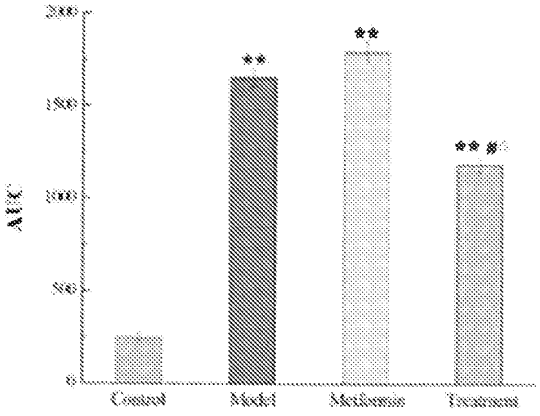


FIG. 34A

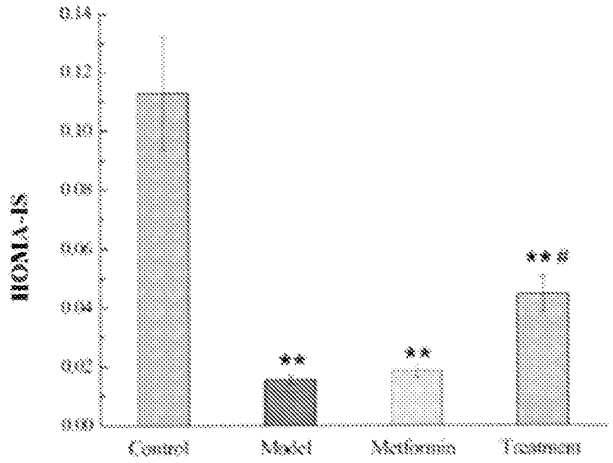


FIG. 34B

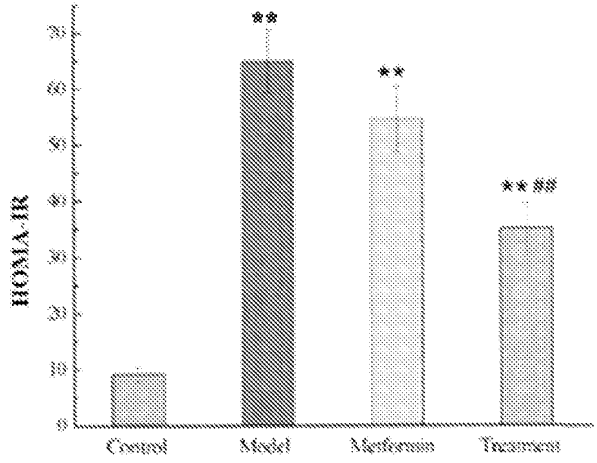


FIG. 35A

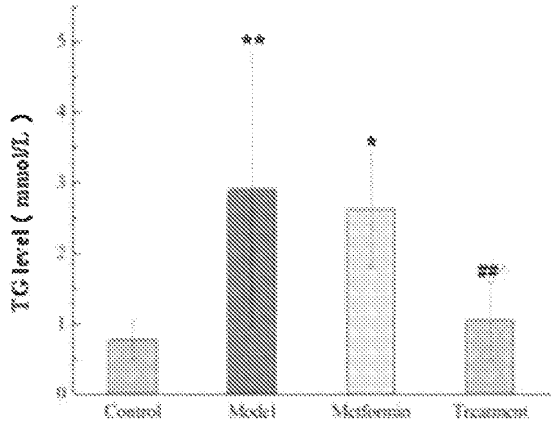


FIG. 35B

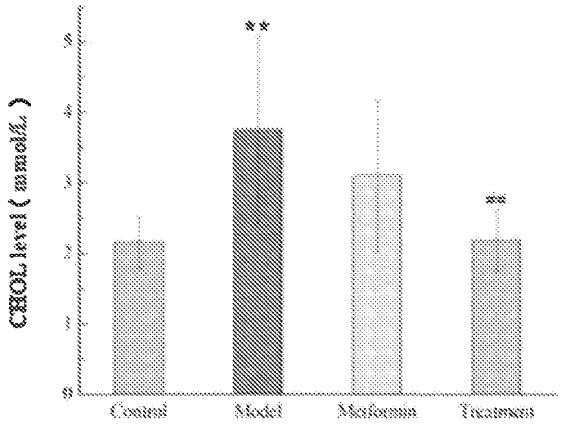


FIG. 35C

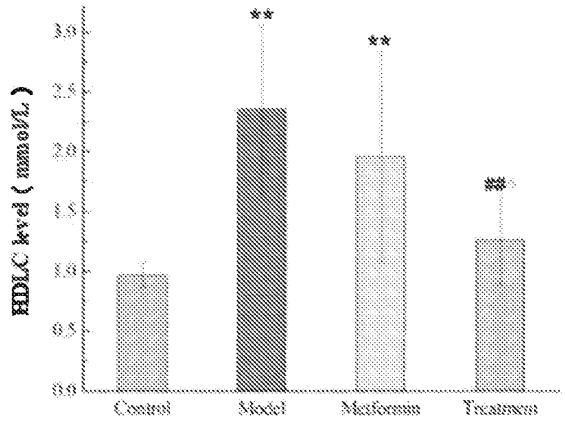


FIG. 35D

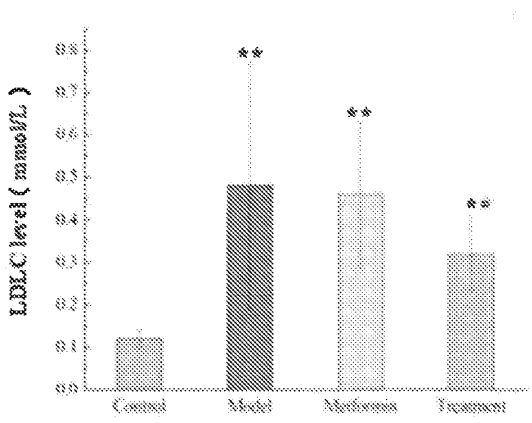


FIG. 36

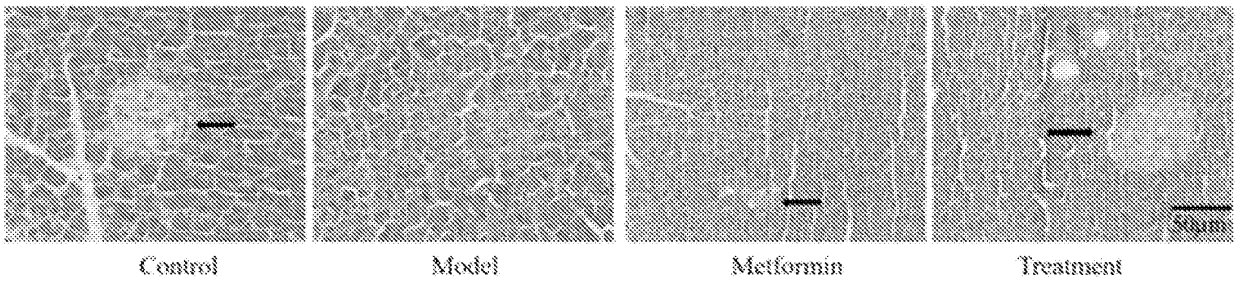


FIG. 37A

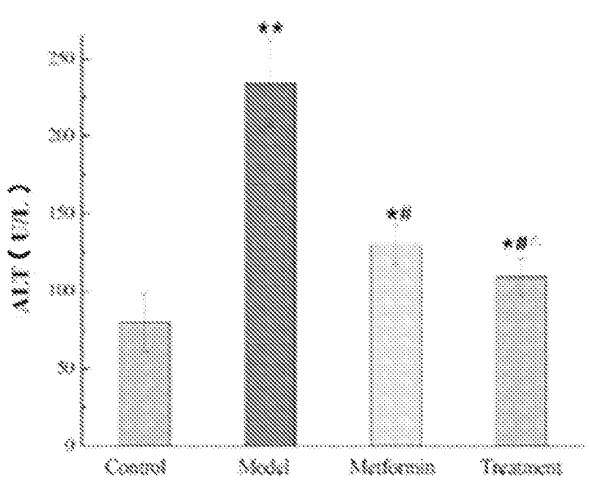


FIG. 37B

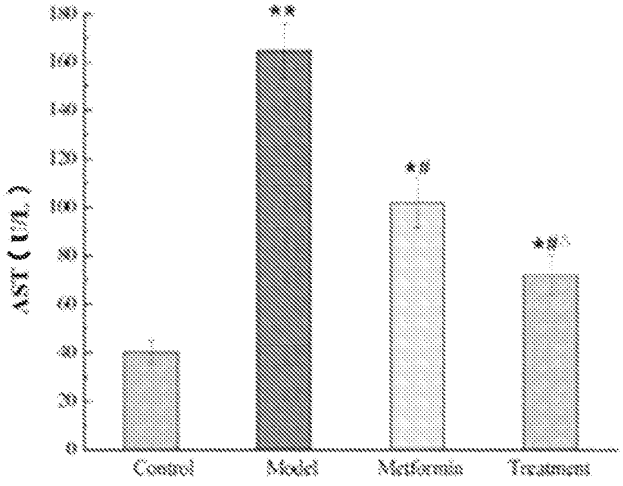


FIG. 38A

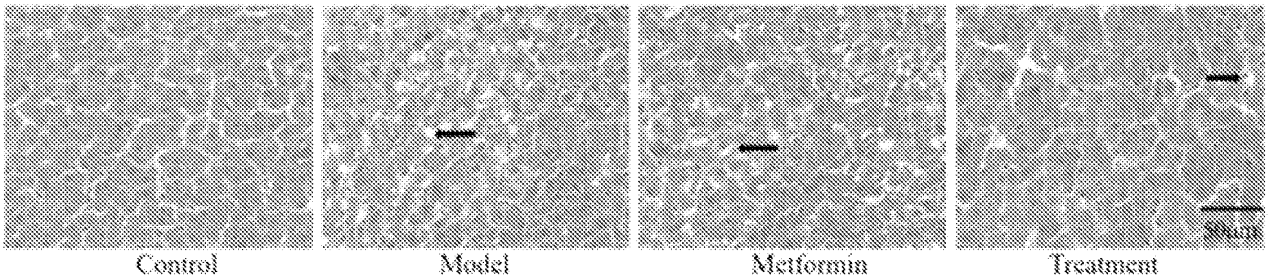


FIG. 38B

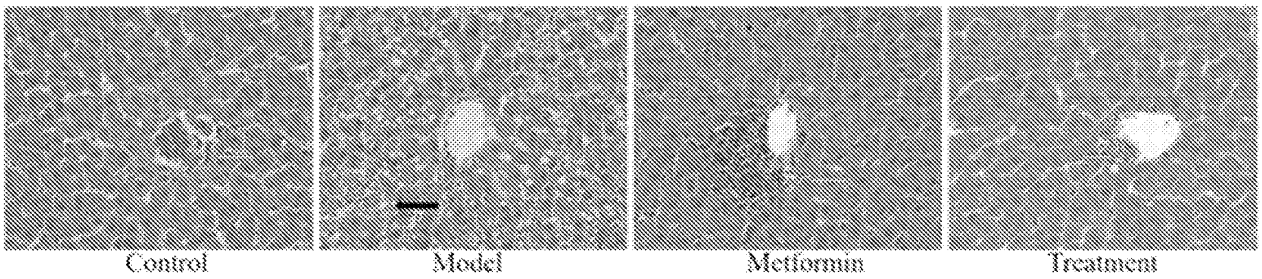


FIG. 39A

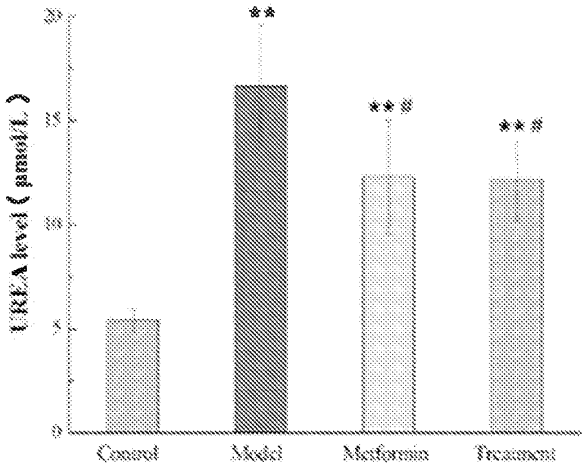


FIG. 39B

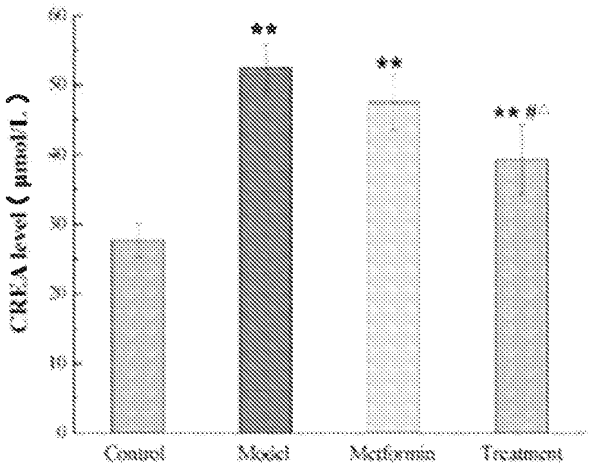


FIG. 40A

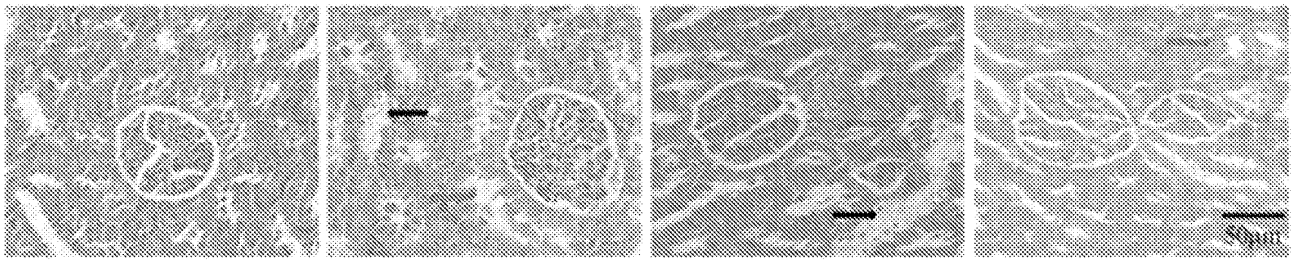


FIG. 40B

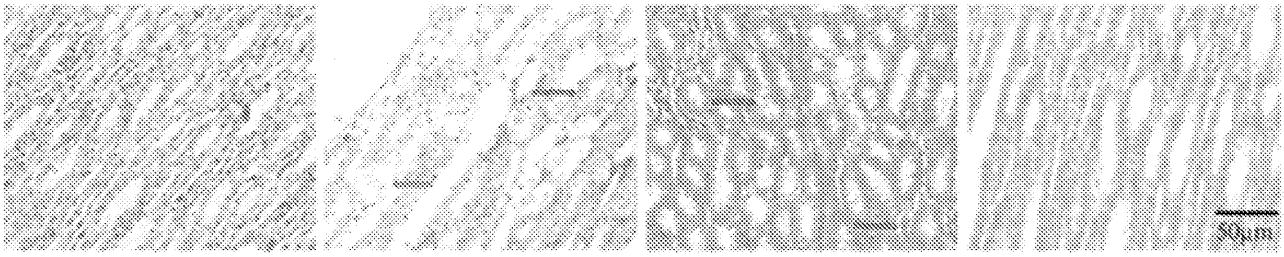


FIG. 41

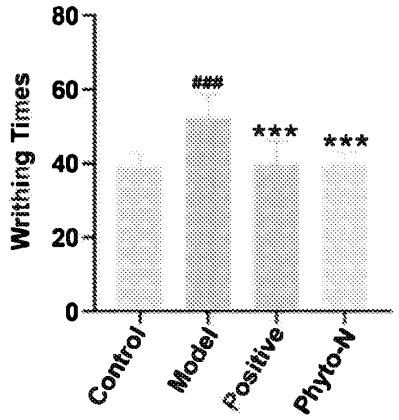


FIG. 42A

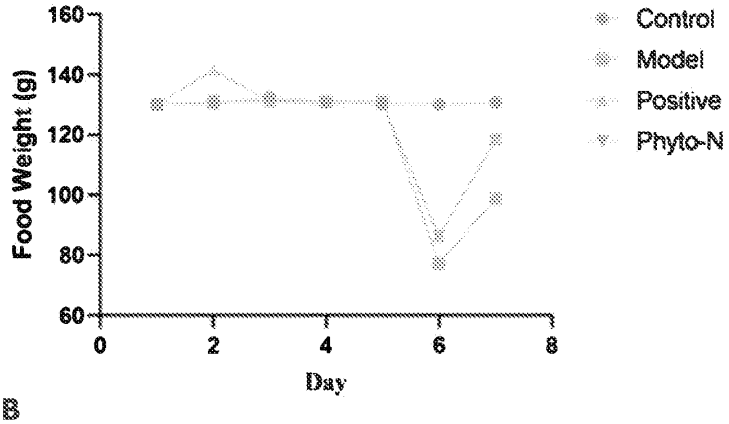


FIG. 43

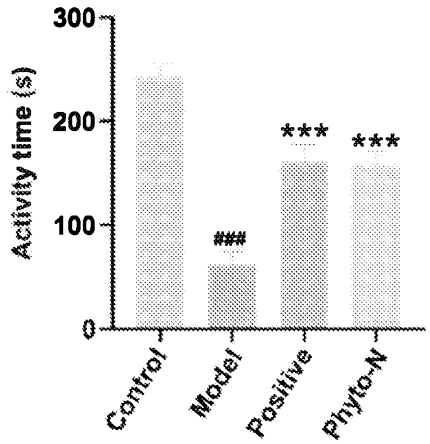


FIG. 42B

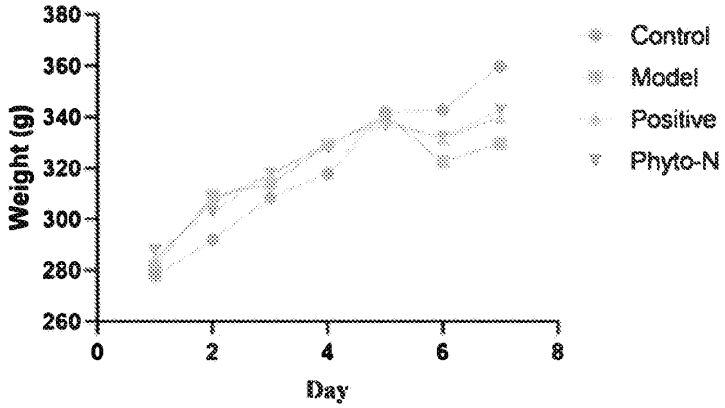


FIG. 44A

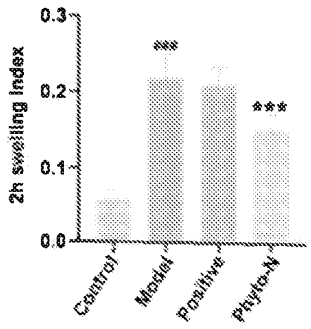


FIG. 44B

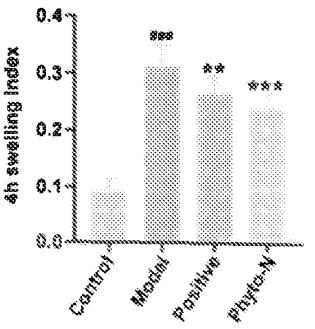


FIG. 44C

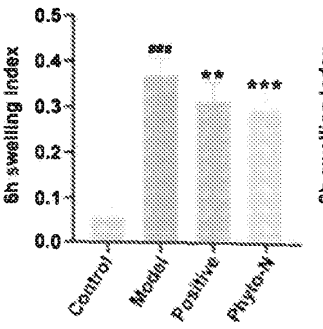


FIG. 44D

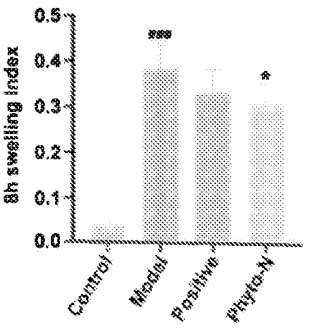


FIG. 44E

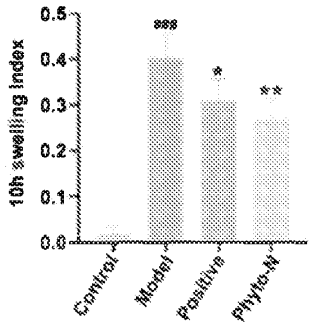


FIG. 44F

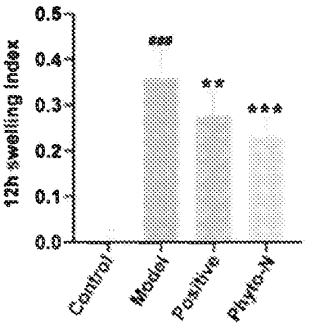


FIG. 44G

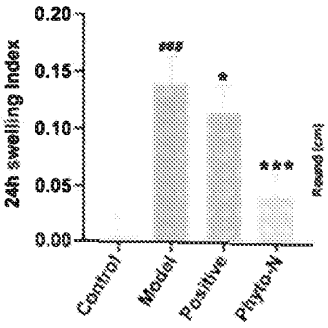


FIG. 44H

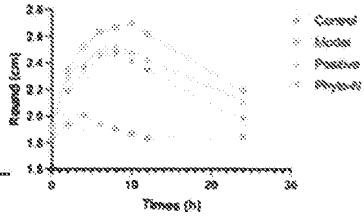


FIG. 45A

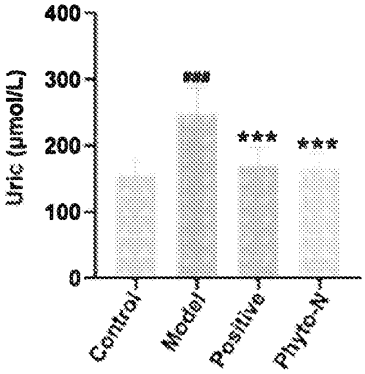


FIG. 45B

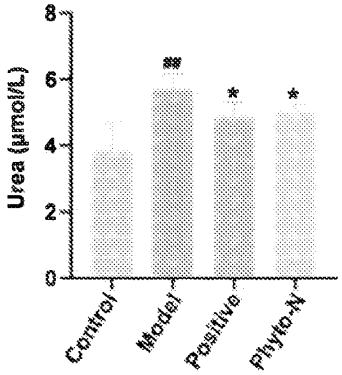


FIG. 45C

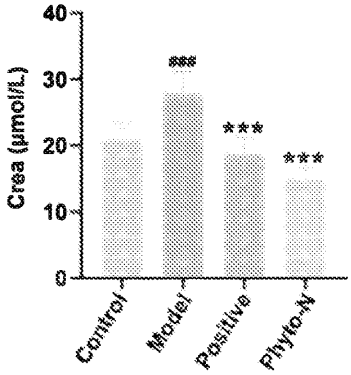


FIG. 45D

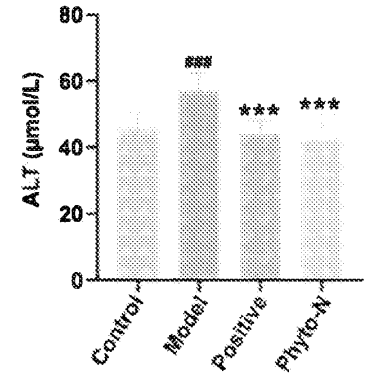


FIG. 45E

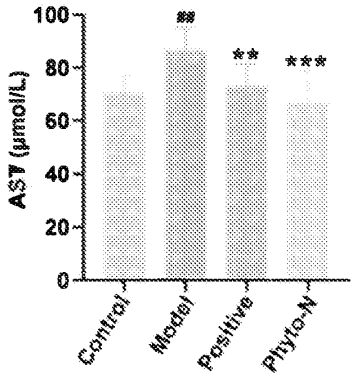


FIG. 46A

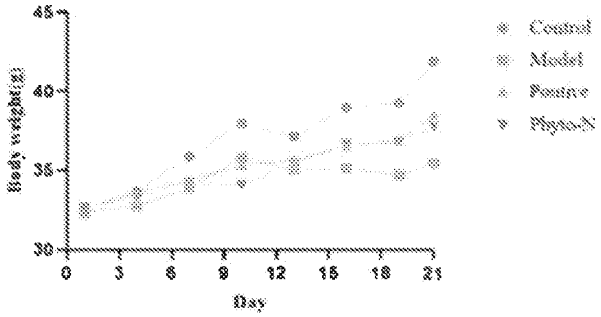


FIG. 64B

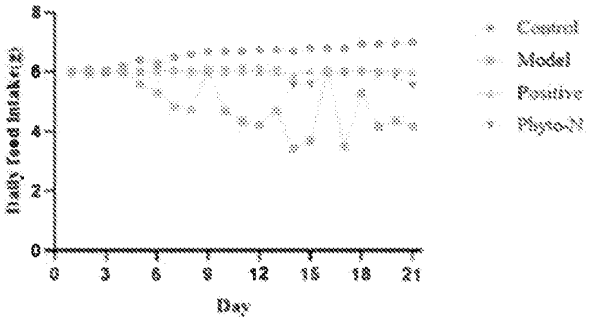


FIG. 47A

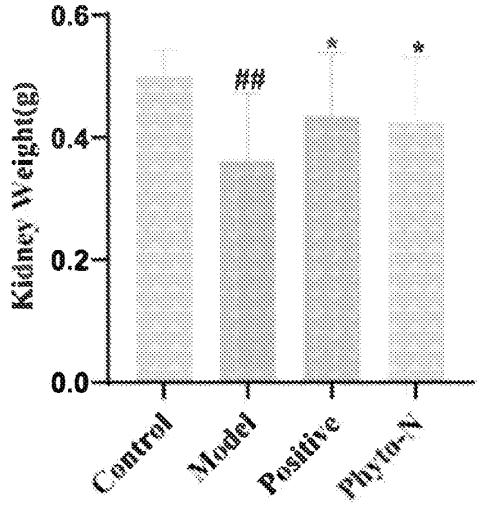


FIG. 47B

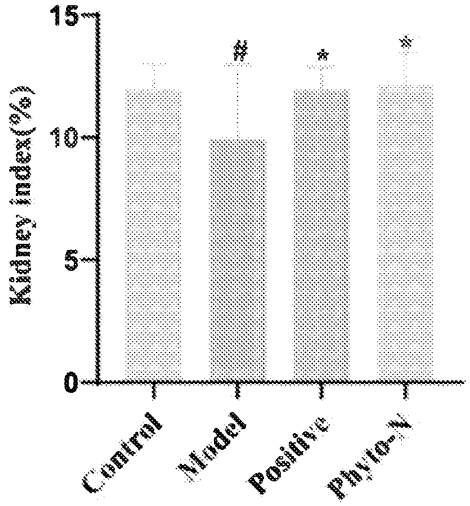


FIG. 48A

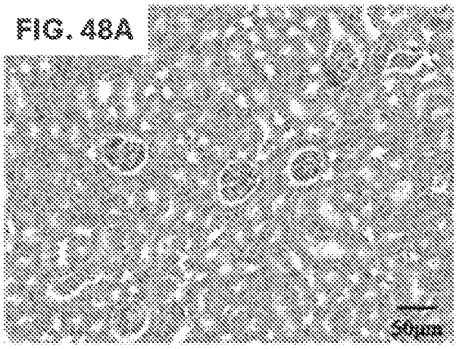


FIG. 48B

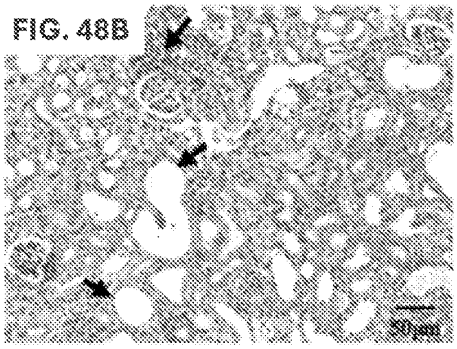


FIG. 48C

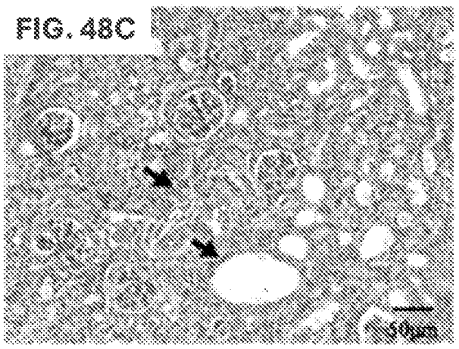


FIG. 48D

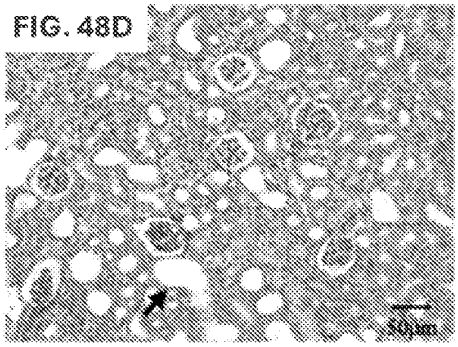


FIG. 49A

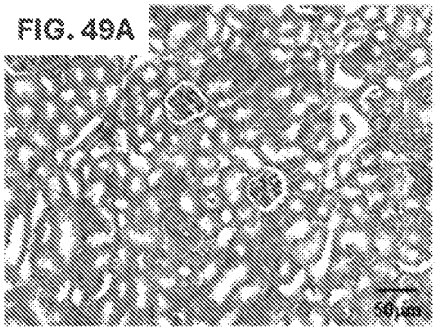


FIG. 49B

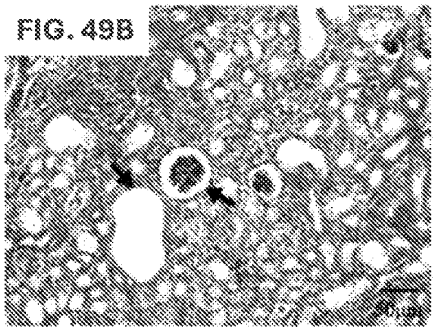


FIG. 49C

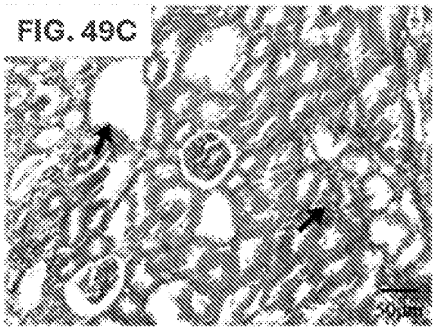


FIG. 49D

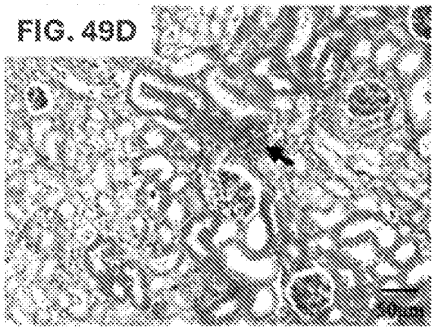


FIG. 50A

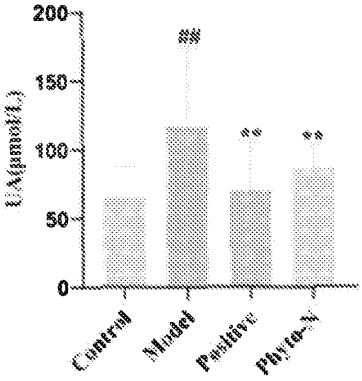


FIG. 50B

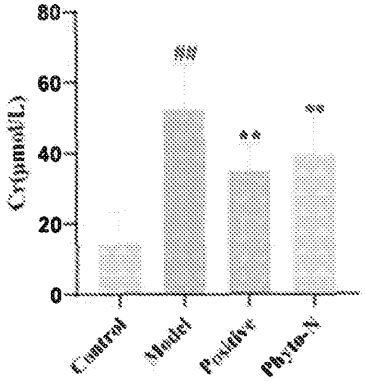


FIG. 50C

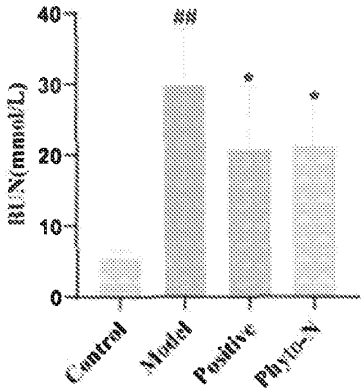


FIG. 51A

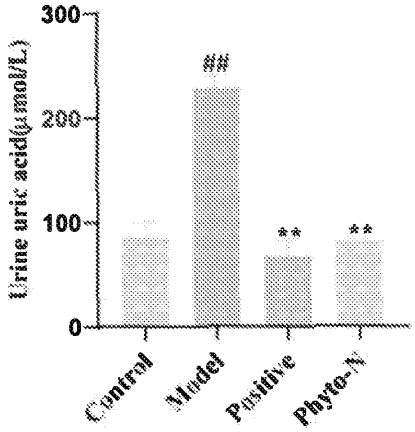


FIG. 51B

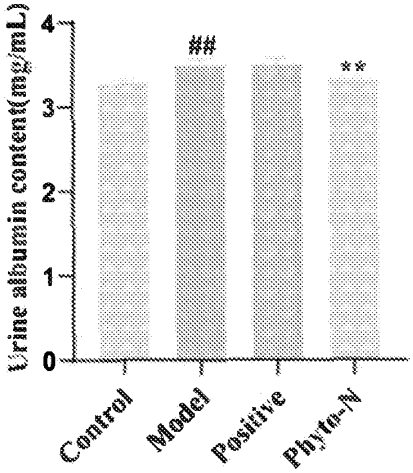


FIG. 52A

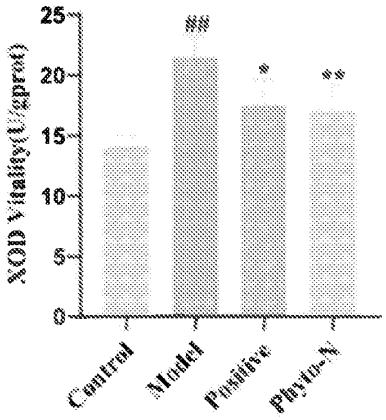


FIG. 52B

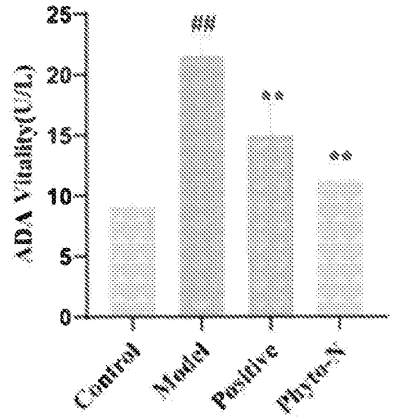


FIG. 52C

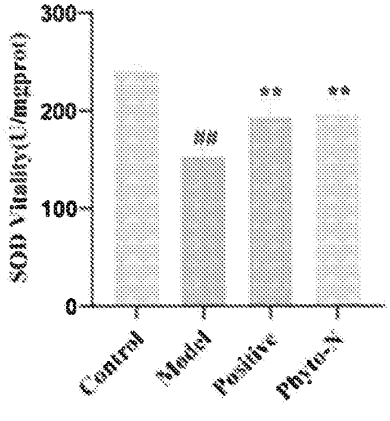


FIG. 53A

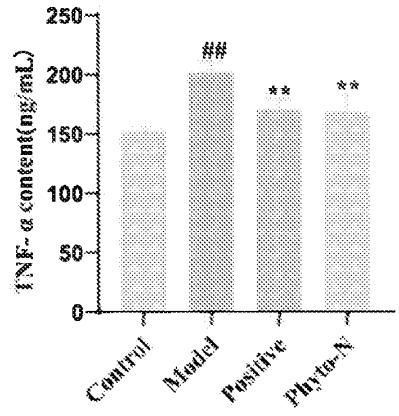


FIG. 53B

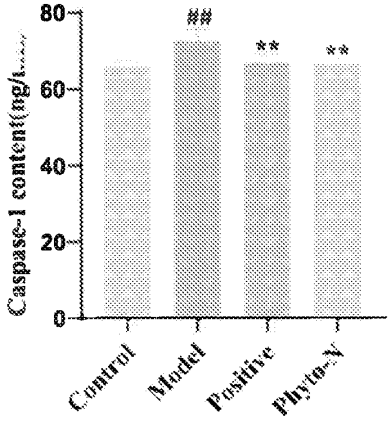


FIG. 54

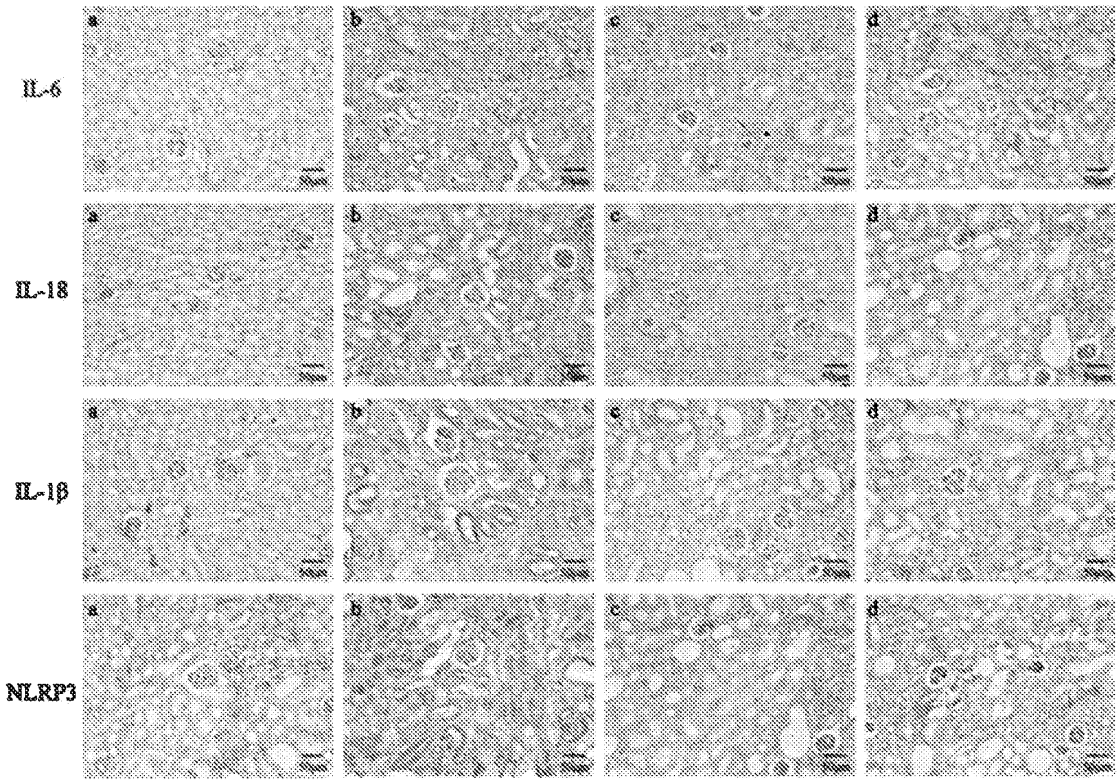


FIG. 55A

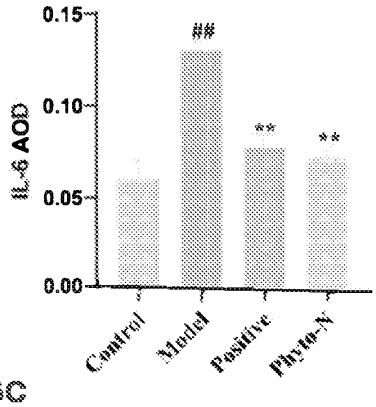


FIG. 55B

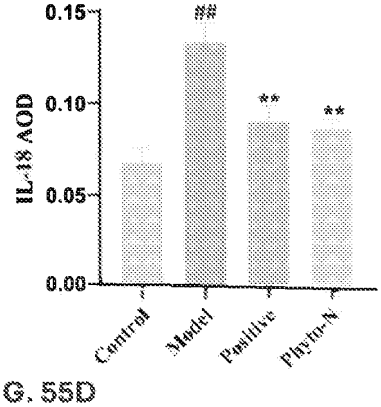


FIG. 55C

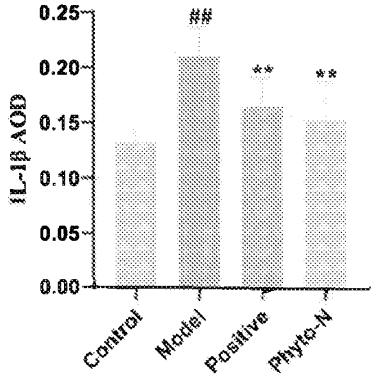


FIG. 55D

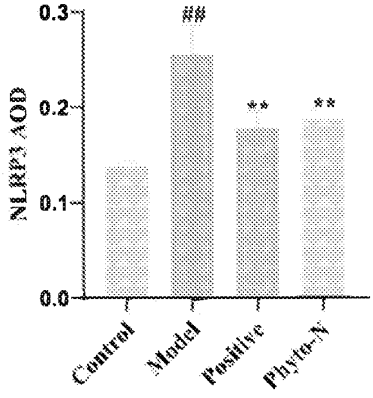


FIG. 56A

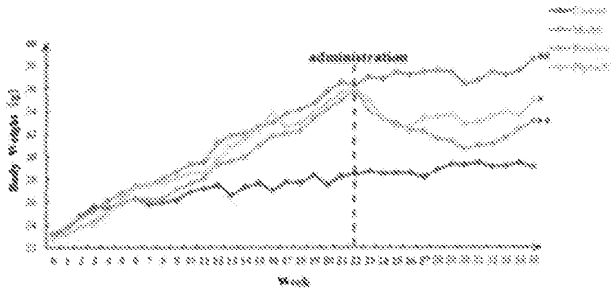


FIG. 56B

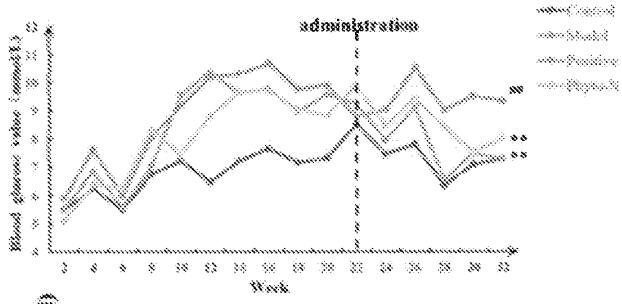


FIG. 56C

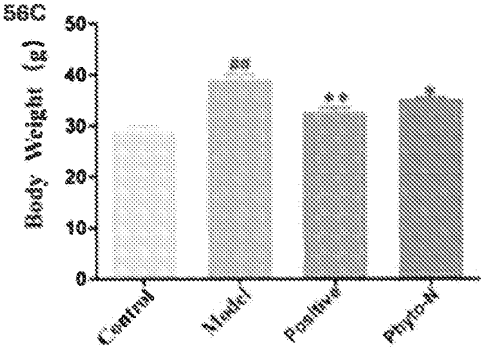


FIG. 56D

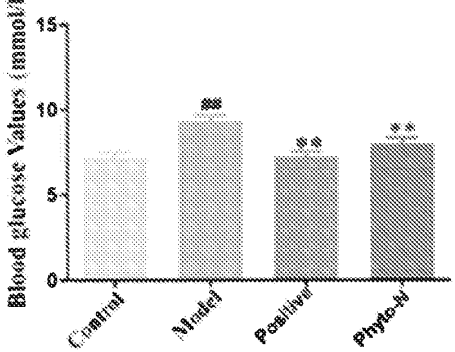


FIG. 57A

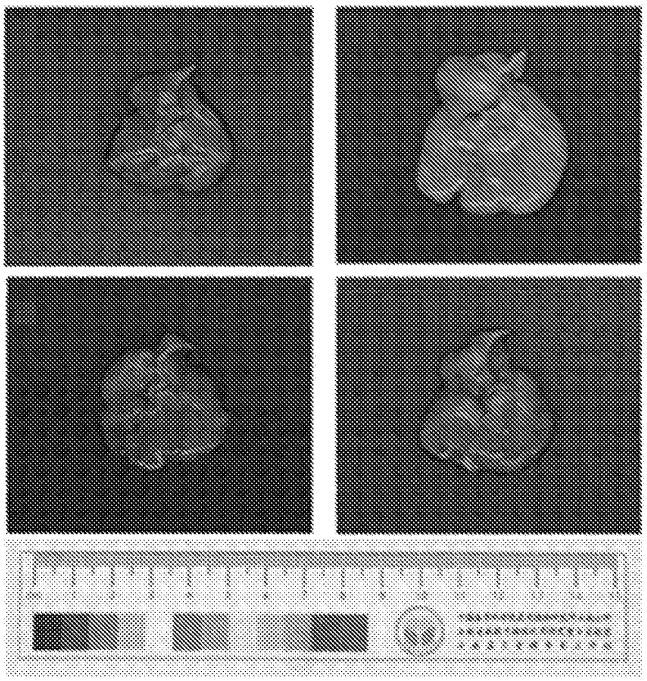


FIG. 57B

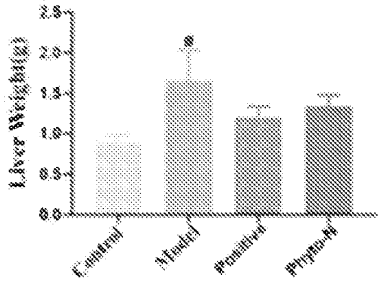


FIG. 57C

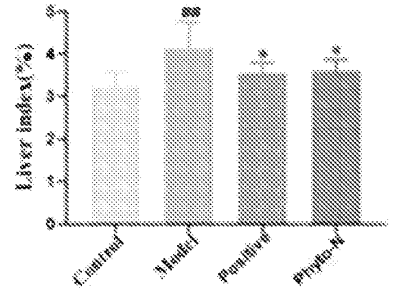


FIG. 58A

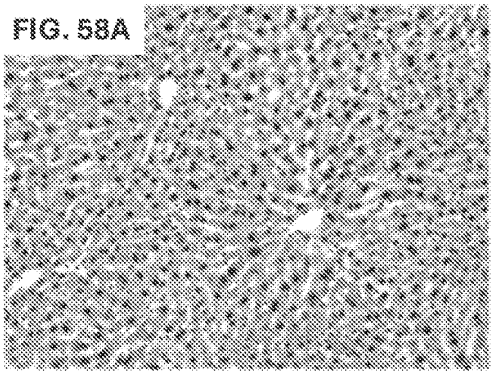


FIG. 58B

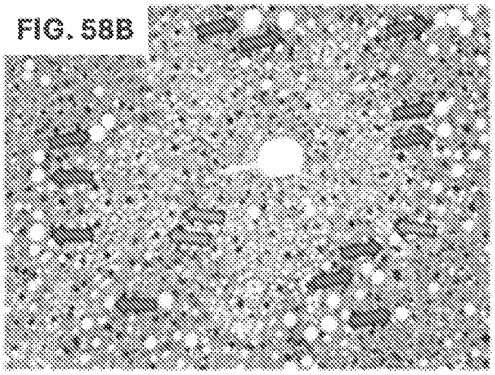


FIG. 58C

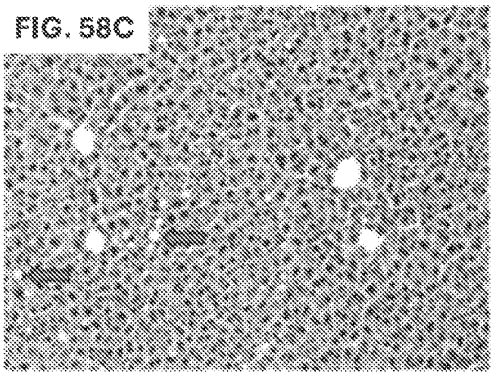


FIG. 58D

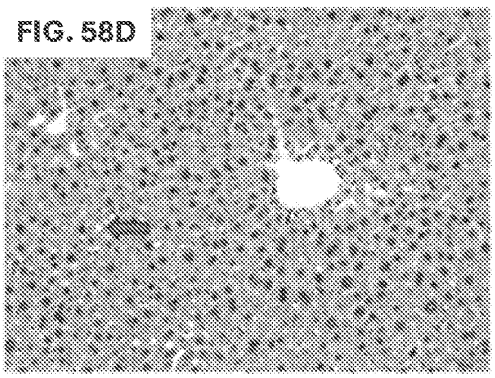


FIG. 59A

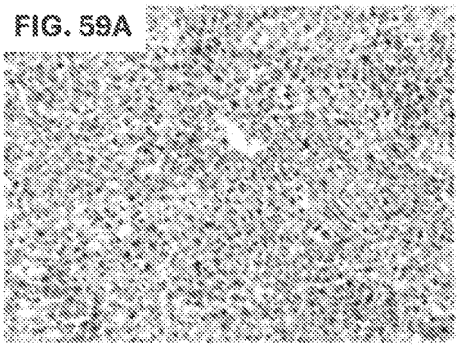


FIG. 59B

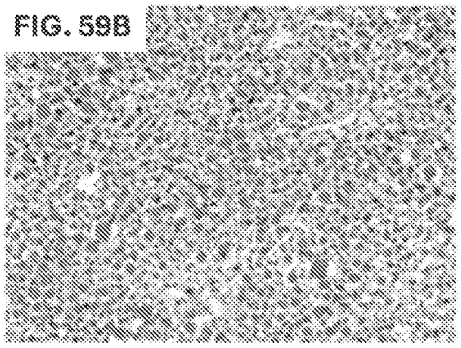


FIG. 59C

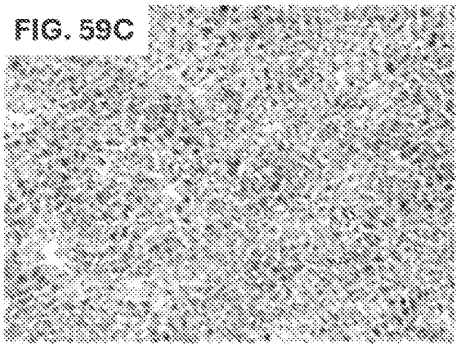


FIG. 59D

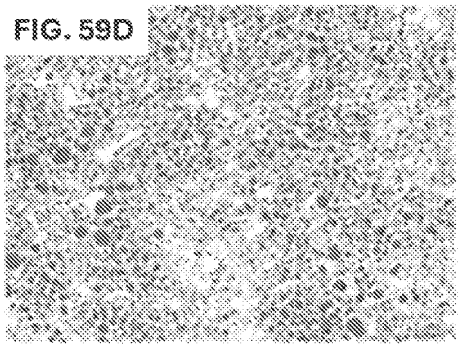


FIG. 60A

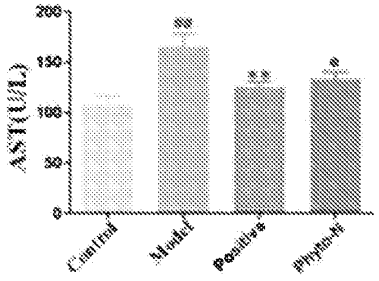


FIG. 60B

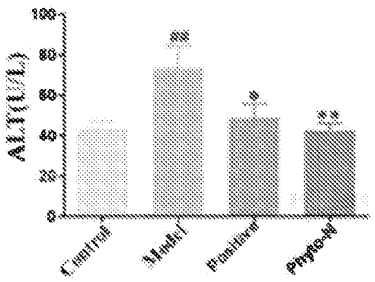


FIG. 60C

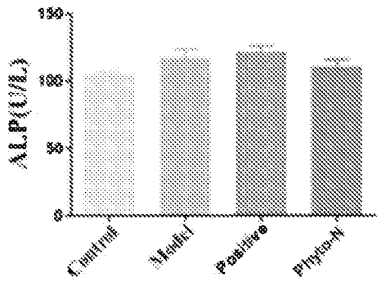


FIG. 60D

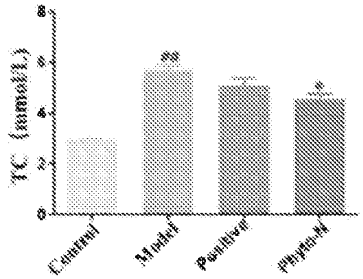


FIG. 60E

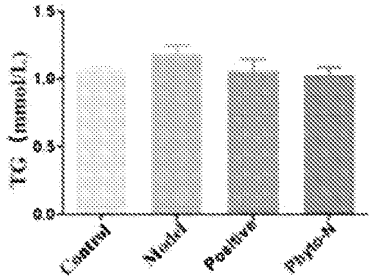


FIG. 61A

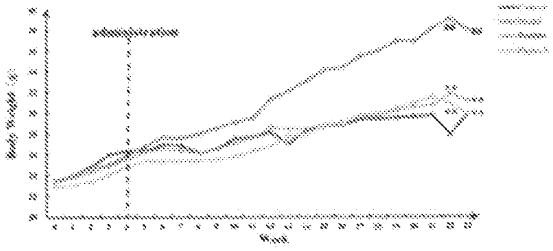


FIG. 61B

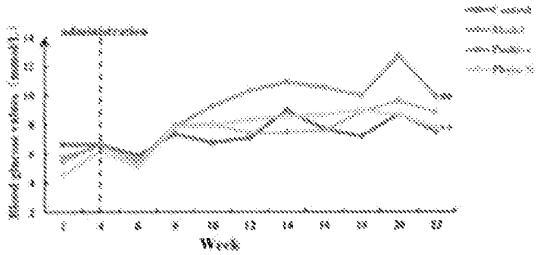


FIG. 61C

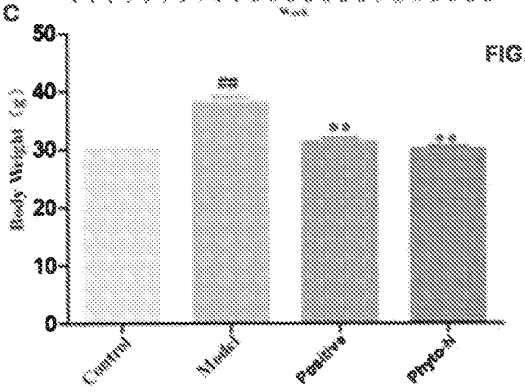


FIG. 61D

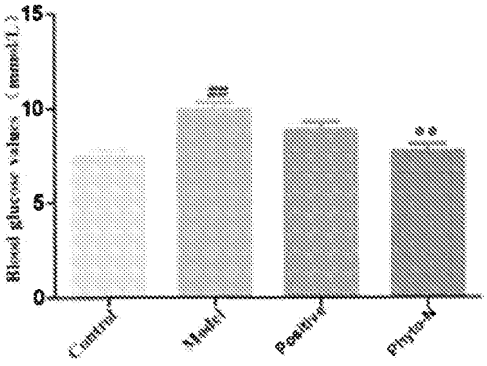


FIG. 62A

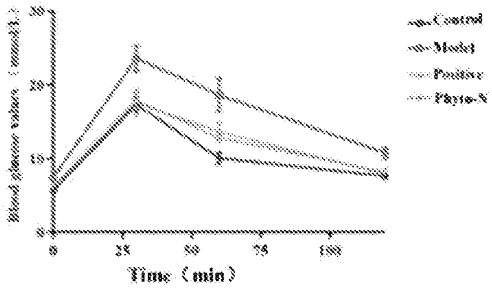


FIG. 62B

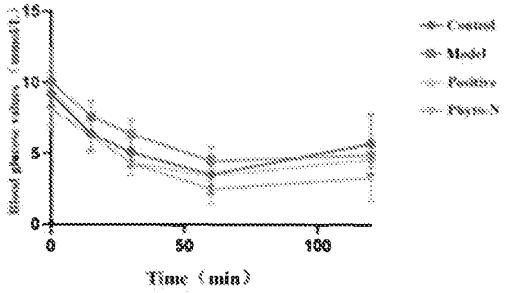


FIG. 62C

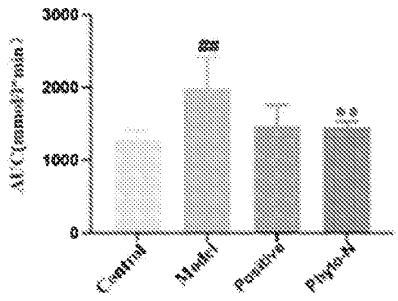


FIG. 62D

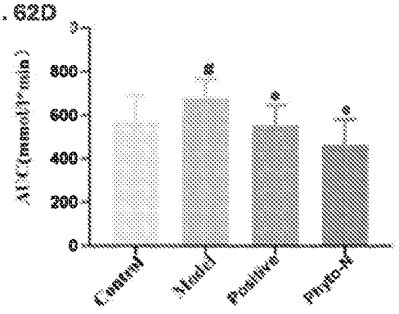


FIG. 63A

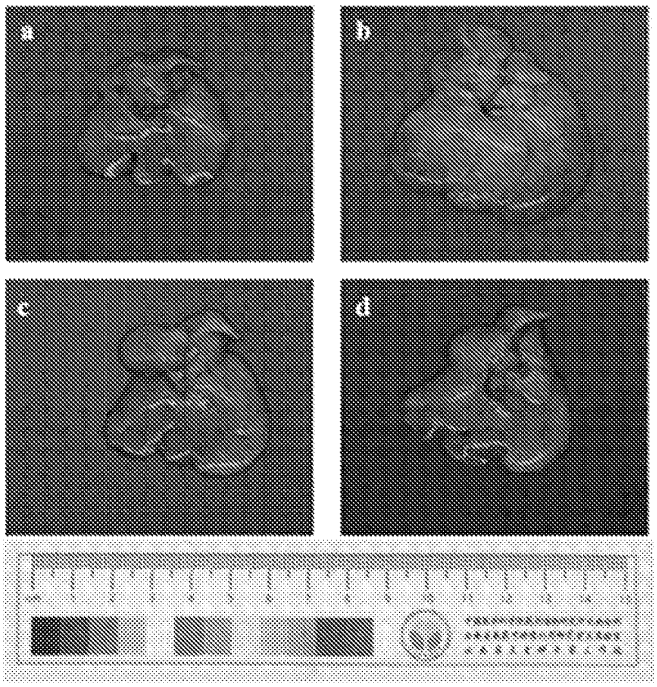


FIG. 63B

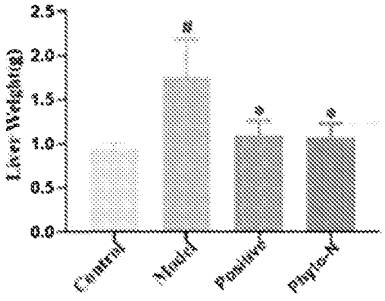


FIG. 63C

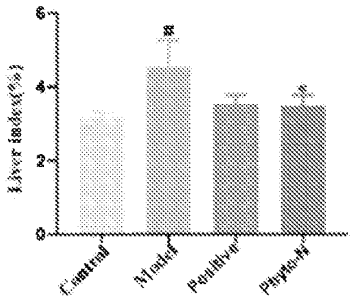


FIG. 64A

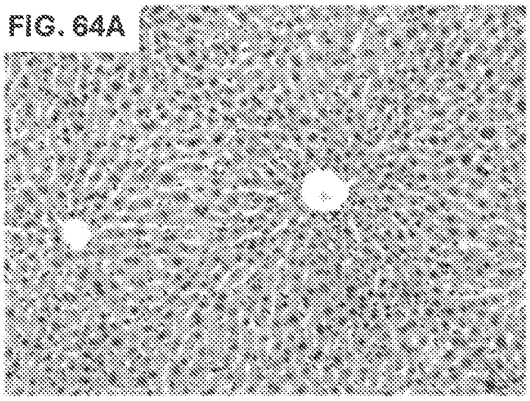


FIG. 64B

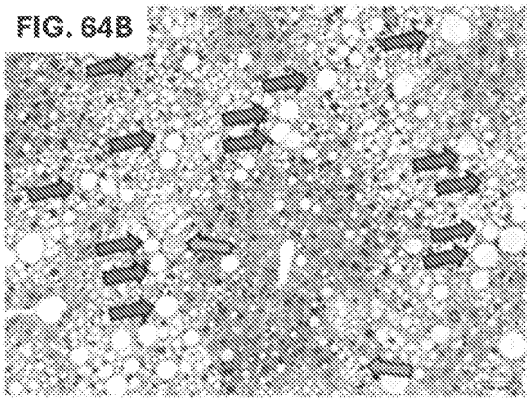


FIG. 64C

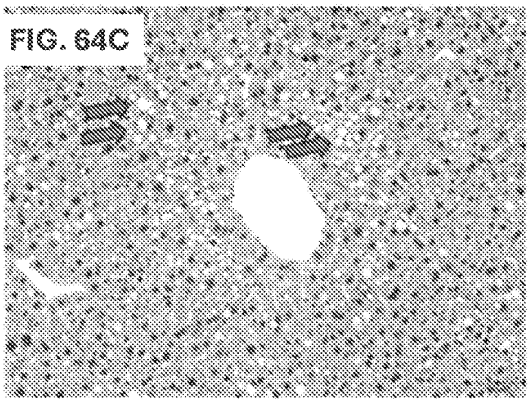


FIG. 64D

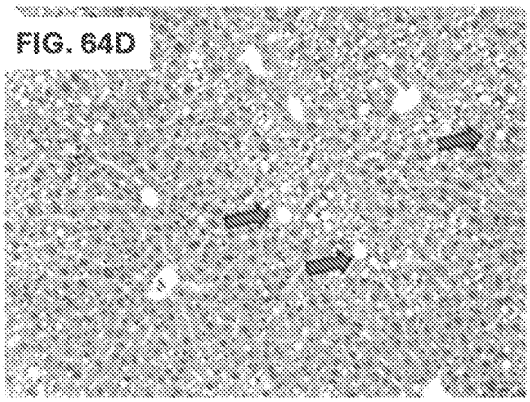


FIG. 65A

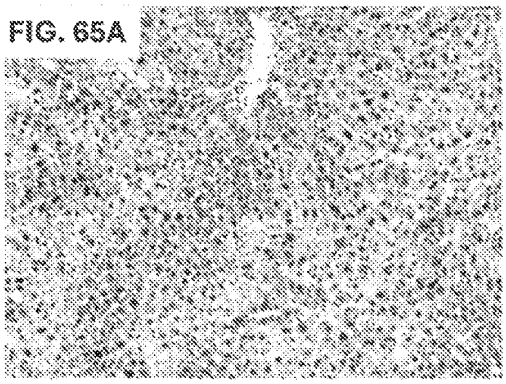


FIG. 65B

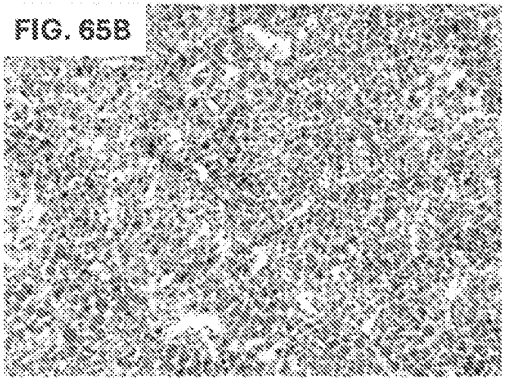


FIG. 65C

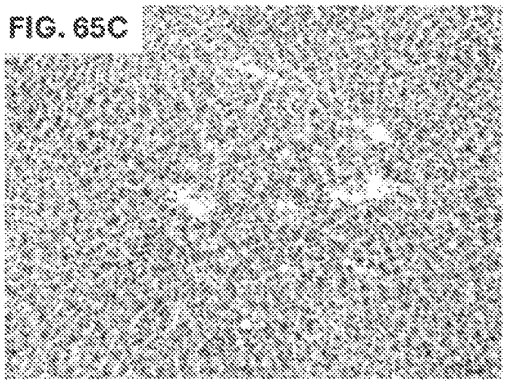


FIG. 65D

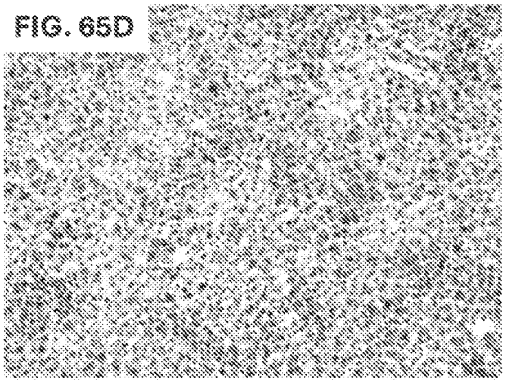


FIG. 66A

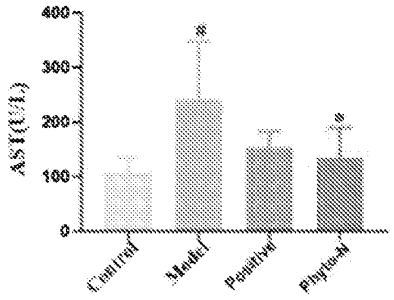


FIG. 66B

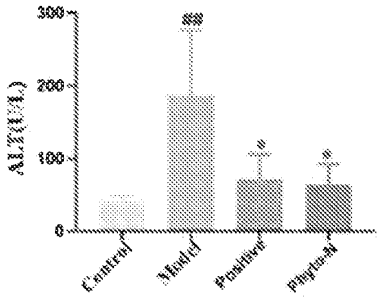


FIG. 66C

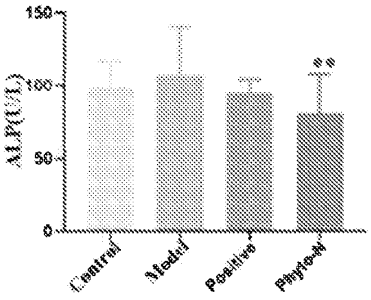


FIG. 66D

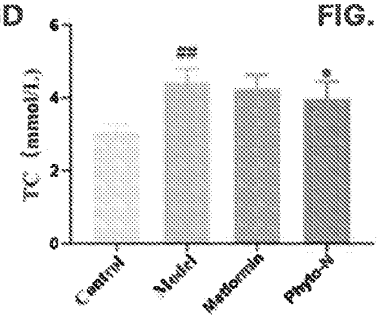


FIG. 66E

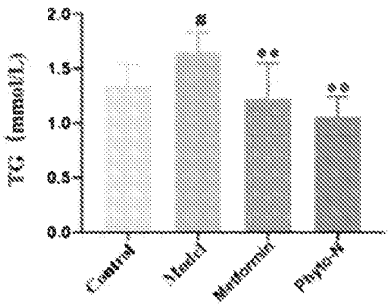


FIG. 67A

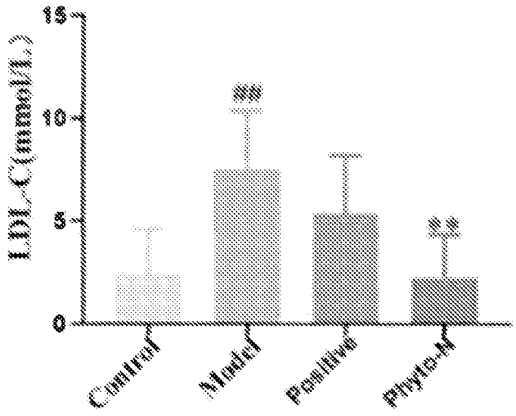


FIG. 67B

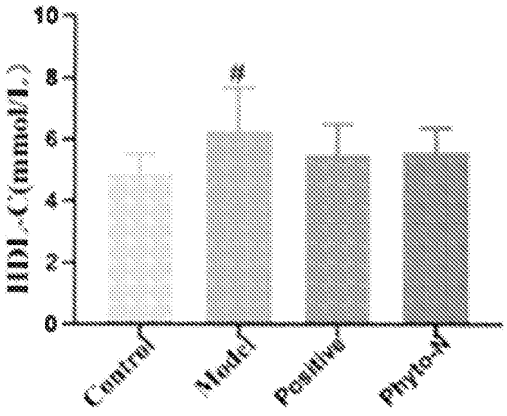


FIG. 68A

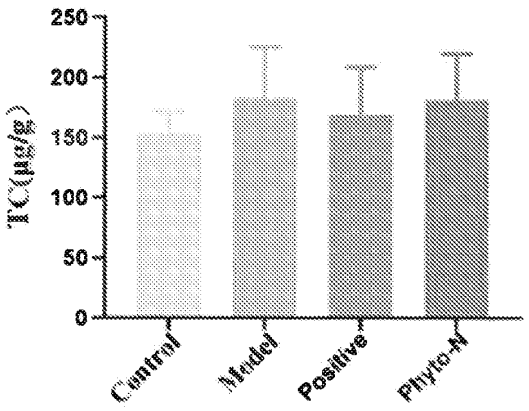


FIG. 68B

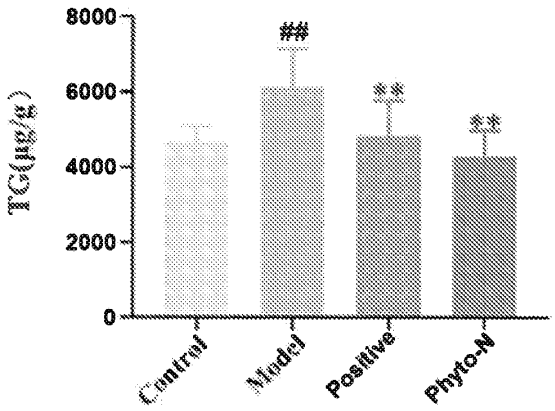
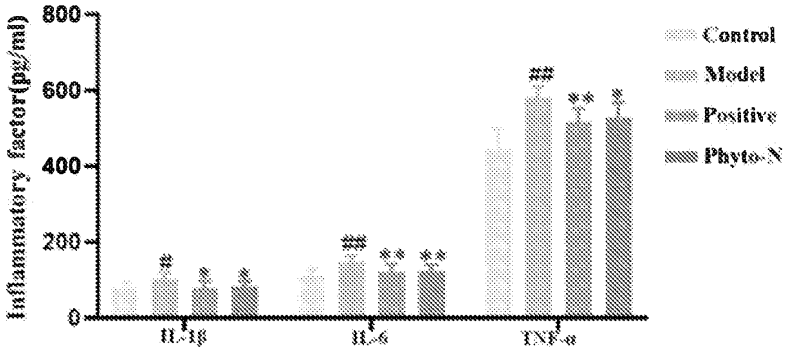


FIG. 69


Inflammatory factor(pg/ml)
800
600
400
200
0
IL-1β
IL-6
TNF-α
Control
Model
Positive
Phyto-N
#
##
**

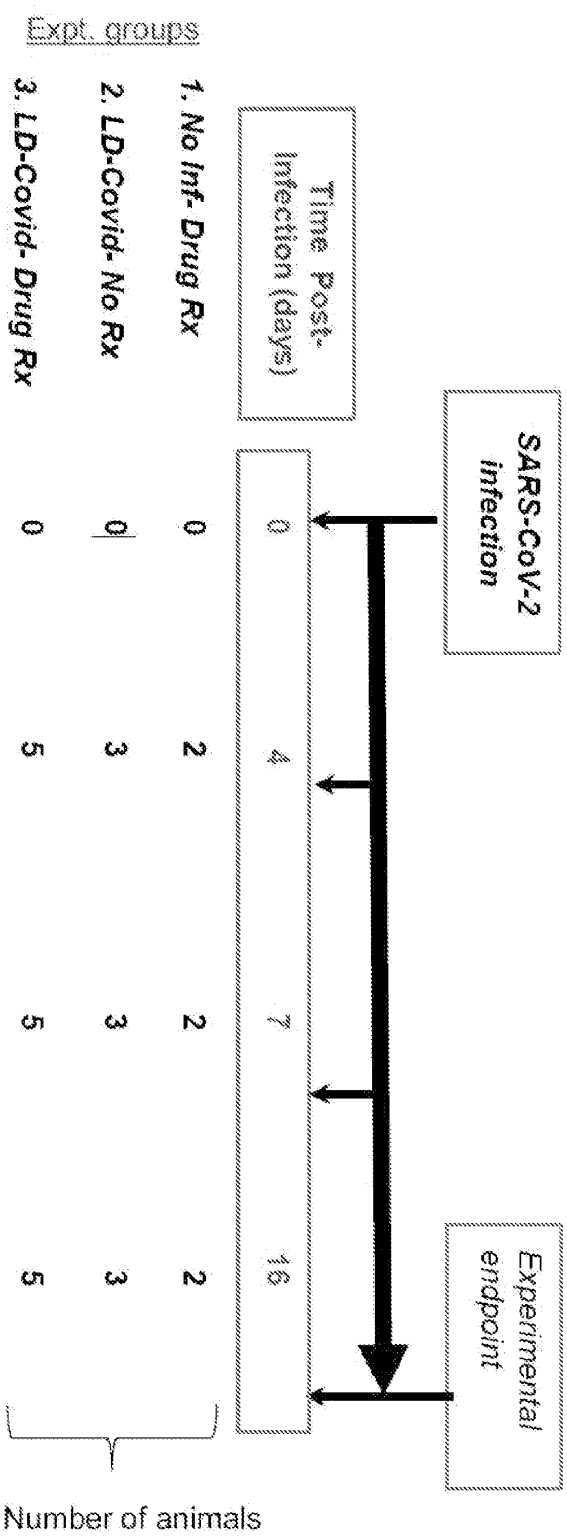

Expt. groups
1. No Inf- Drug Rx
2. LD-Covid- No Rx
3. LD-Covid- Drug Rx
Time Post-Infection (days)
0
4
7
16
SARS-CoV-2 infection
Experimental endpoint
0
2
2
2
0
3
3
3
0
5
5
5
Number of animals

FIG. 70

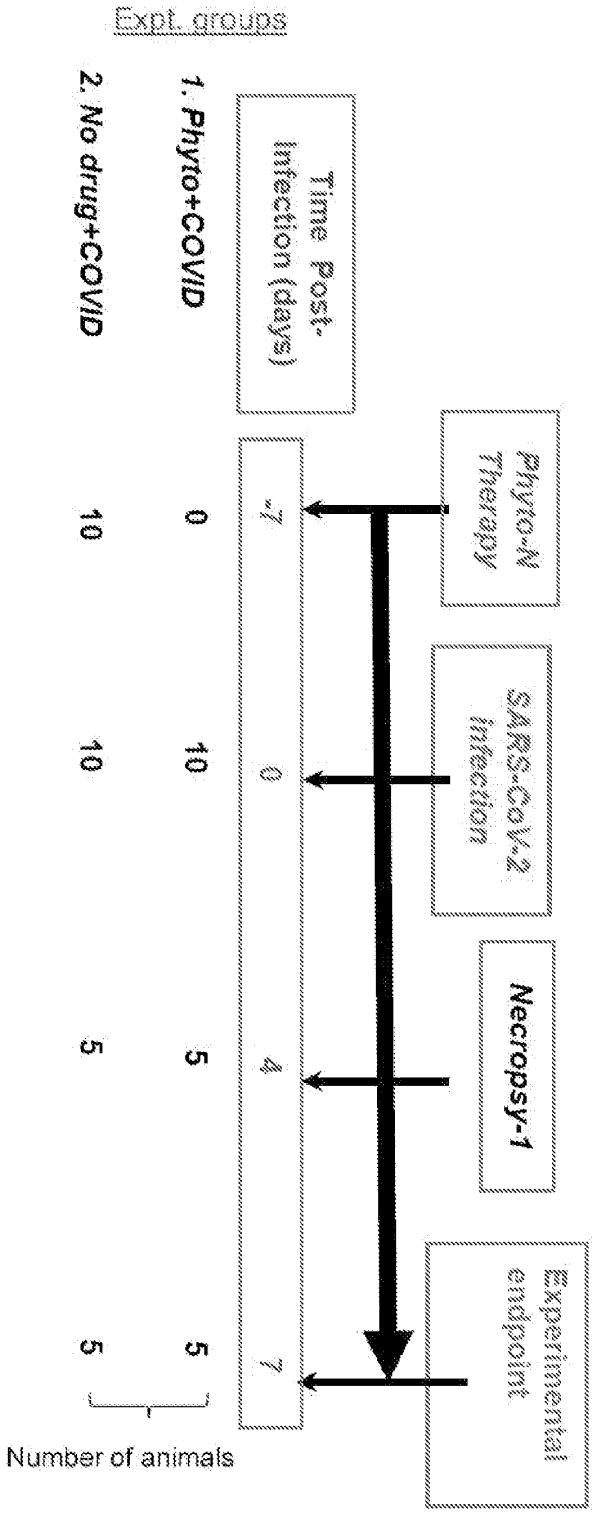

Expt. groups
1. Phyto+COVID
2. No drug+COVID
Time Post-Infection (days)
Phyto-N Therapy
SARS-CoV-2 infection
Necropsy-1
Experimental endpoint
-7
0
4
7
10
10
5
5
10
10
5
5
Number of animals

FIG. 71

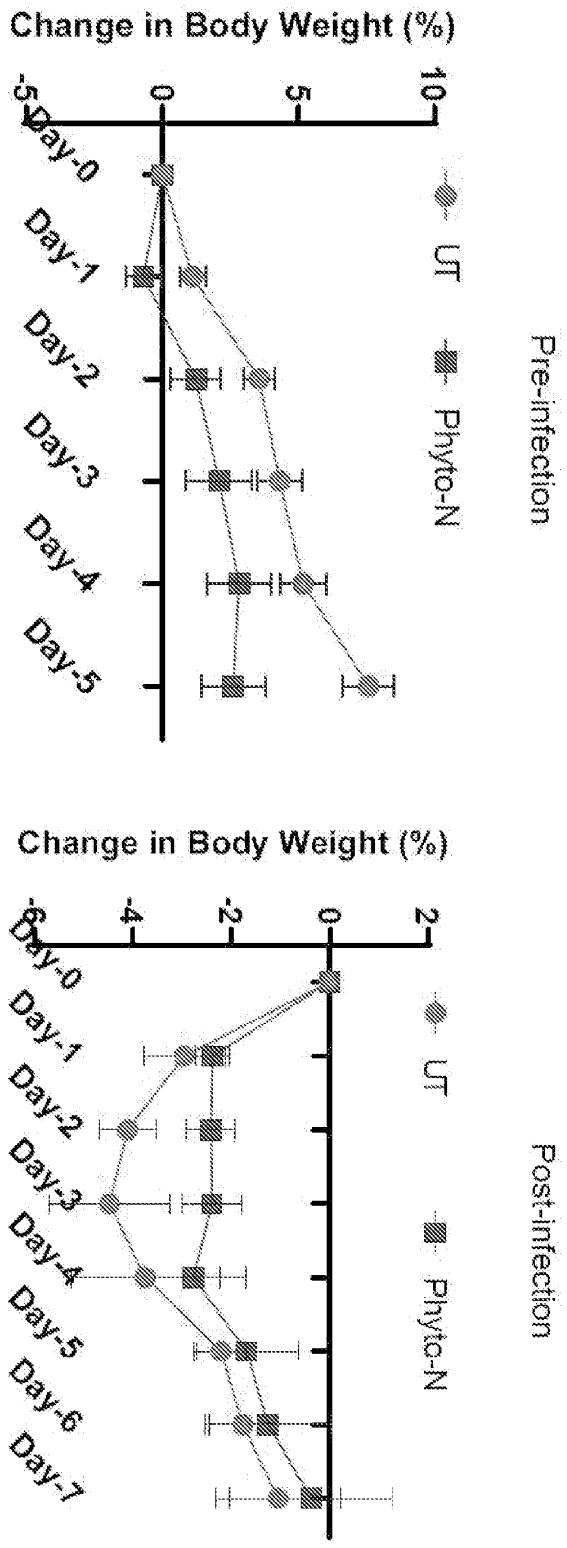

Change in Body Weight (%)
-5
0
5
10
Day-0
Day-1
Day-2
Day-3
Day-4
Day-5
UT
Phyto-N
Pre-infection
Change in Body Weight (%)
-6
-4
-2
0
2
Day-0
Day-1
Day-2
Day-3
Day-4
Day-5
Day-6
Day-7
UT
Phyto-N
Post-infection

FIG. 72

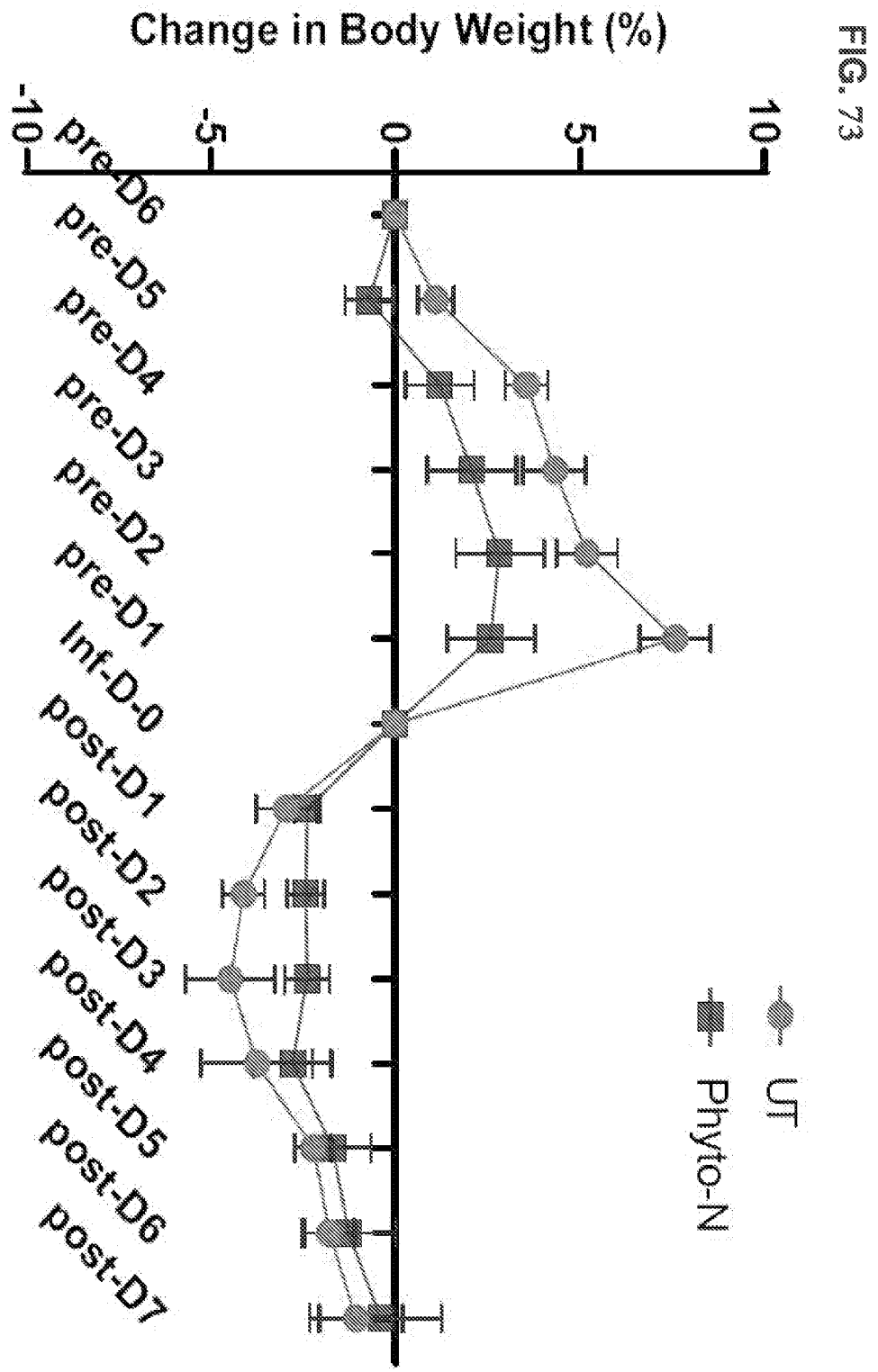

Change in Body Weight (%)
-10
-5
0
5
10
pre-D6
pre-D5
pre-D4
pre-D3
pre-D2
pre-D1
Inf-D-0
post-D1
post-D2
post-D3
post-D4
post-D5
post-D6
post-D7
UT
Phyto-N

FIG. 73

FIG. 74

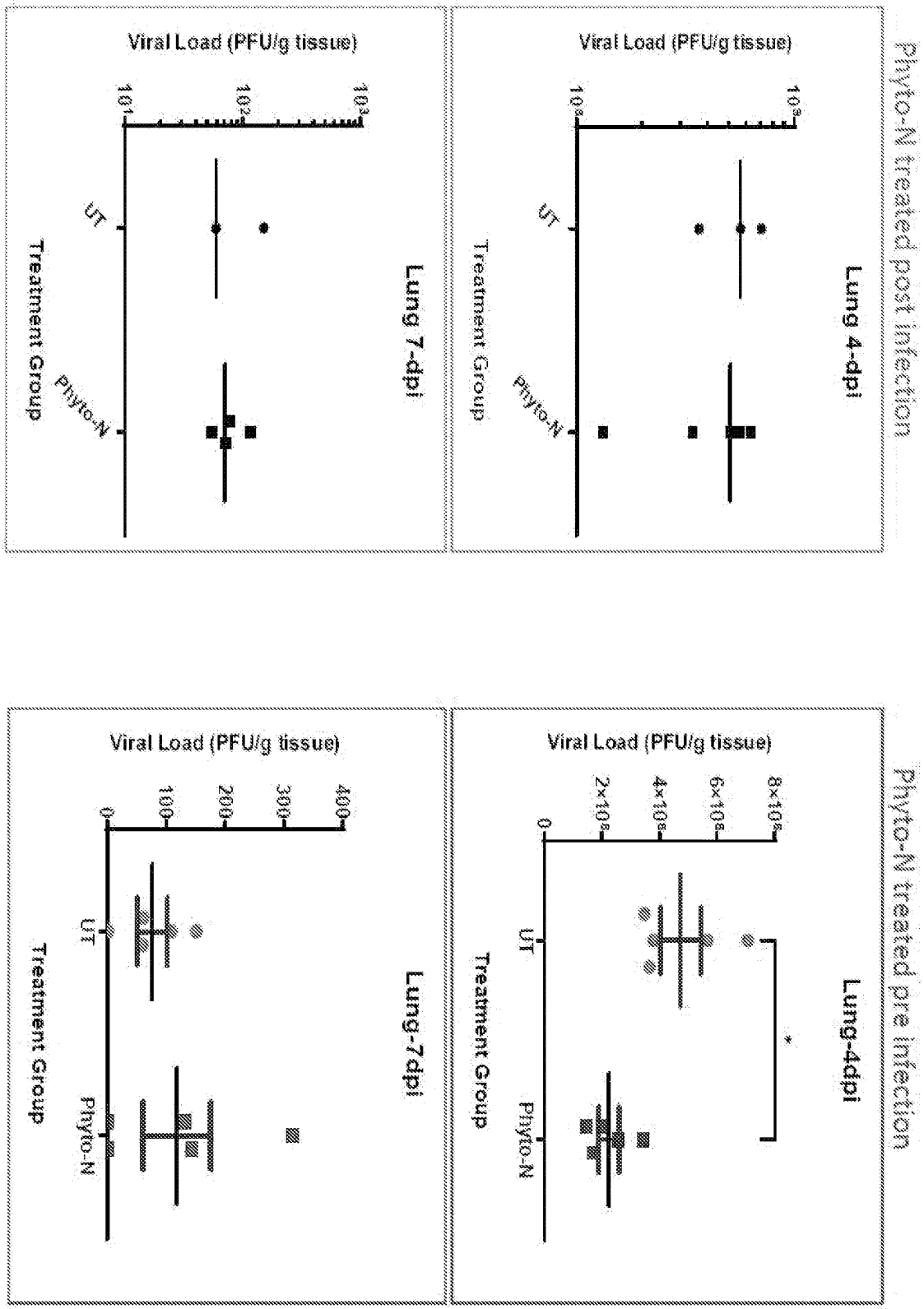
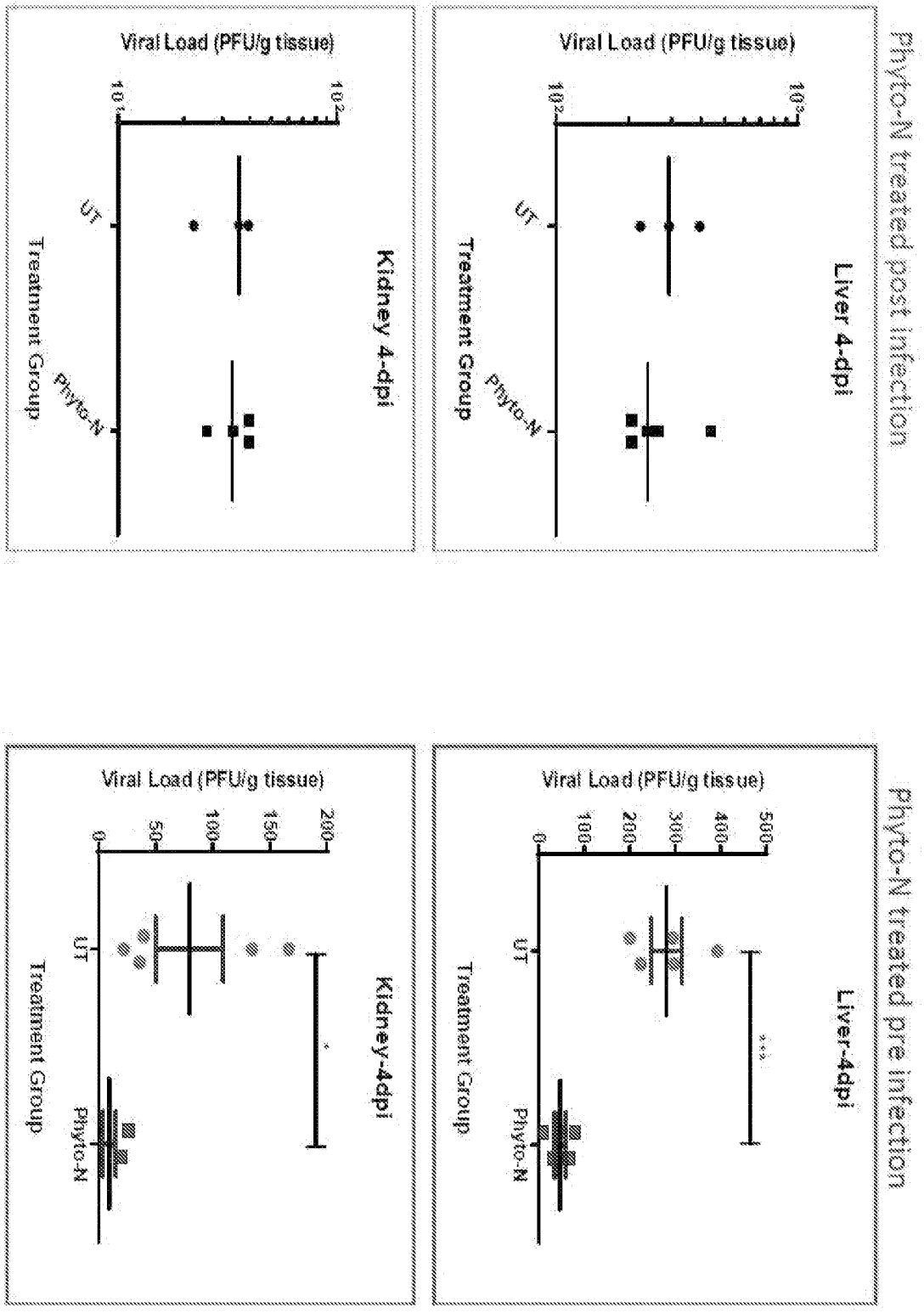

Phyto-N treated post infection
Lung 4-dpi
Viral Load (PFU/g tissue)
Treatment Group
UT
Phyto-N
Lung 7-dpi
Viral Load (PFU/g tissue)
Treatment Group
UT
Phyto-N
Phyto-N treated pre infection
Lung-4dpi
Viral Load (PFU/g tissue)
Treatment Group
UT
Phyto-N
Lung-7dpi
Viral Load (PFU/g tissue)
Treatment Group
UT
Phyto-N

FIG. 75


Phyto-N treated post infection
Liver 4-dpi
Kidney 4-dpi
Viral Load (PFU/g tissue)
Treatment Group
UT
Phyto-N
Phyto-N treated pre infection
Liver-4dpi
Kidney-4dpi
0
50
100
150
200
300
400
500
*
***

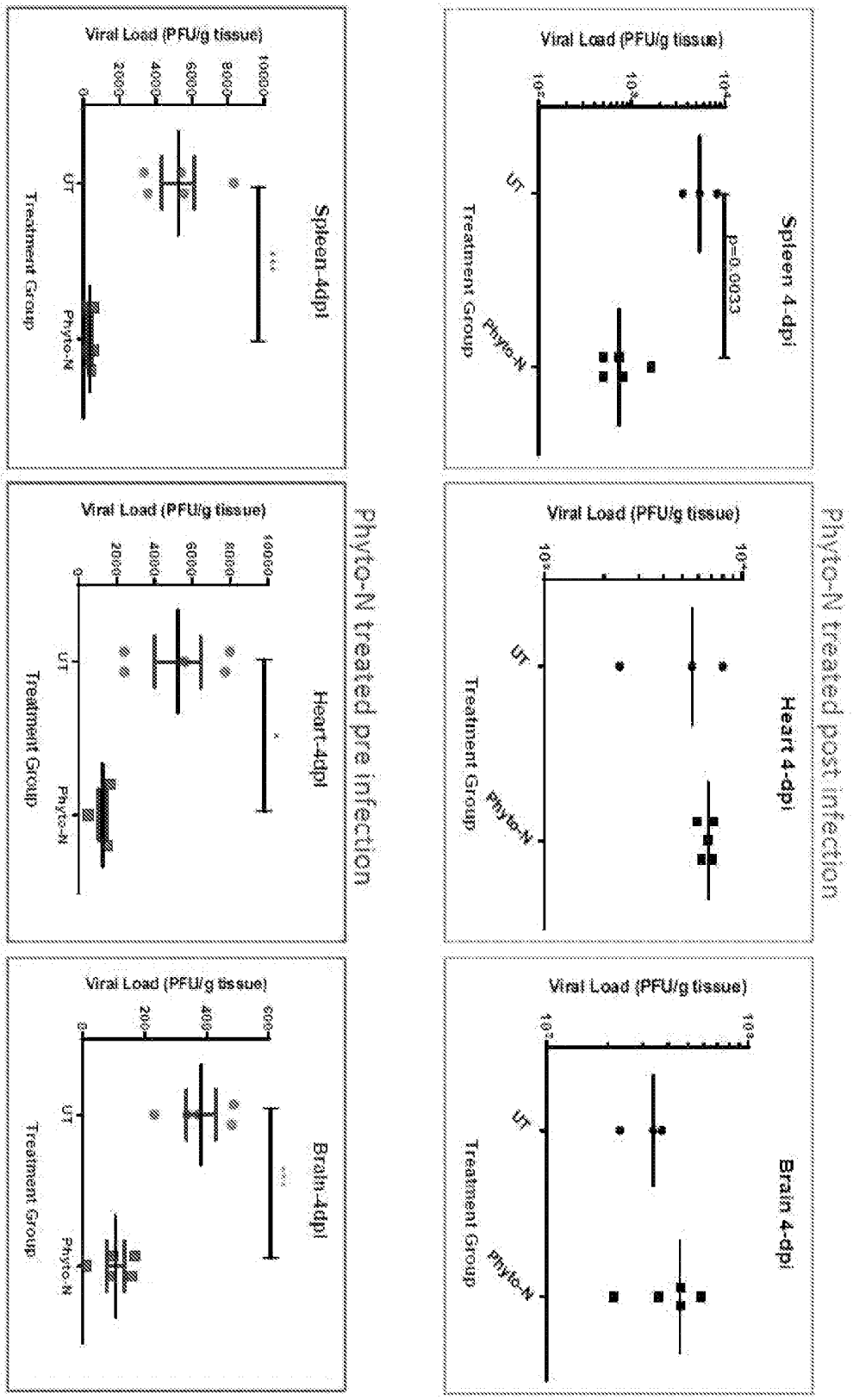

Phyto-N treated pre infection
Phyto-N treated post infection
Viral Load (PFU/g tissue)
Spleen-4dpi
Heart-4dpi
Brain-4dpi
Spleen 4-dpi
Heart 4-dpi
Brain 4-dpi
Treatment Group
UT
Phyto-N
p=0.0033

FIG. 76

FIG. 77

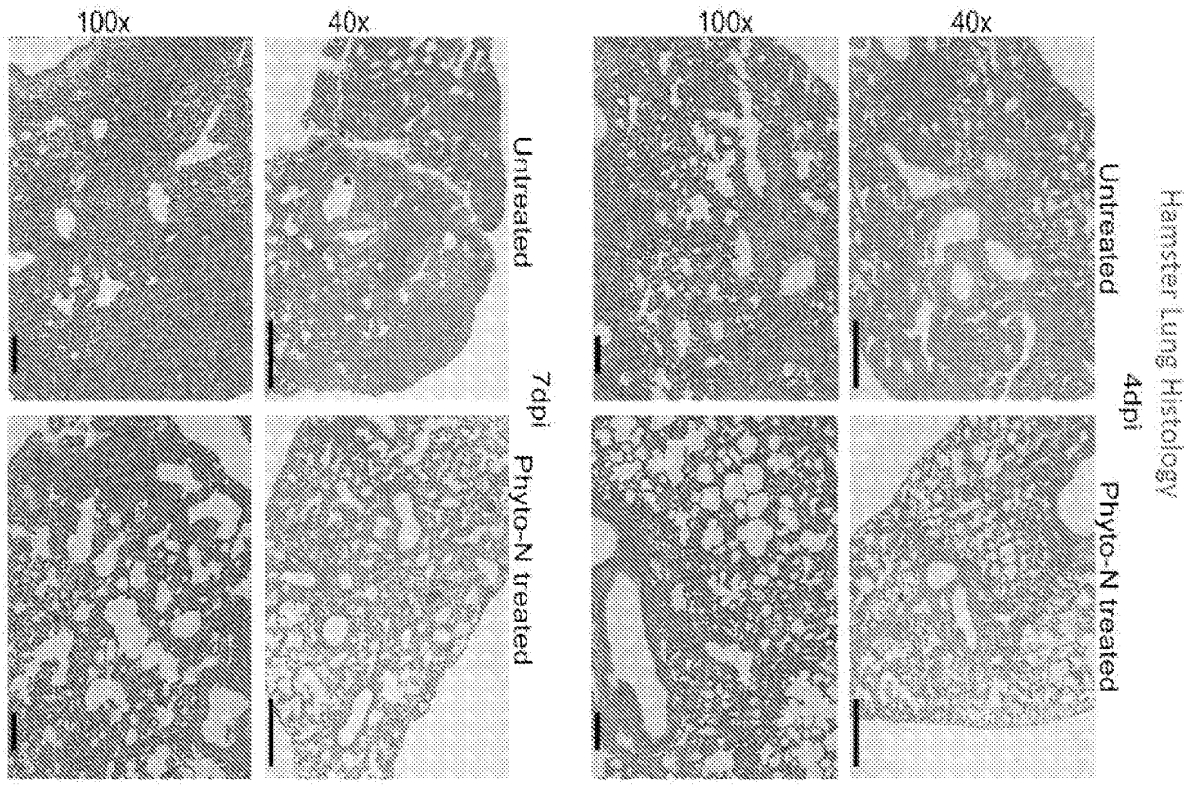

Hamster Lung Histology
4dpi
7dpi
100x
40x
Untreated
Phyto-N treated

FIG. 78

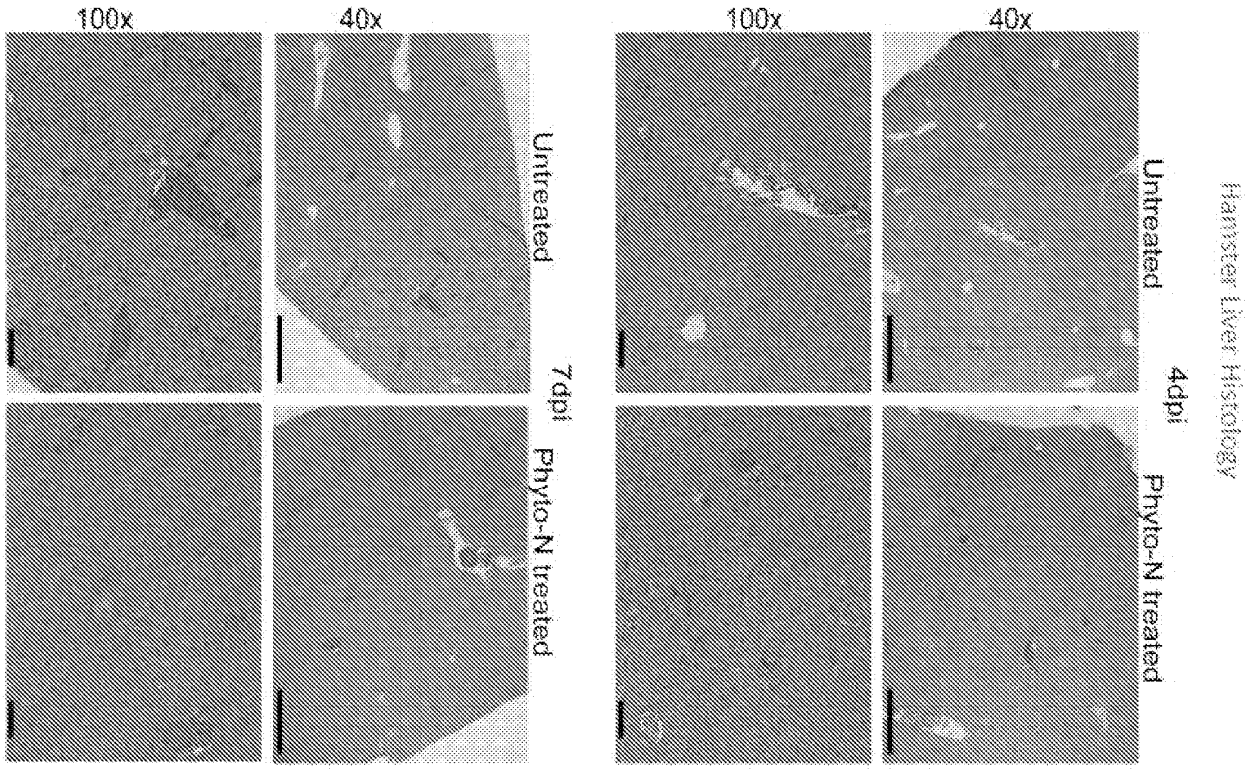

Hamster Liver Histology
100x
40x
Untreated
4dpi
Phyto-N treated
100x
40x
Untreated
7dpi
Phyto-N treated

FIG. 79

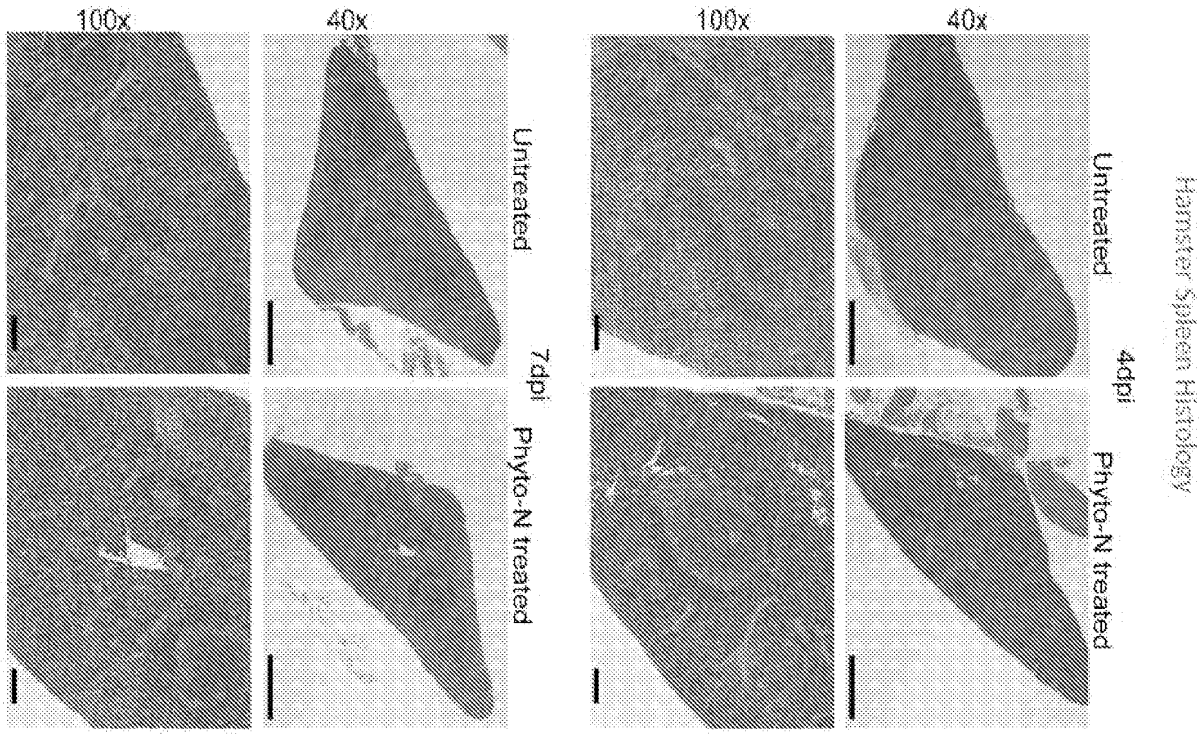

Hamster Spleen Histology
100x
40x
100x
40x
Untreated
4dpi
Phyto-N treated
Untreated
7dpi
Phyto-N treated

FIG. 80

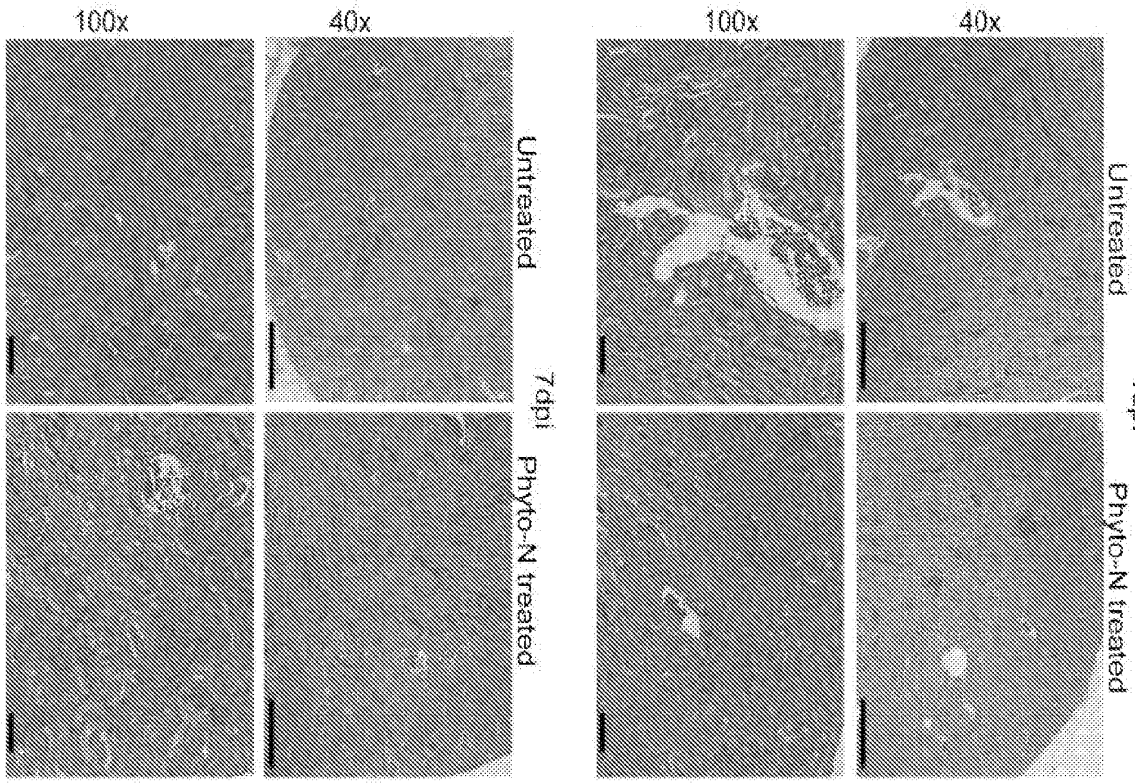
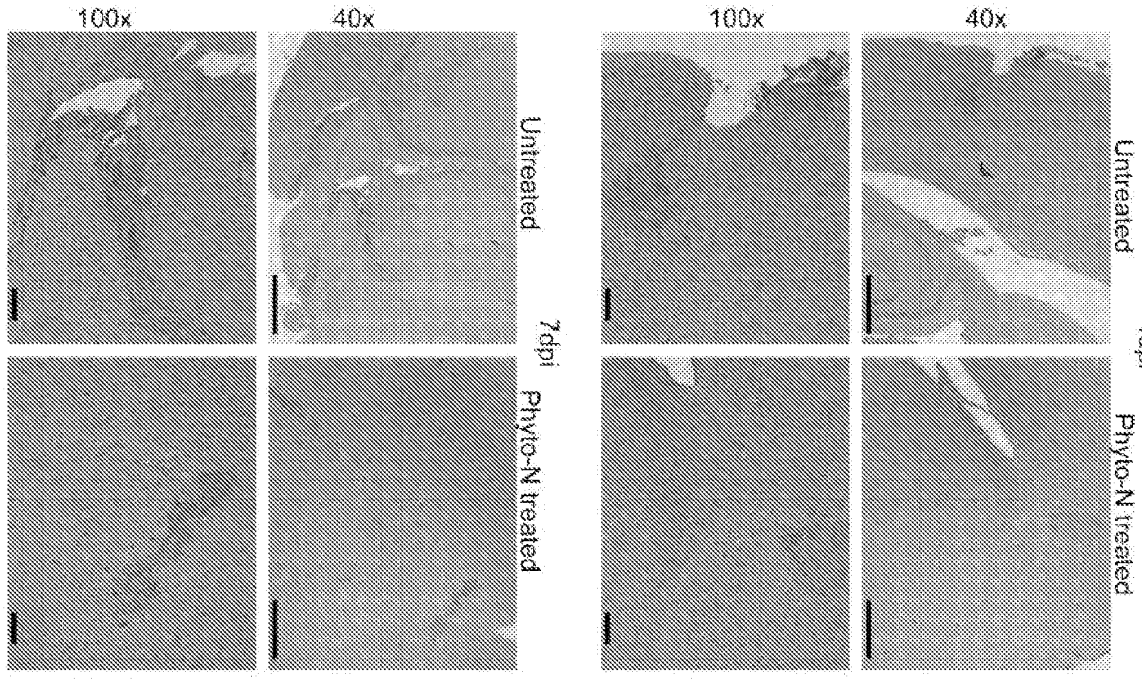

Hamster Kidney Histology
100x
40x
100x
40x
Untreated
4dpi
Phyto-N treated
Untreated
7dpi
Phyto-N treated

FIG. 81


Hamster Brain Histology
100x
40x
100x
40x
Untreated
4dpi
Phyto-N treated
Untreated
7dpi
Phyto-N treated

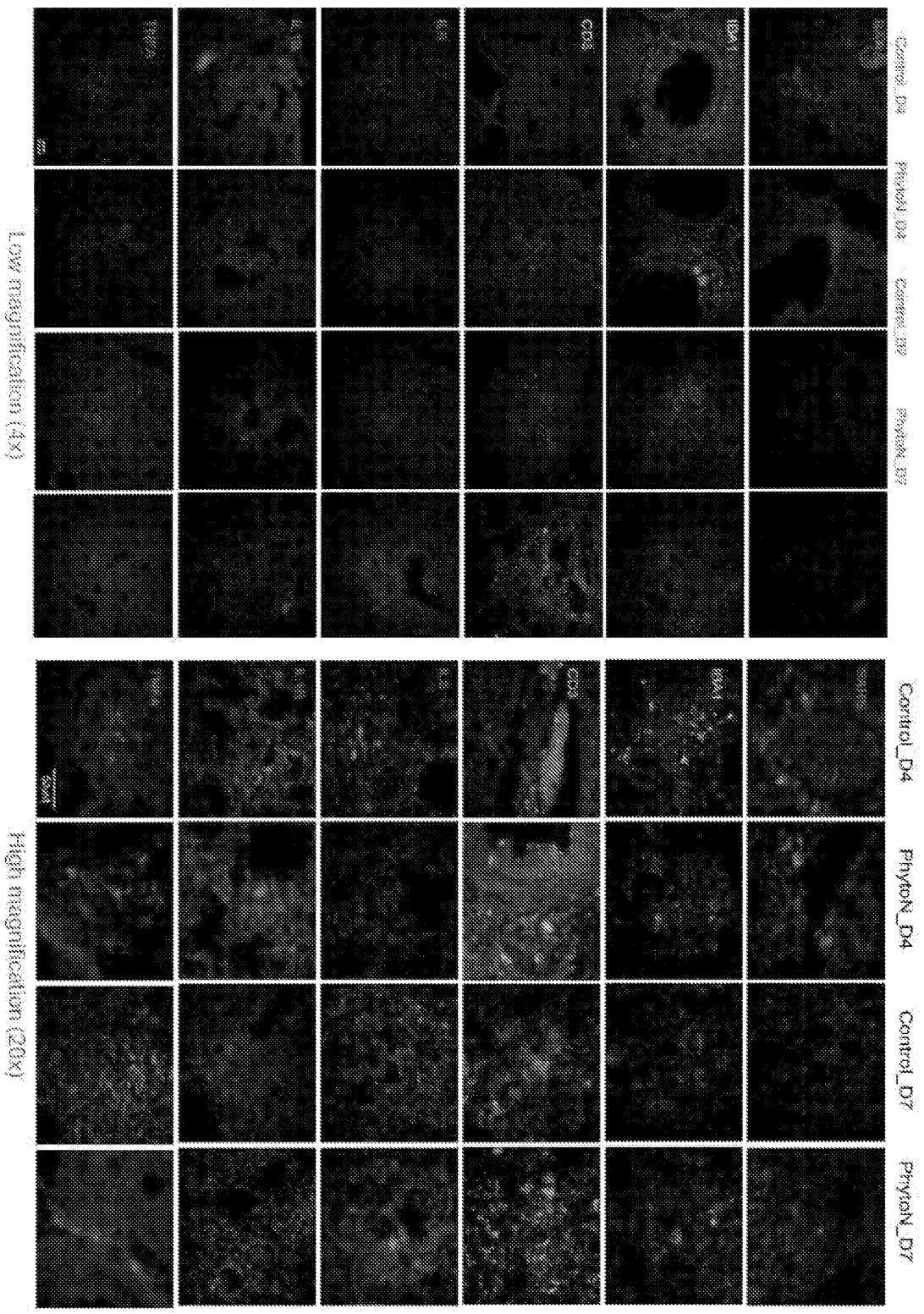

Control_D4
PhytoN_D4
Control_D7
PhytoN_D7
Low magnification (4x)
High magnification (20x)
50um

FIG. 82

FIG. 83

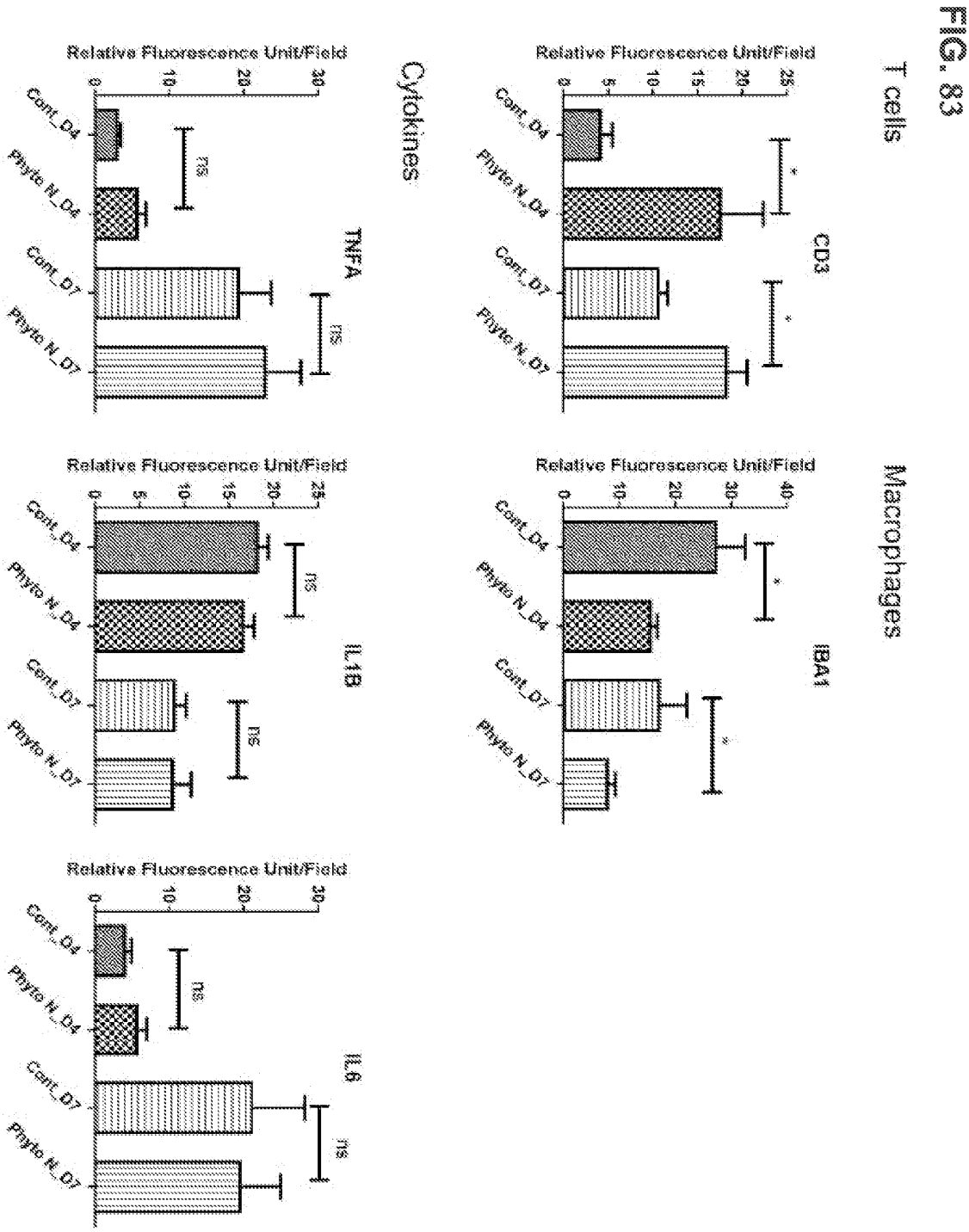

T cells
Macrophages
Cytokines
Relative Fluorescence Unit/Field
Cont_D4
Phyto N_D4
Cont_D7
Phyto N_D7
CD3
IBA1
TNFA
IL1B
IL6
*
ns

FIG. 84

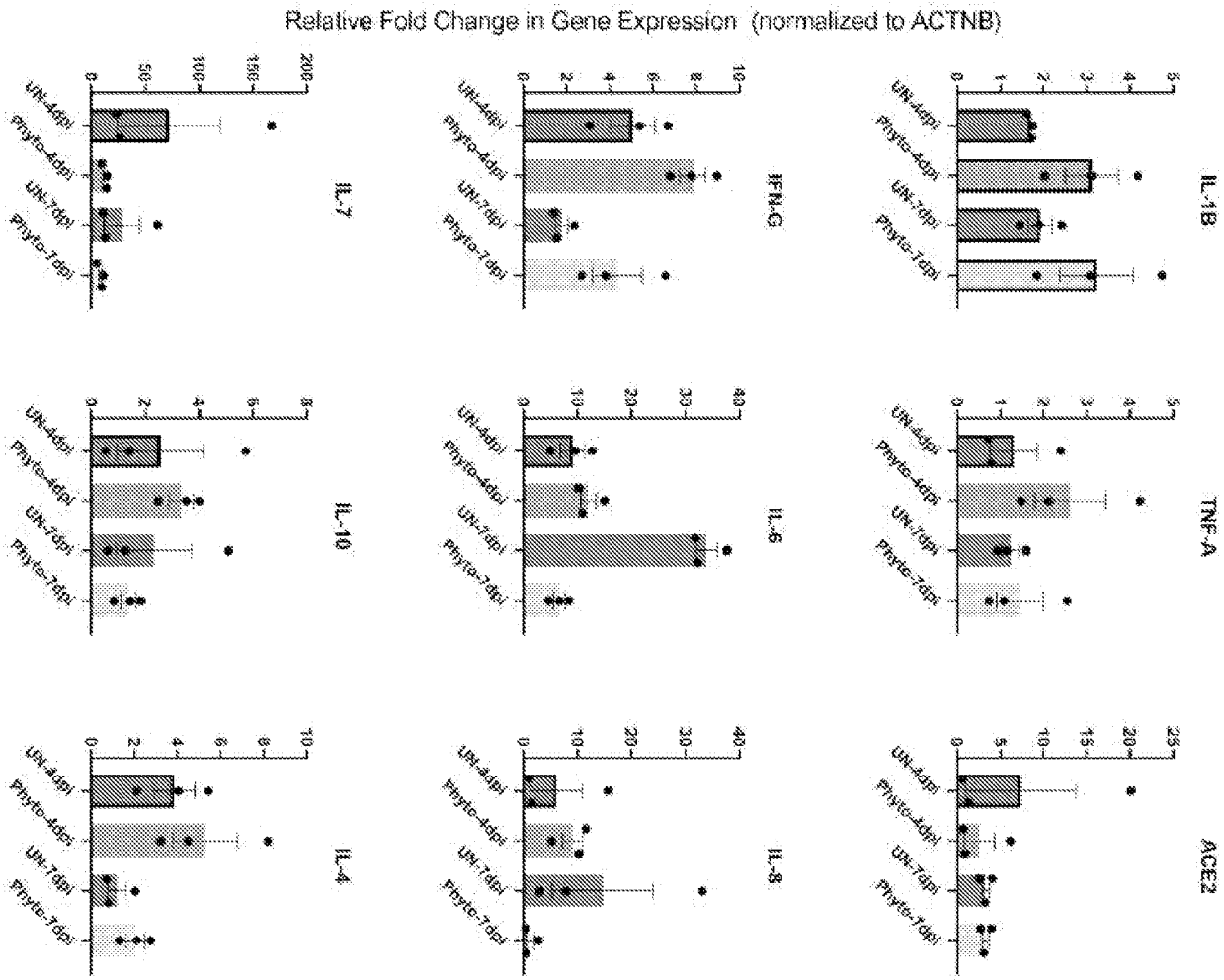

Relative Fold Change in Gene Expression (normalized to ACTNB)
IL-1B
IFN-G
IL-7
TNF-A
IL-6
IL-10
ACE2
IL-8
IL-4
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi

FIG. 84 cont.

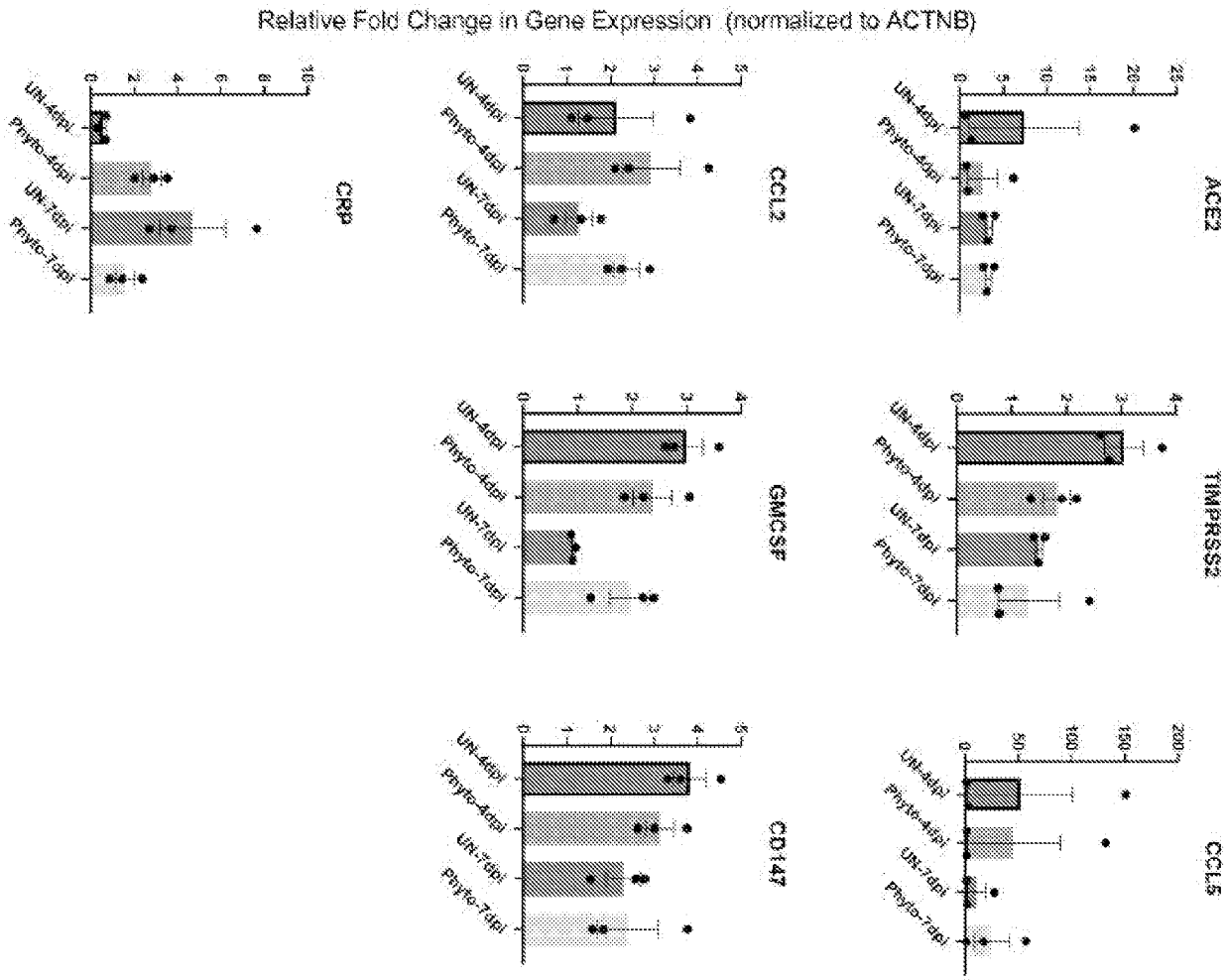

Relative Fold Change in Gene Expression (normalized to ACTNB)
ACE2
TMPRSS2
CCL5
CCL2
GMCSF
CD147
CRP
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi

FIG. 85

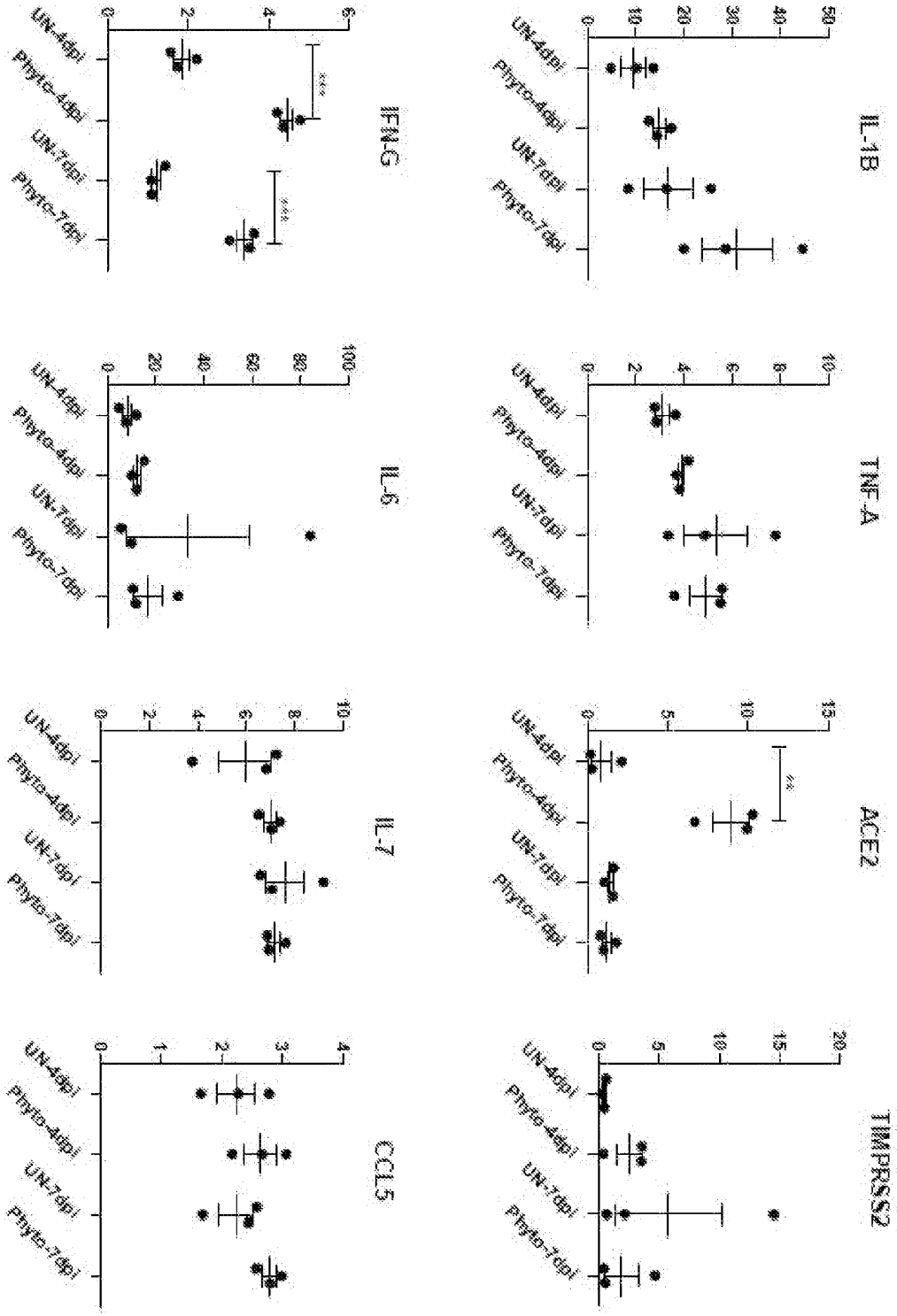

Fold-change
IL-1B
IFN-G
TNF-A
IL-6
ACE2
IL-7
TMPRSS2
CCL5
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi

FIG. 85 cont.

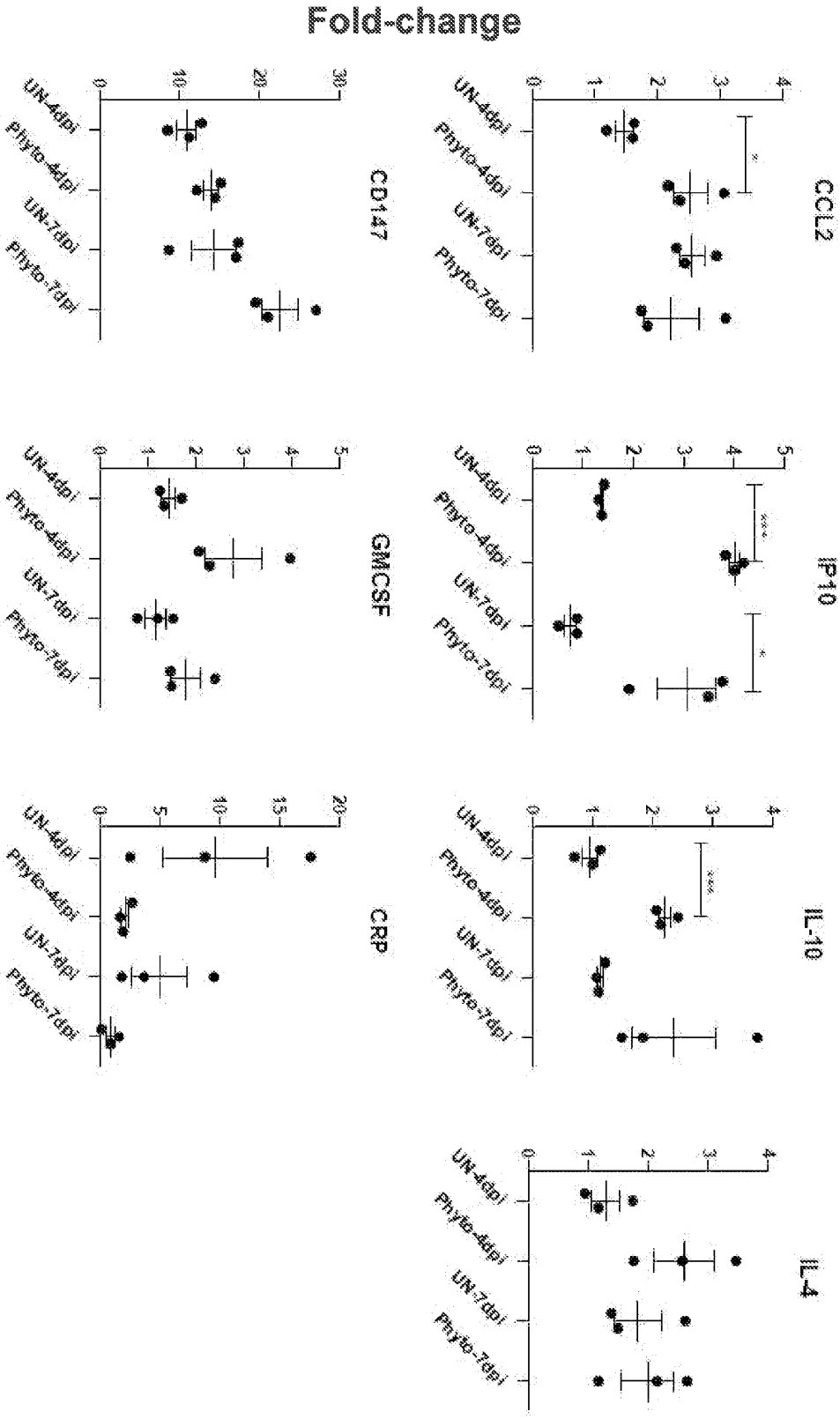

Fold-change
CCL2
IP10
IL-10
IL-4
CD147
GMCSF
CRP
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi

FIG. 86

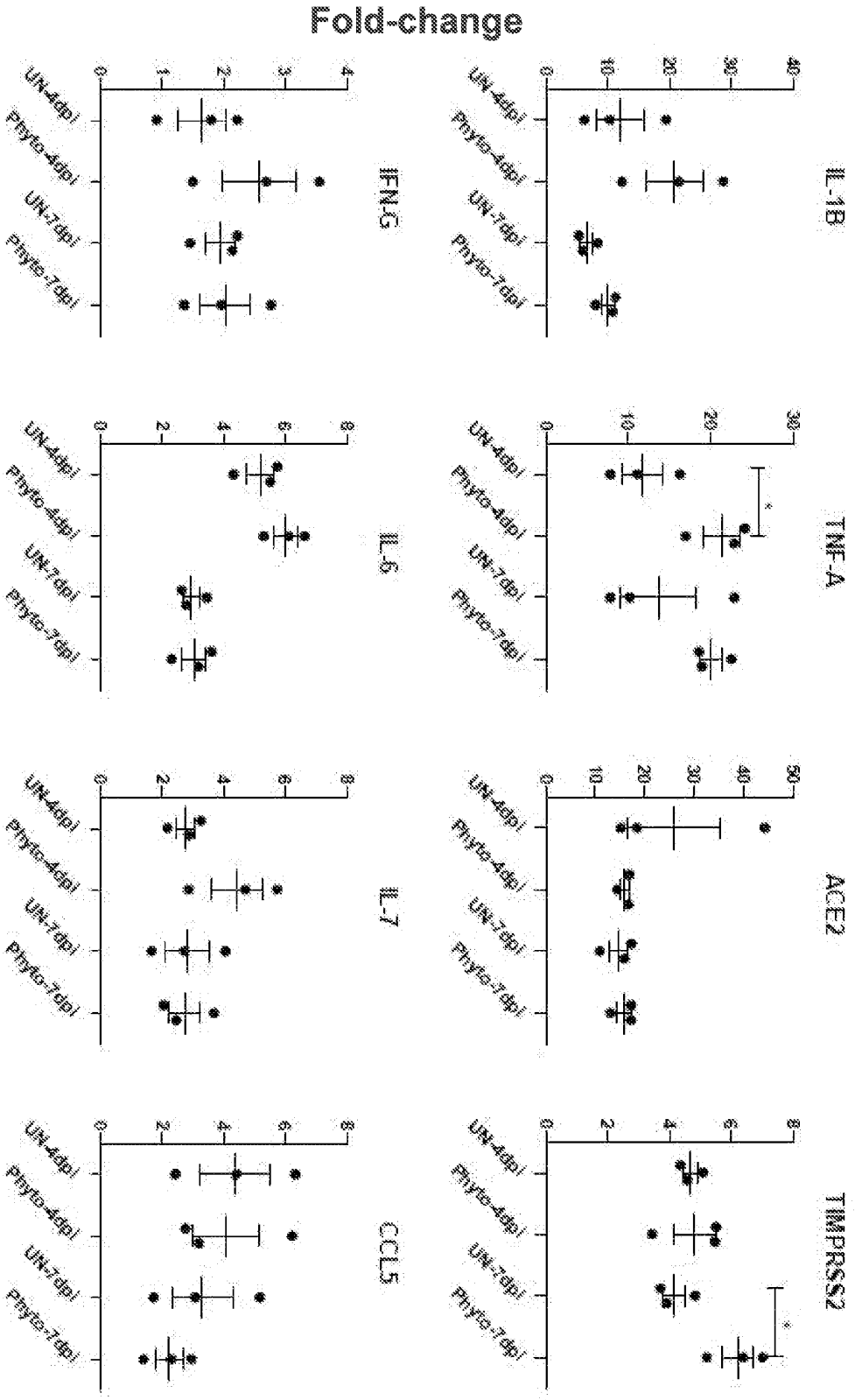

Fold-change
IL-1B
IFNG
TNF-A
IL-6
ACE2
IL-7
TMPRSS2
CCL5
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi
*

FIG. 86 cont.

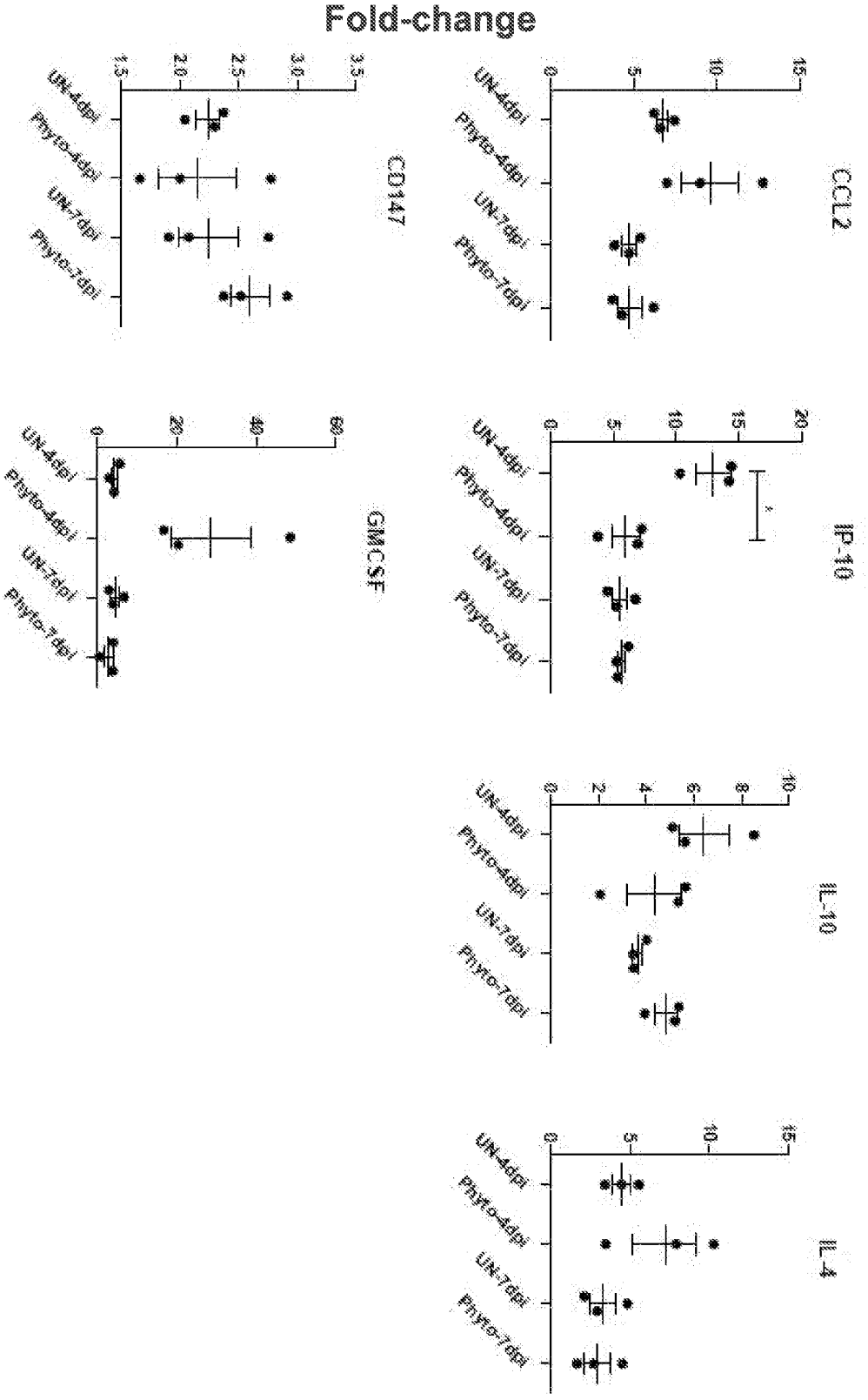

Fold-change
CD147
GMCSF
CCL2
IP-10
IL-10
IL-4
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi

FIG. 87

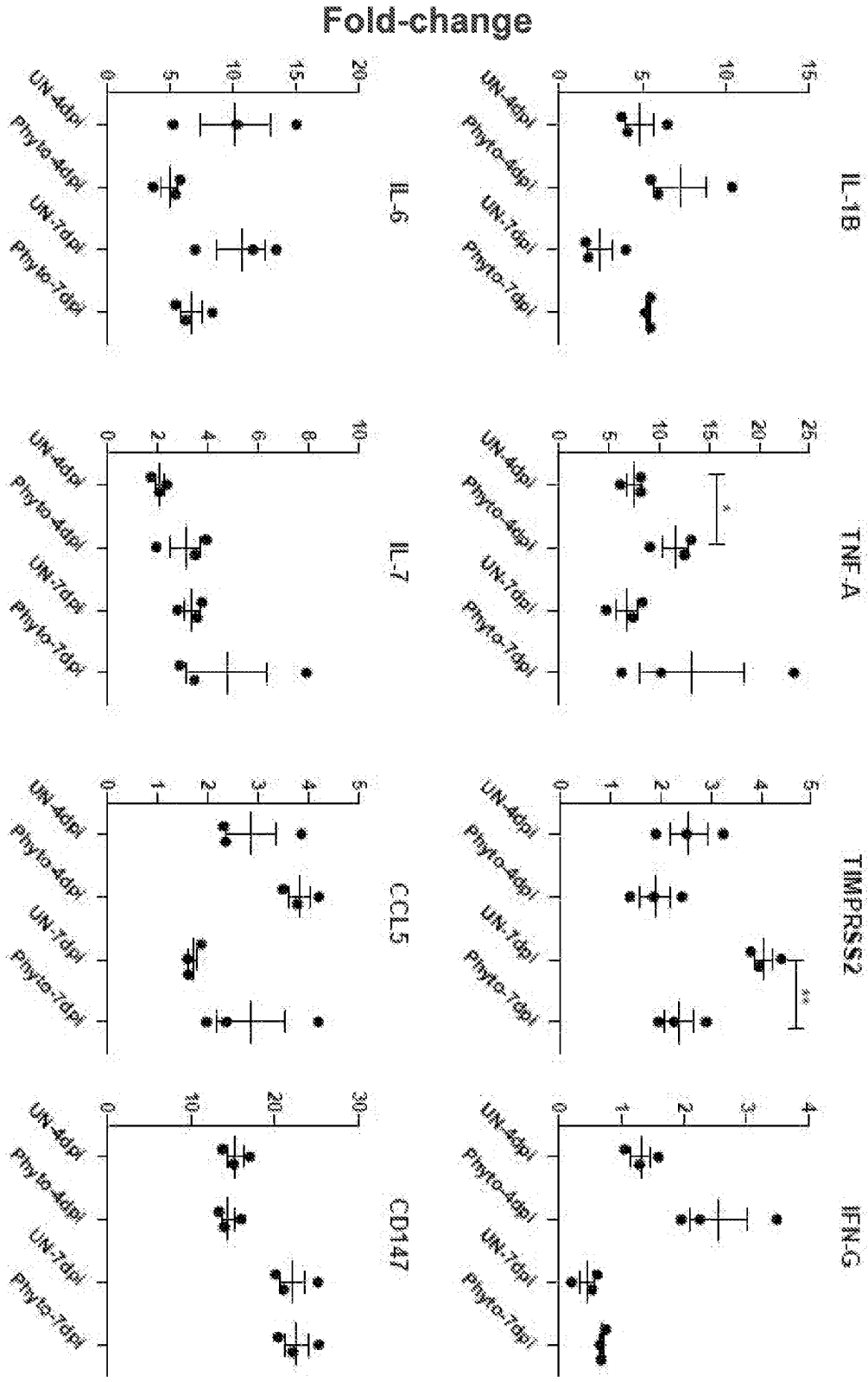

Fold-change
IL-1B
TNF-A
TMPRSS2
IFN-G
IL-6
IL-7
CCL5
CD147
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi
*
**

FIG. 87 cont.

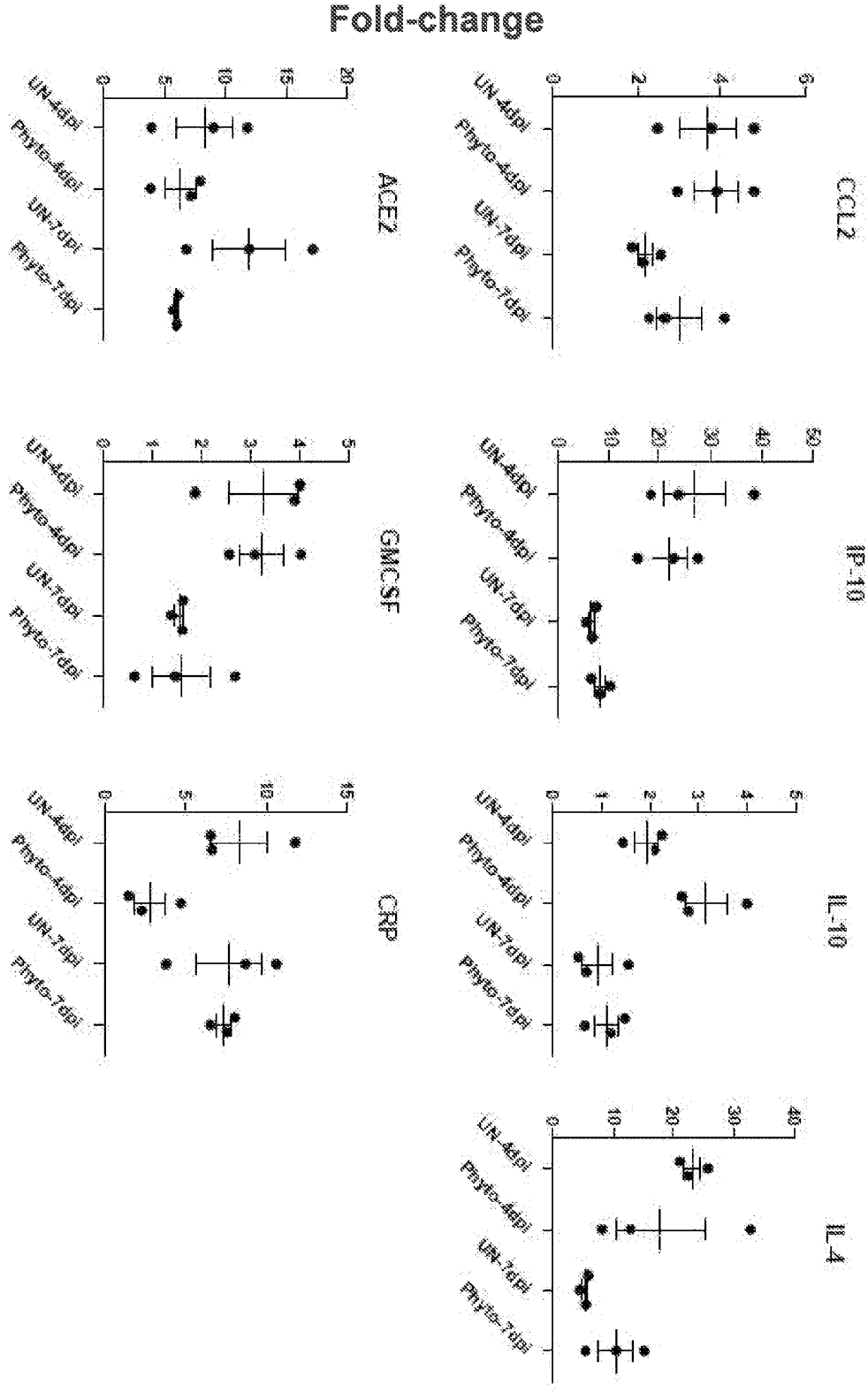
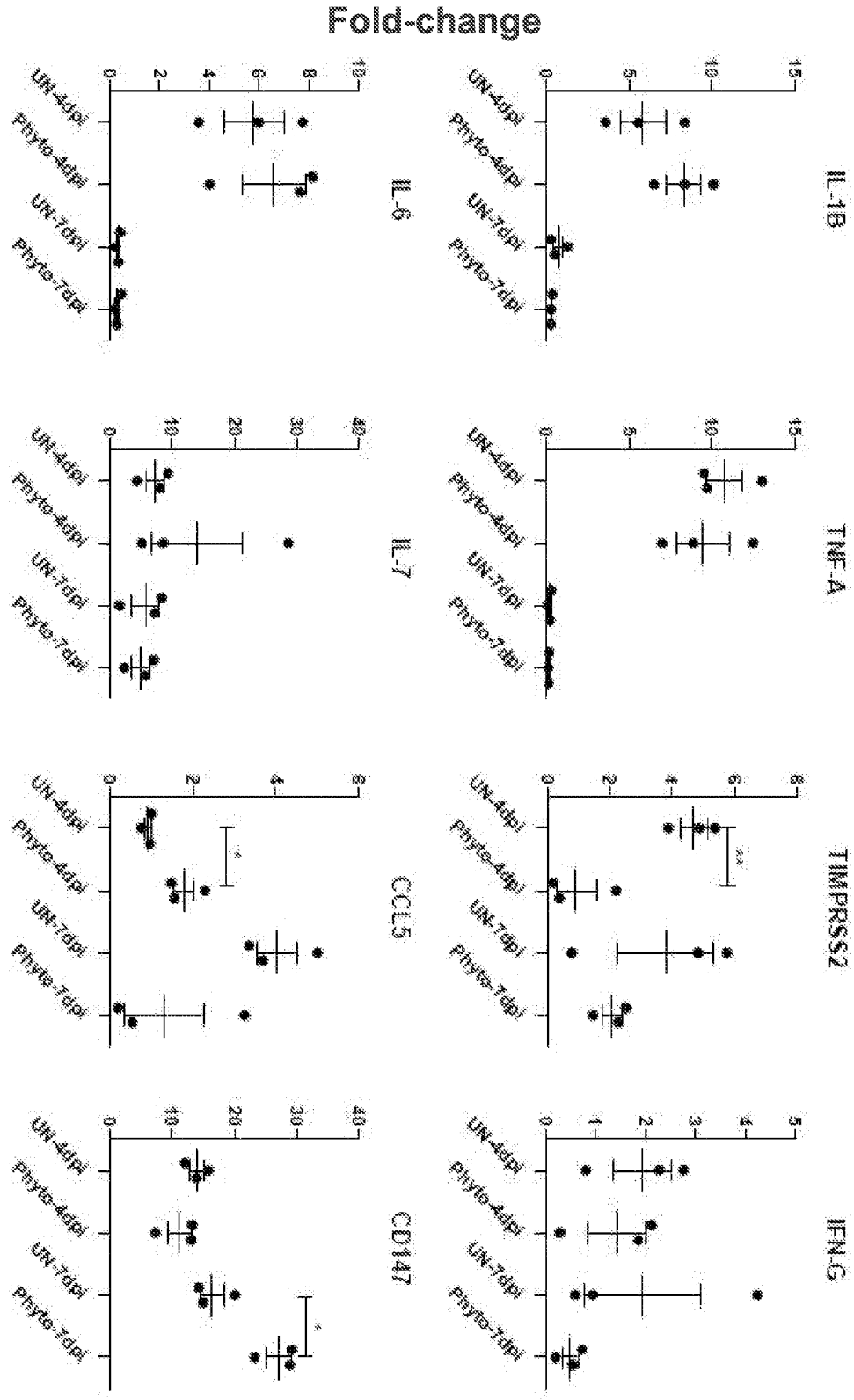

Fold-change
CCL2
IP-10
IL-10
IL-4
ACE2
GMCSF
CRP
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi

FIG. 88


Fold-change
IL-1B
IL-6
TNF-A
IL-7
TMPRSS2
CCL5
IFN-G
CD147
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi
*
**
*

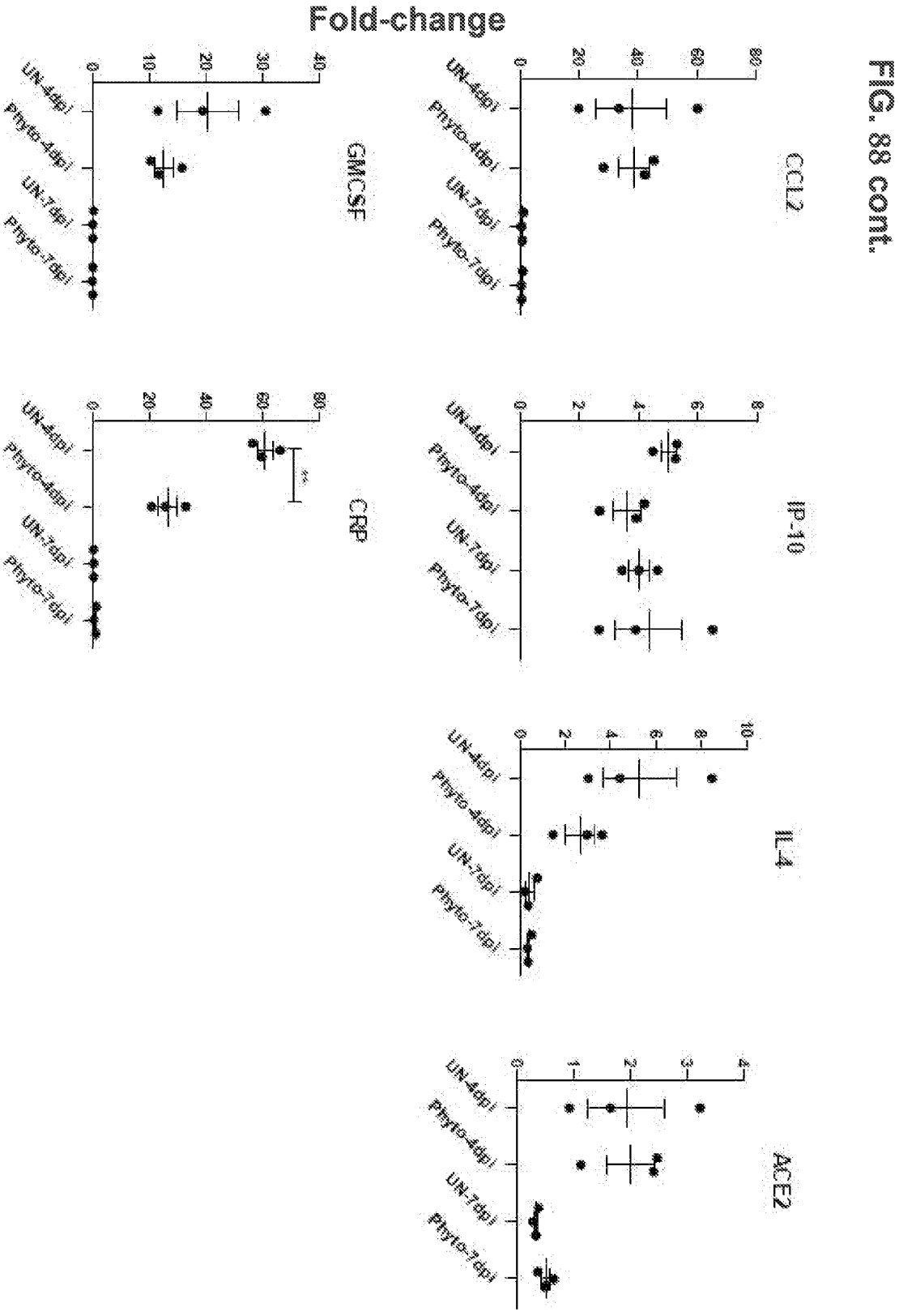
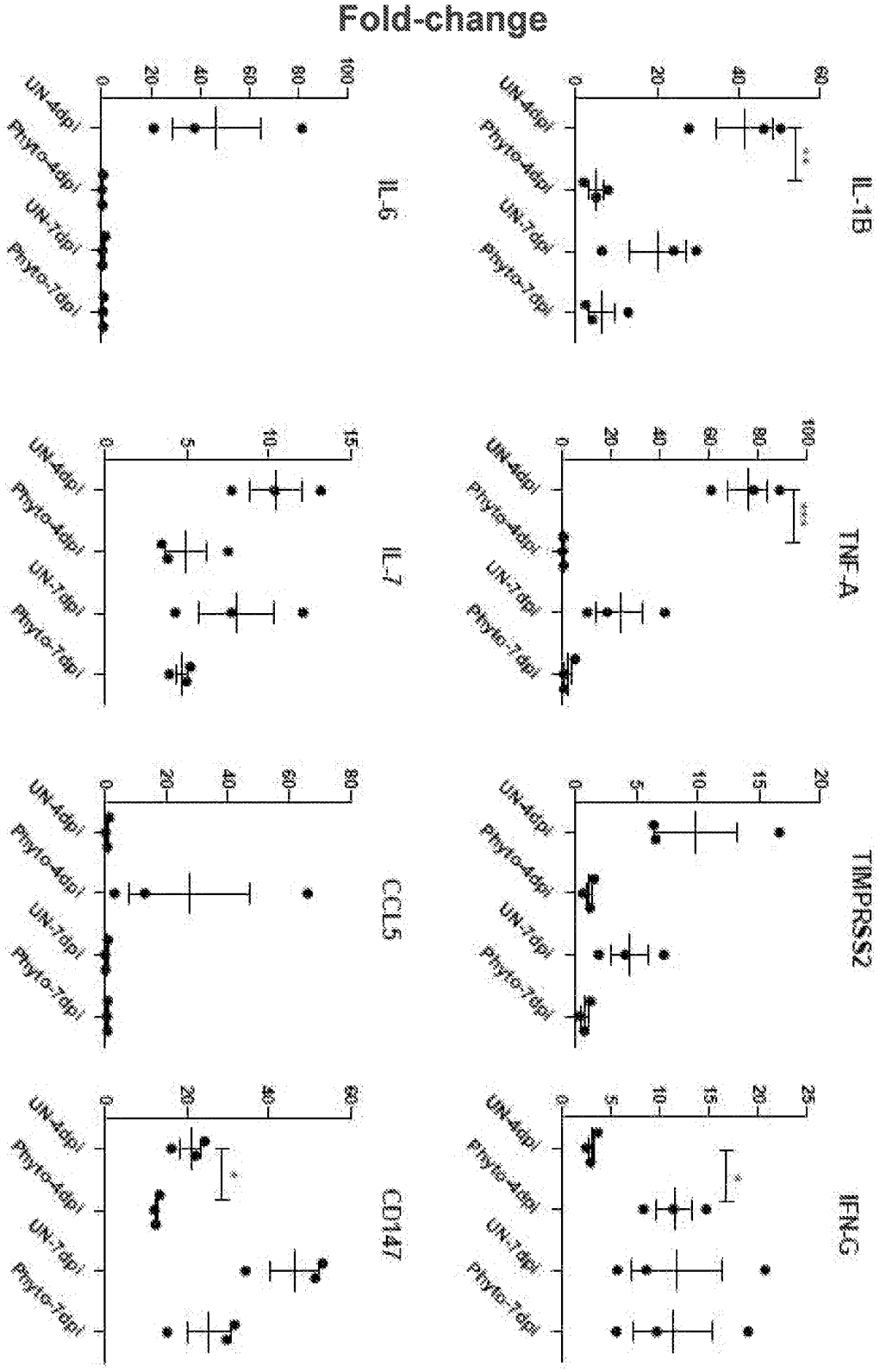

Fold-change
CCL2
GMCSF
IP-10
CRP
IL4
ACE2
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi

FIG. 88 cont.

FIG. 89


Fold-change
IL-1B
IL-6
TNF-A
IL-7
TMPRSS2
CCL5
IFN-G
CD147
UN-4dpi
Phyto-4dpi
UN-7dpi
Phyto-7dpi

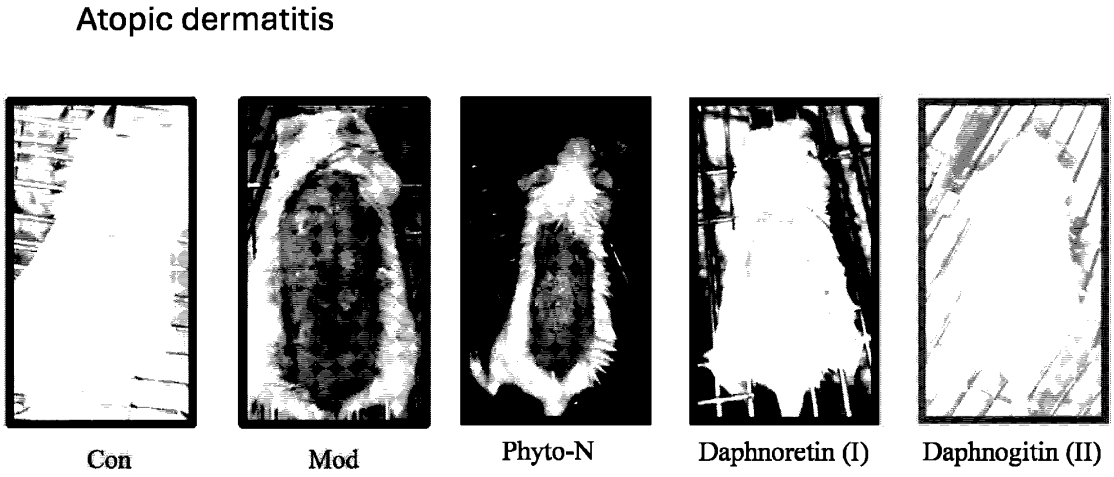


Fig.90 Animals from atopic dermatitis model: Blank group, model group, Phyto-N, Group Daphnoretin (I) and Group Daphnogitin (II) mouse skin condition

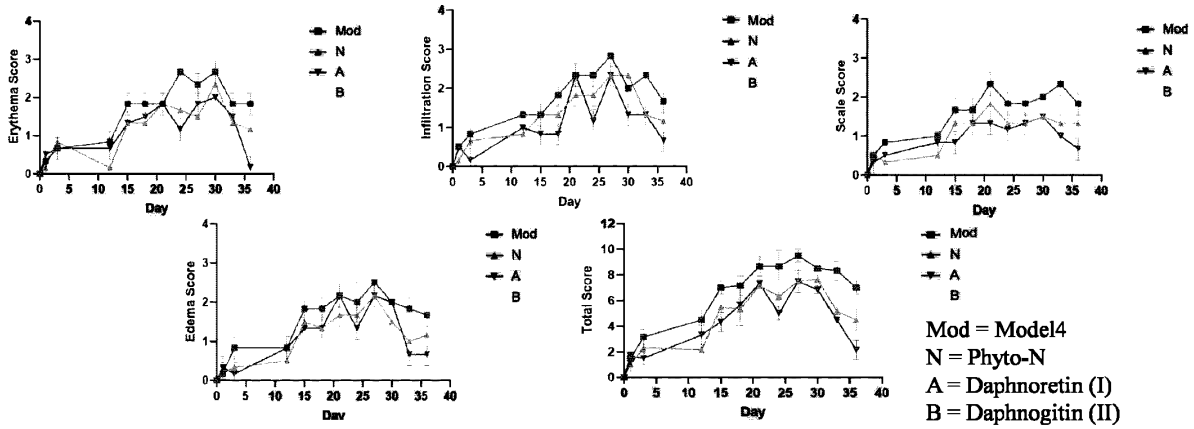


Fig. 91 Change plot of skin erythema, infiltration, scales, edema, and skin lesions in mice (Model group (Mod) Phyto-N (N) , Daphnoretin (I) (A) and Daphnogitin (II) (B)) ($x \pm S$, n=7)

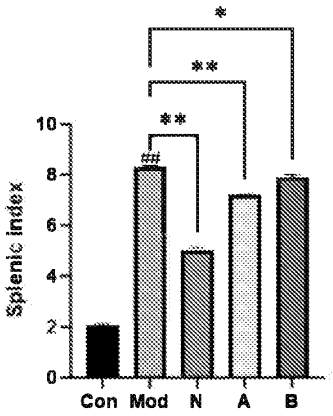


Fig. 92 Spleen index of mice in blank group (Con), model group (Mod), Phyto-N group (N), Daphnoretin (I) group (A) and Daphnogitin(II) group (B) ($x \pm S$, $n = 7$)

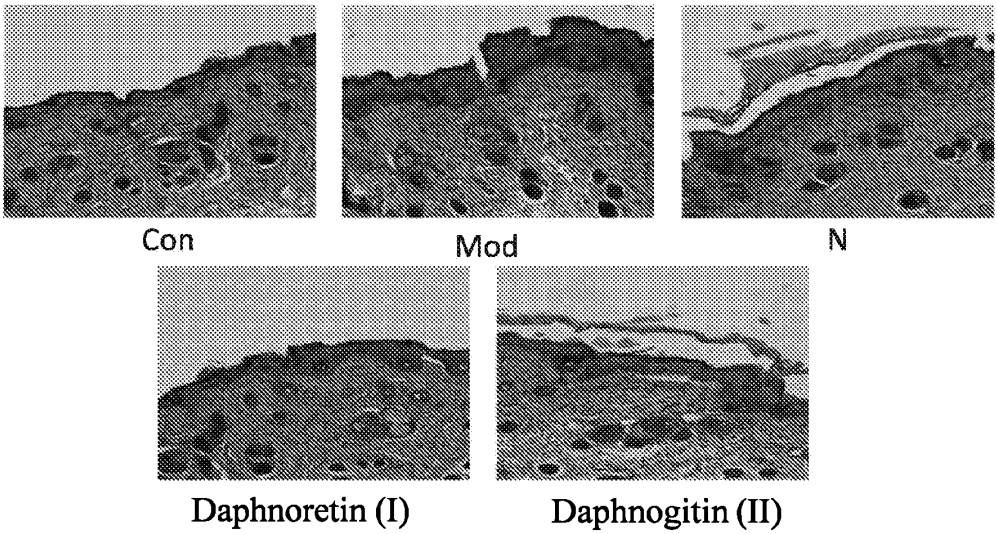


Fig. 93 HE staining of back skin tissue of mice in blank group (Con) model group (Mod), Phyto-N group, Daphnoretin (I) group and Daphnogitin (II) group (100x)

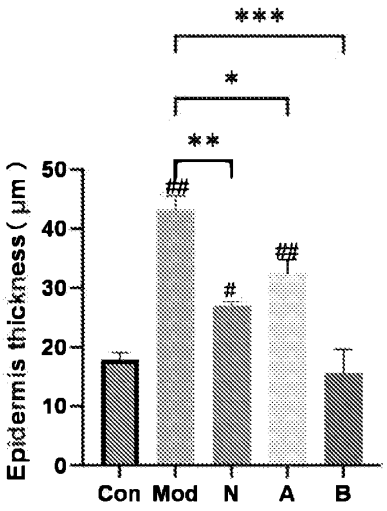


Fig. 94: Epidermal thickness of blank (Con), model (Mod), and treated group (Phyto-N (N), Daphnoretin (I) (A) and Daphnogitin (II) (B) (x ± S, n=7). Compared with the blank control group,$^{\#}P<0.05$,$^{\#\#}P<0.01$;compared with the model group, $^{*}P<0.05$,$^{**}P<0.01$

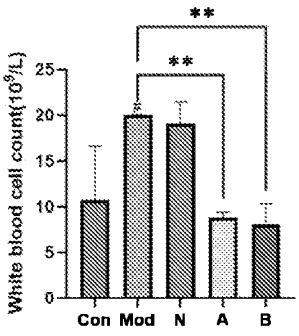


Fig. 95: Number of white blood cells (X ±S, N = 7 blank (Con), model (Mod), and treated group (Phyto-N (N), Daphnoretin (I) (A) and Daphnogitin (II) (B) **P<0.01

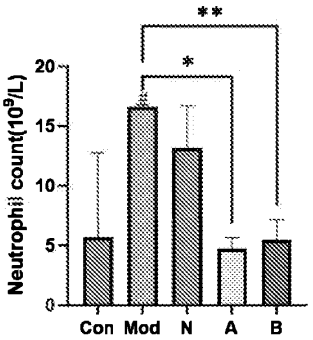


Fig. 96: Number of neutrophils (X ±S, N = 7 blank (Con), model (Mod), and treated group (Phyto-N (N), Daphnoretin (I) (A) and Daphnogitin (II) (B), *P<0.05,**P<0.01

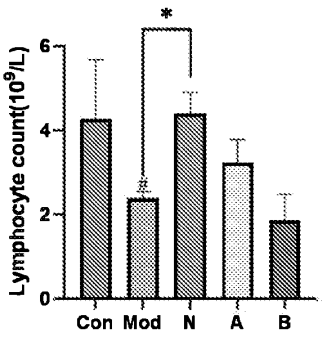


Fig. 97: Number of lymphocytes (X ±S, N = 7 blank (Con), model (Mod), and treated group (Phyto-N (N), Daphnoretin (I) (A) and Daphnogitin (II) (B), *P<0.05

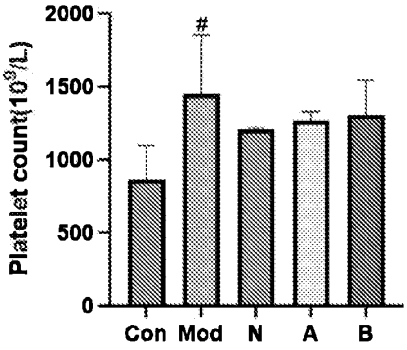


Fig. 98: Number of platelets (X ±S, N = 7 blank (Con), model (Mod), and treated group (Phyto-N (N), Daphnoretin (I) (A) and Daphnogitin (II) (B). P<0.05.

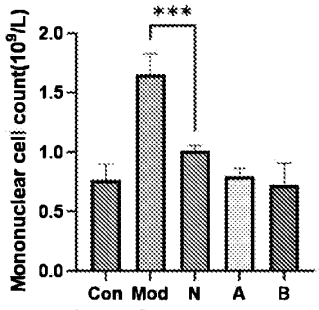


Fig.10 Number of monocytes (X±S, n=7)

Fig. 99: Number of monocytes (X ±S, N = 7 blank (Con), model (Mod), and treated group (Phyto-N (N), Daphnoretin (I) (A) and Daphnogitin (II) (B), ,***P<0.01

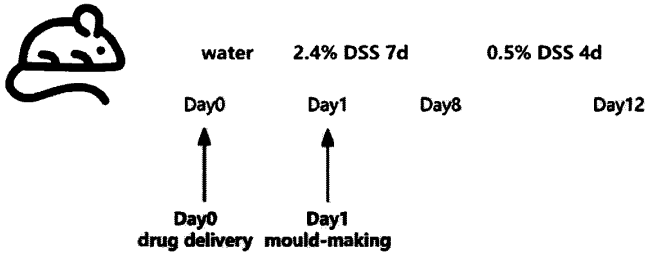


Figure 100: Acute colitis experimental flow

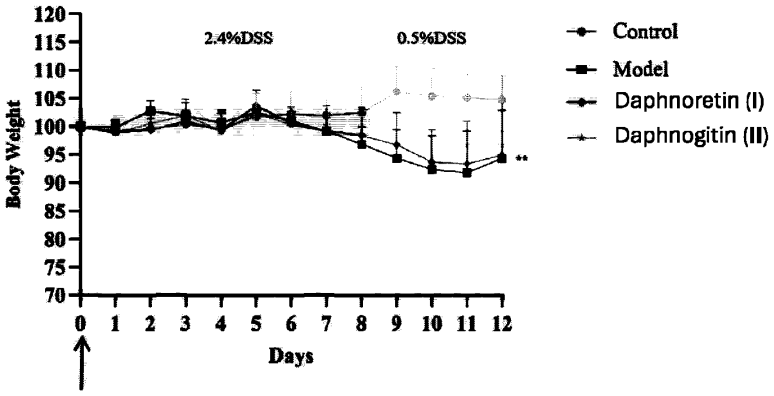


Figure 101 Line graph of percent body weight change in mice

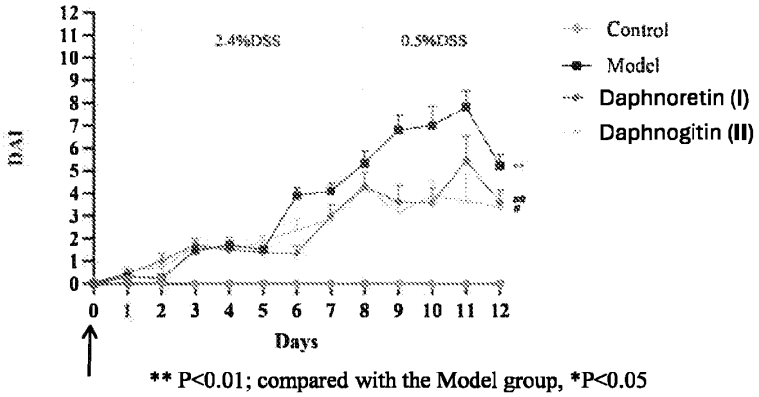


Figure 102: Line graph of DAI scores in mice

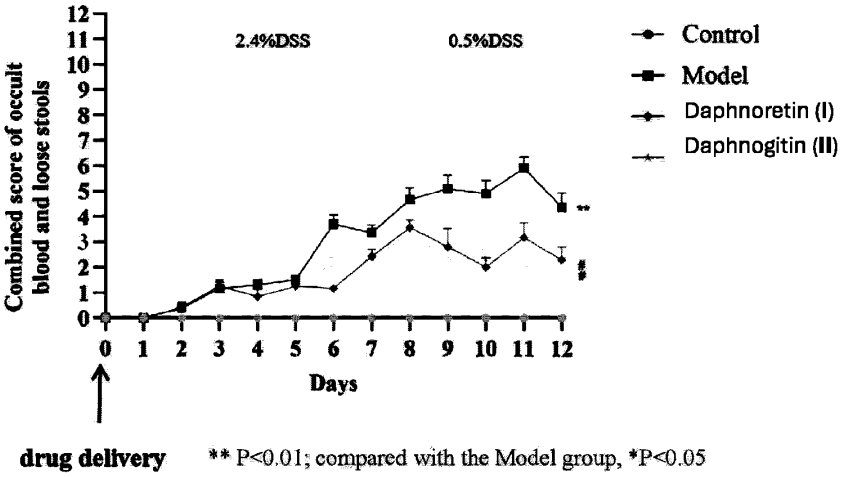


Figure 103: Line graph of occult blood and stool dilution scores in mice

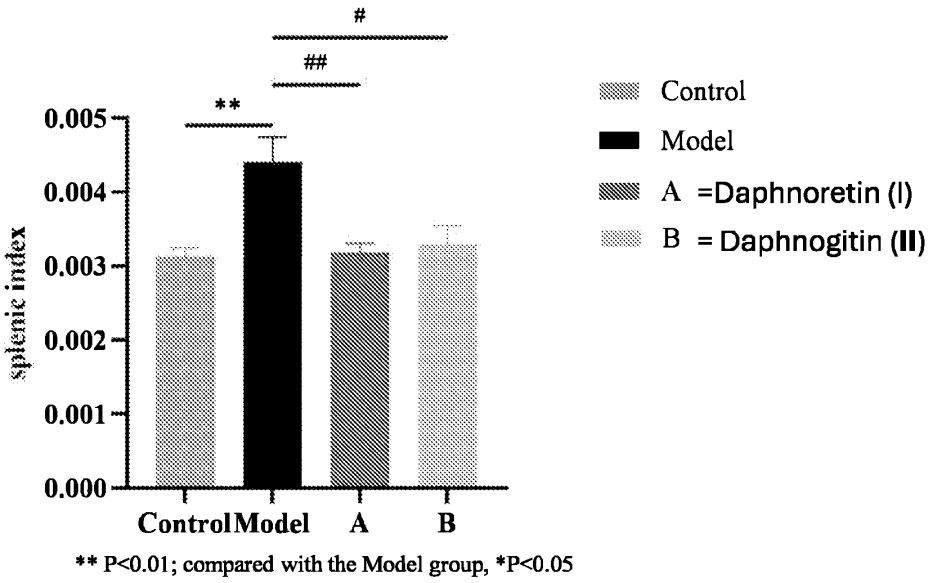
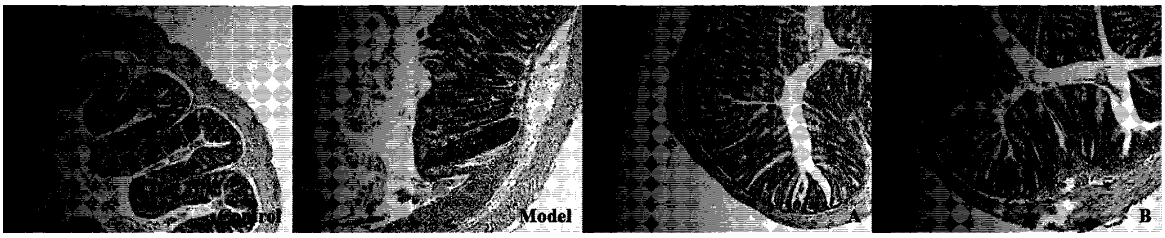


Figure 104: Histogram of mouse spleen index Daphnoretin (I) and Daphnogitin (II)



A = Daphnoretin (**I**), B = Daphnogitin (**II**)

Figure 105: H&E staining of colon of mice in each group of mice in acute colitis model (100x)