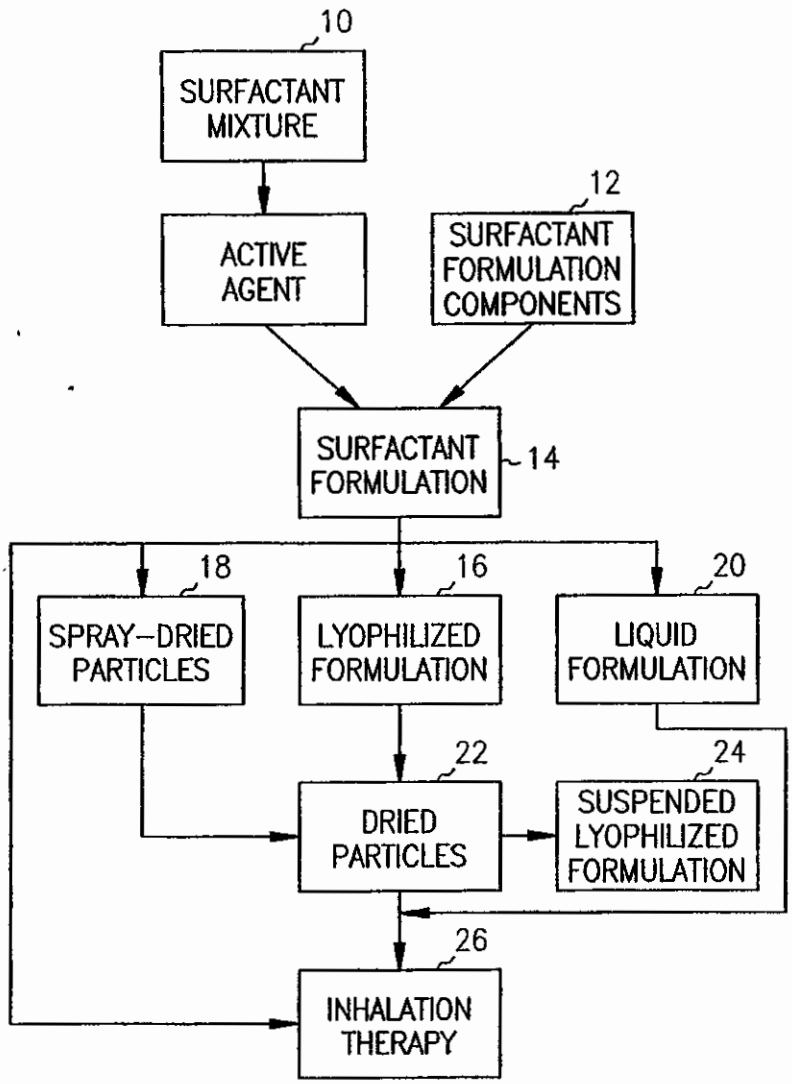
10
SURFACTANT MIXTURE
12
ACTIVE AGENT
SURFACTANT FORMULATION COMPONENTS
SURFACTANT FORMULATION
14
18
16
20
SPRAY-DRIED PARTICLES
LYOPHILIZED FORMULATION
LIQUID FORMULATION
22
24
DRIED PARTICLES
SUSPENDED LYOPHILIZED FORMULATION
26
INHALATION THERAPY

FIG. 1

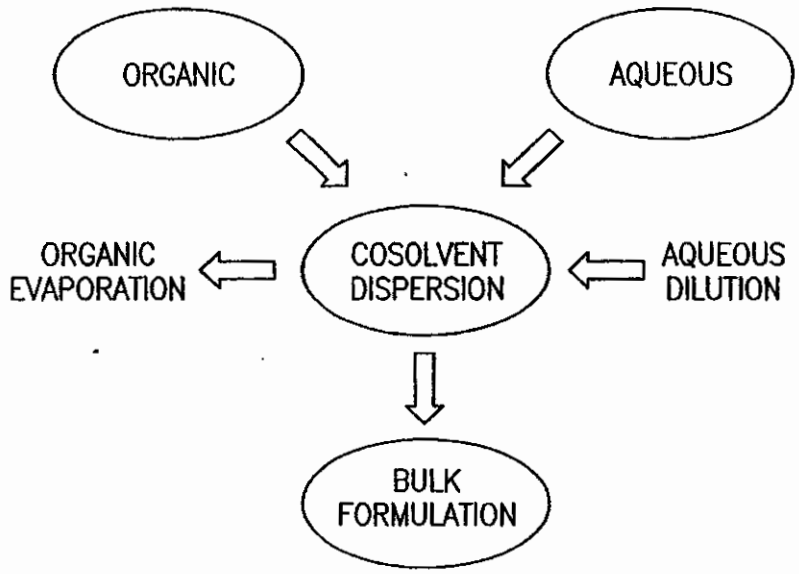
ORGANIC
AQUEOUS
ORGANIC EVAPORATION
COSOLVENT DISPERSION
AQUEOUS DILUTION
BULK FORMULATION

FIG. 2A

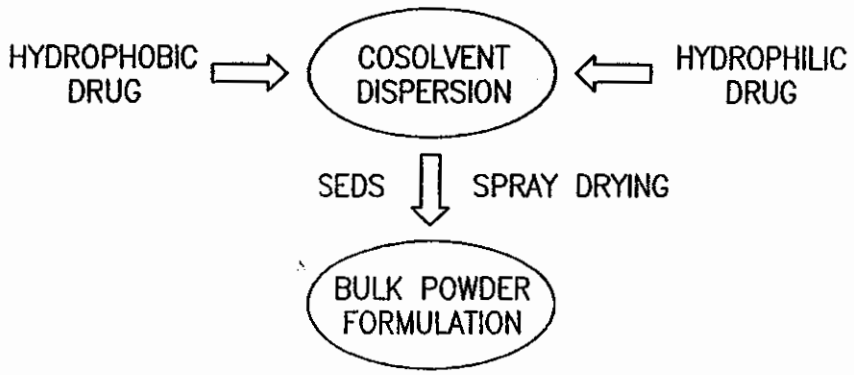
HYDROPHOBIC DRUG
COSOLVENT DISPERSION
HYDROPHILIC DRUG
SEDS
SPRAY DRYING
BULK POWDER FORMULATION

FIG. 2B



FIG. 3A

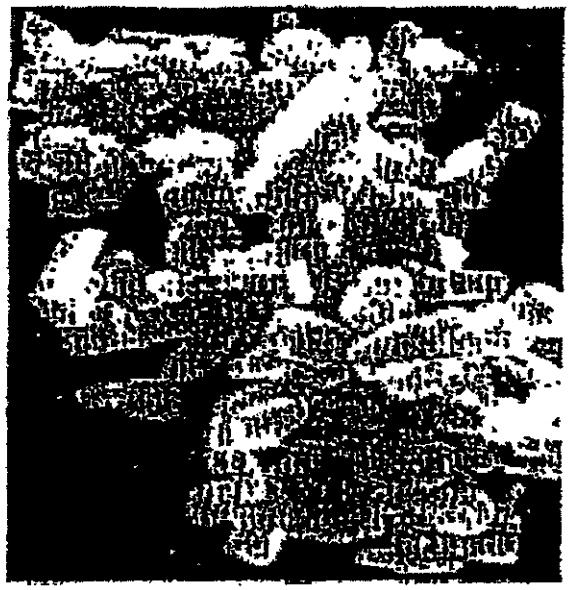

FIG. 3B

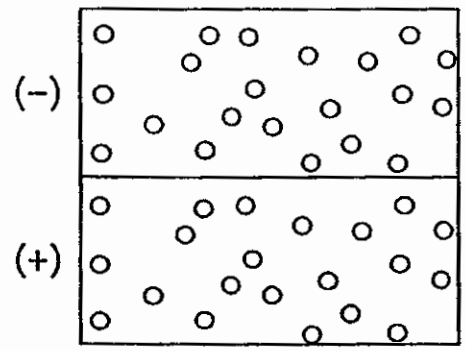


FIG. 4A

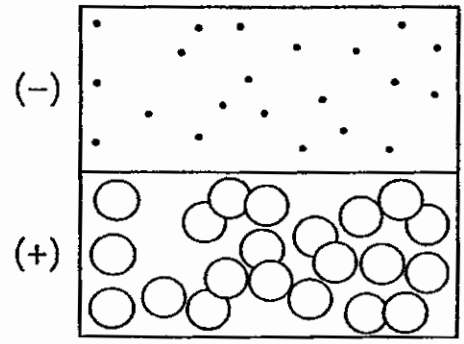


FIG. 4B

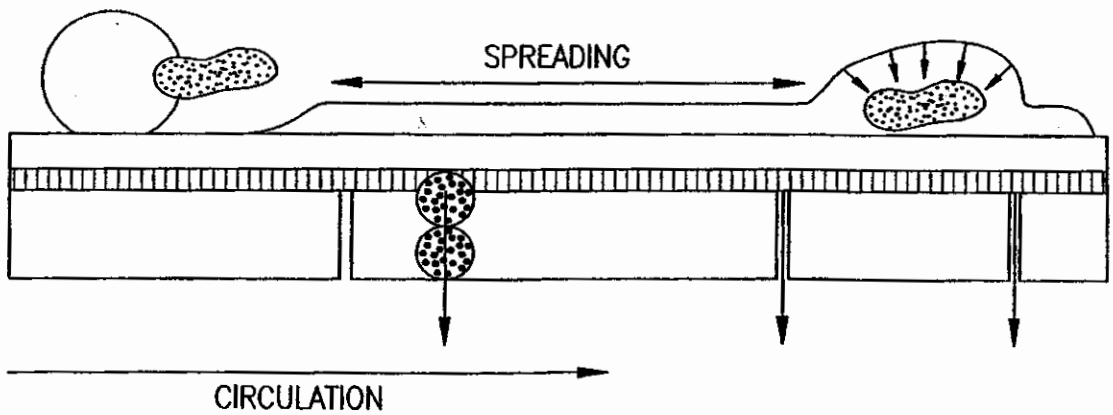


FIG. 4C

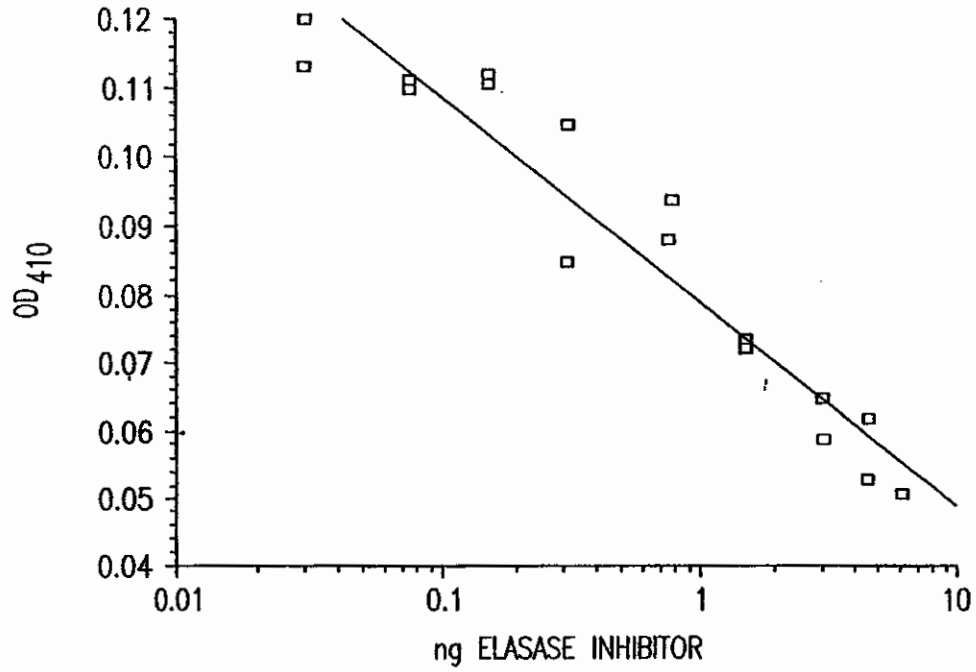
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
OD410
0.01
0.1
1
10
ng ELASASE INHIBITOR

FIG. 5A

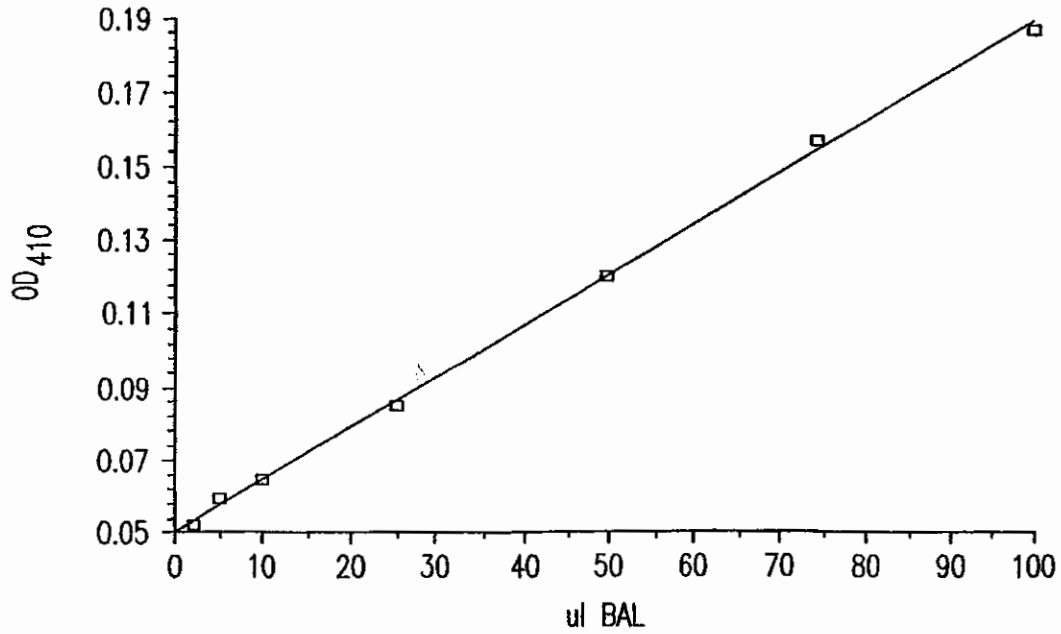
0.19
0.17
0.15
0.13
0.11
0.09
0.07
0.05
OD410
0
10
20
30
40
50
60
70
80
90
100
ul BAL

FIG. 5B

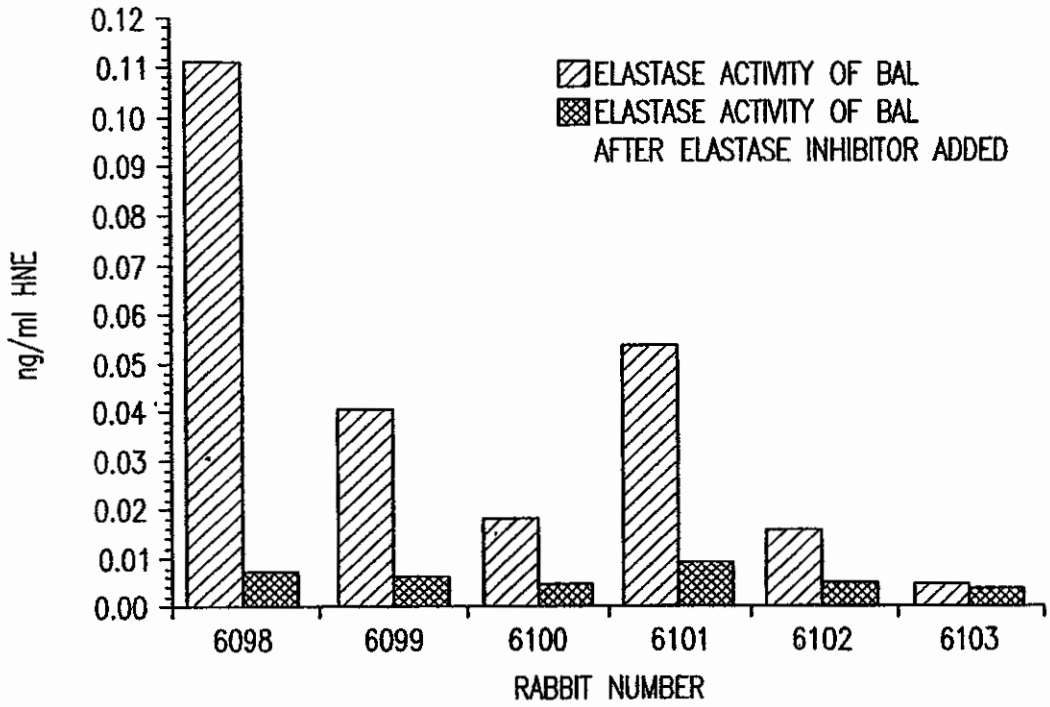
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
ng/ml HNE
ELASTASE ACTIVITY OF BAL
ELASTASE ACTIVITY OF BAL
AFTER ELASTASE INHIBITOR ADDED
6098
6099
6100
6101
6102
6103
RABBIT NUMBER

FIG. 6A

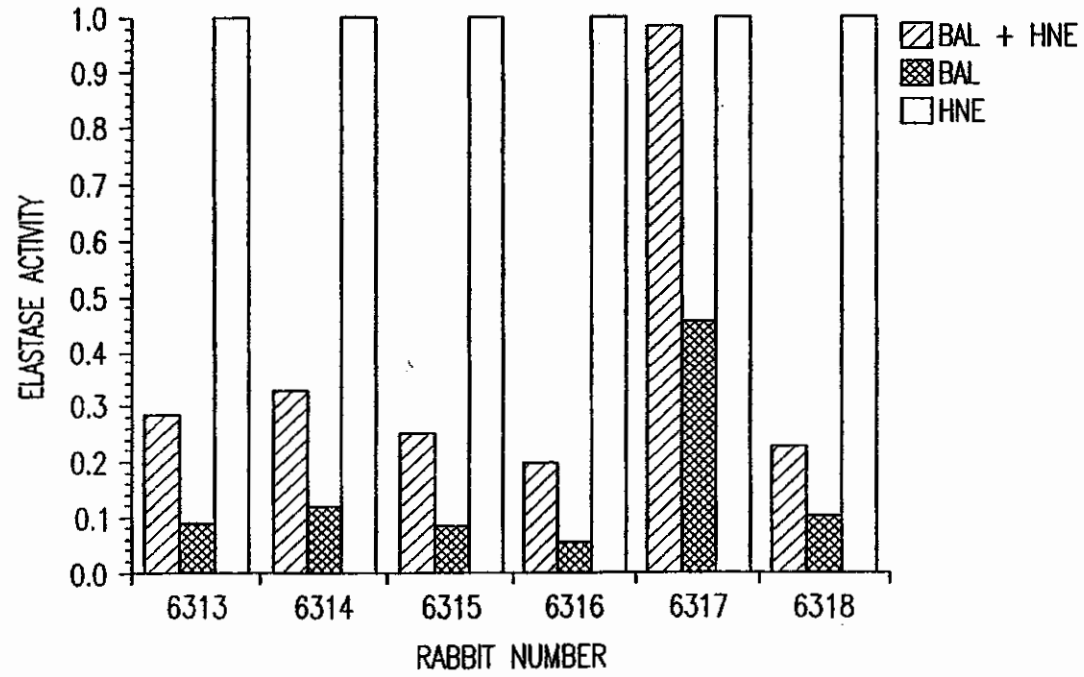
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
ELASTASE ACTIVITY
BAL + HNE
BAL
HNE
6313
6314
6315
6316
6317
6318
RABBIT NUMBER

FIG. 6B

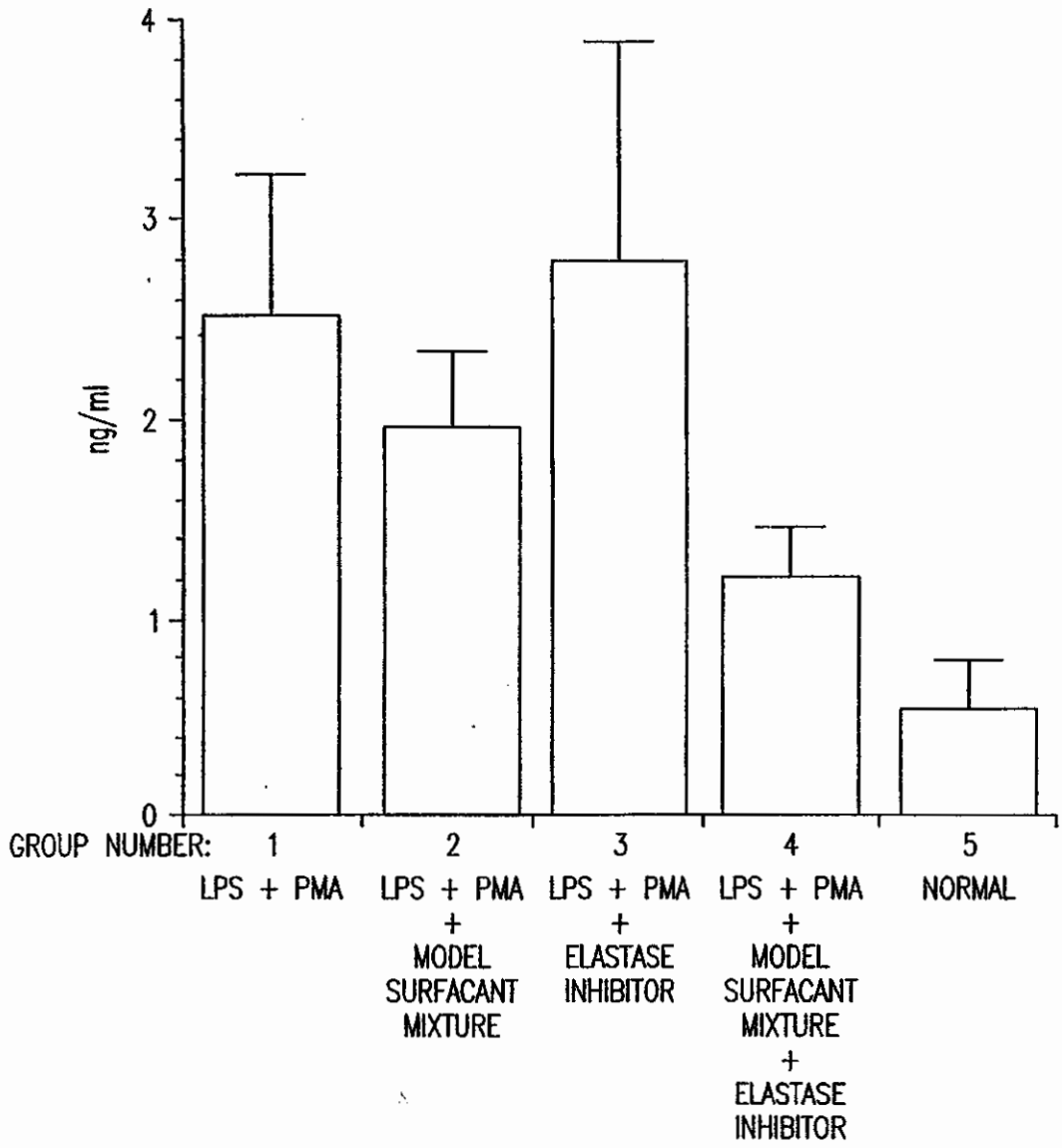
4
3
2
1
0
ng/ml
GROUP NUMBER: 1
LPS + PMA
2
LPS + PMA + MODEL SURFACANT MIXTURE
3
LPS + PMA + ELASTASE INHIBITOR
4
LPS + PMA + MODEL SURFACANT MIXTURE + ELASTASE INHIBITOR
5
NORMAL

FIG. 7A

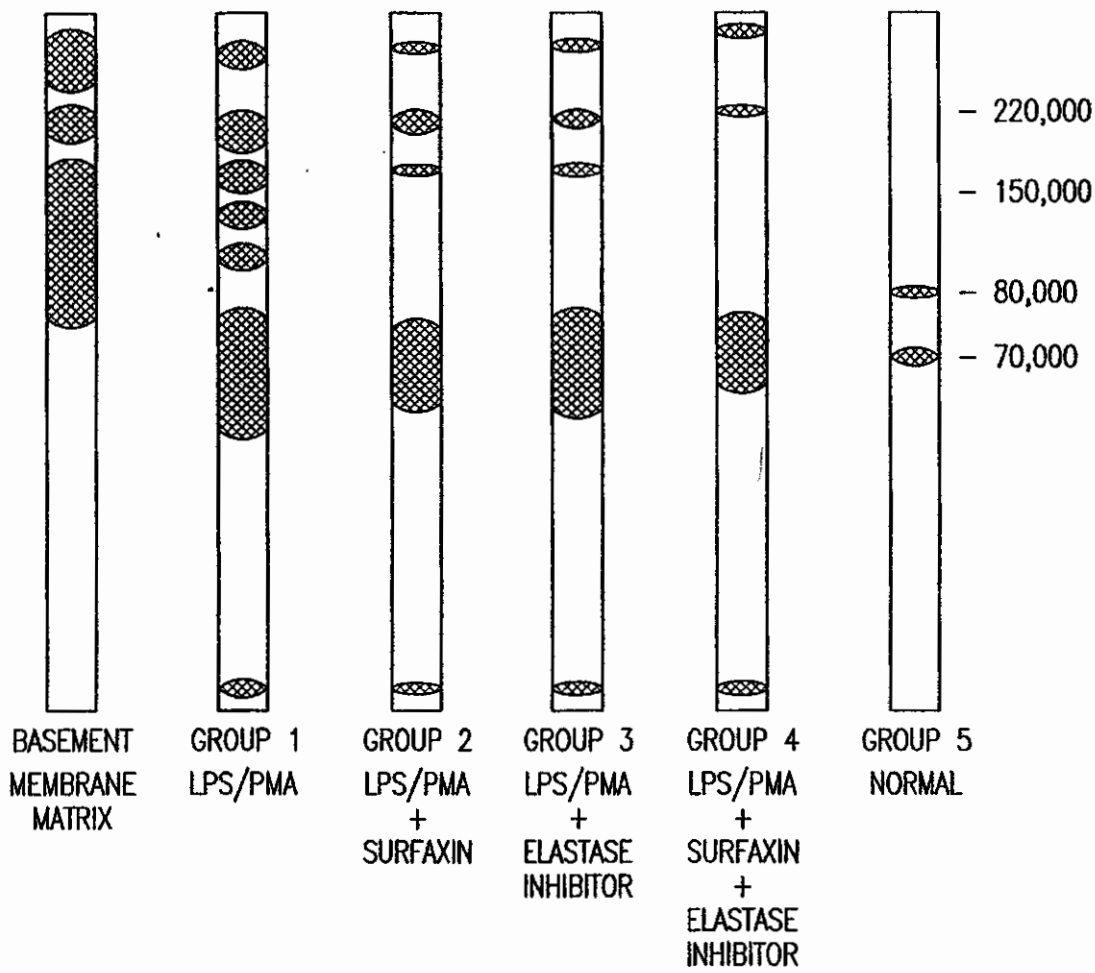
220,000
150,000
80,000
70,000
BASEMENT MEMBRANE MATRIX
GROUP 1 LPS/PMA
GROUP 2 LPS/PMA + SURFAXIN
GROUP 3 LPS/PMA + ELASTASE INHIBITOR
GROUP 4 LPS/PMA + SURFAXIN + ELASTASE INHIBITOR
GROUP 5 NORMAL

FIG. 7B

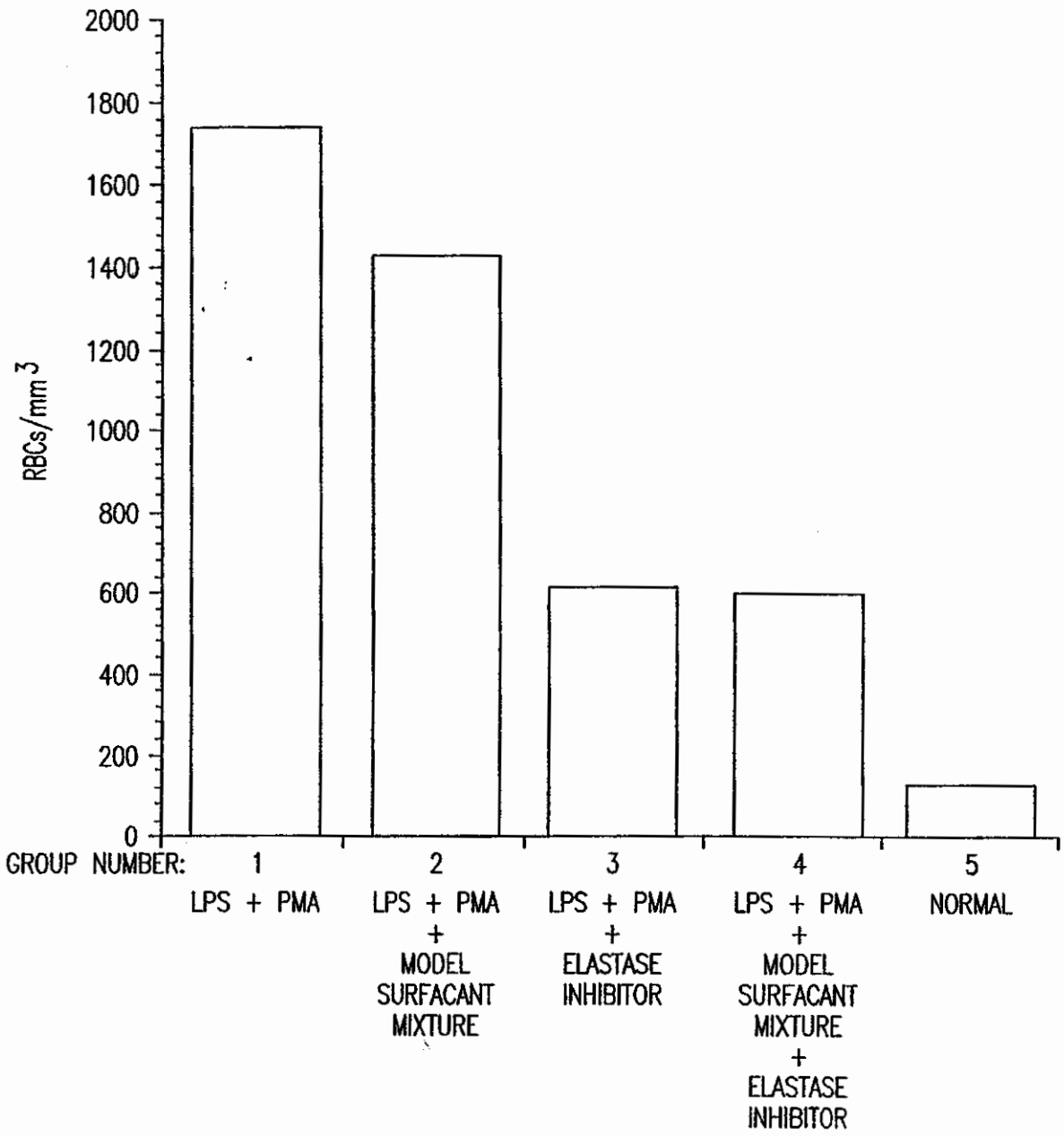
2000
1800
1600
1400
1200
1000
800
600
400
200
0
RBCs/mm 3
GROUP NUMBER:
1
LPS + PMA
2
LPS + PMA + MODEL SURFACANT MIXTURE
3
LPS + PMA + ELASTASE INHIBITOR
4
LPS + PMA + MODEL SURFACANT MIXTURE + ELASTASE INHIBITOR
5
NORMAL

FIG. 7C

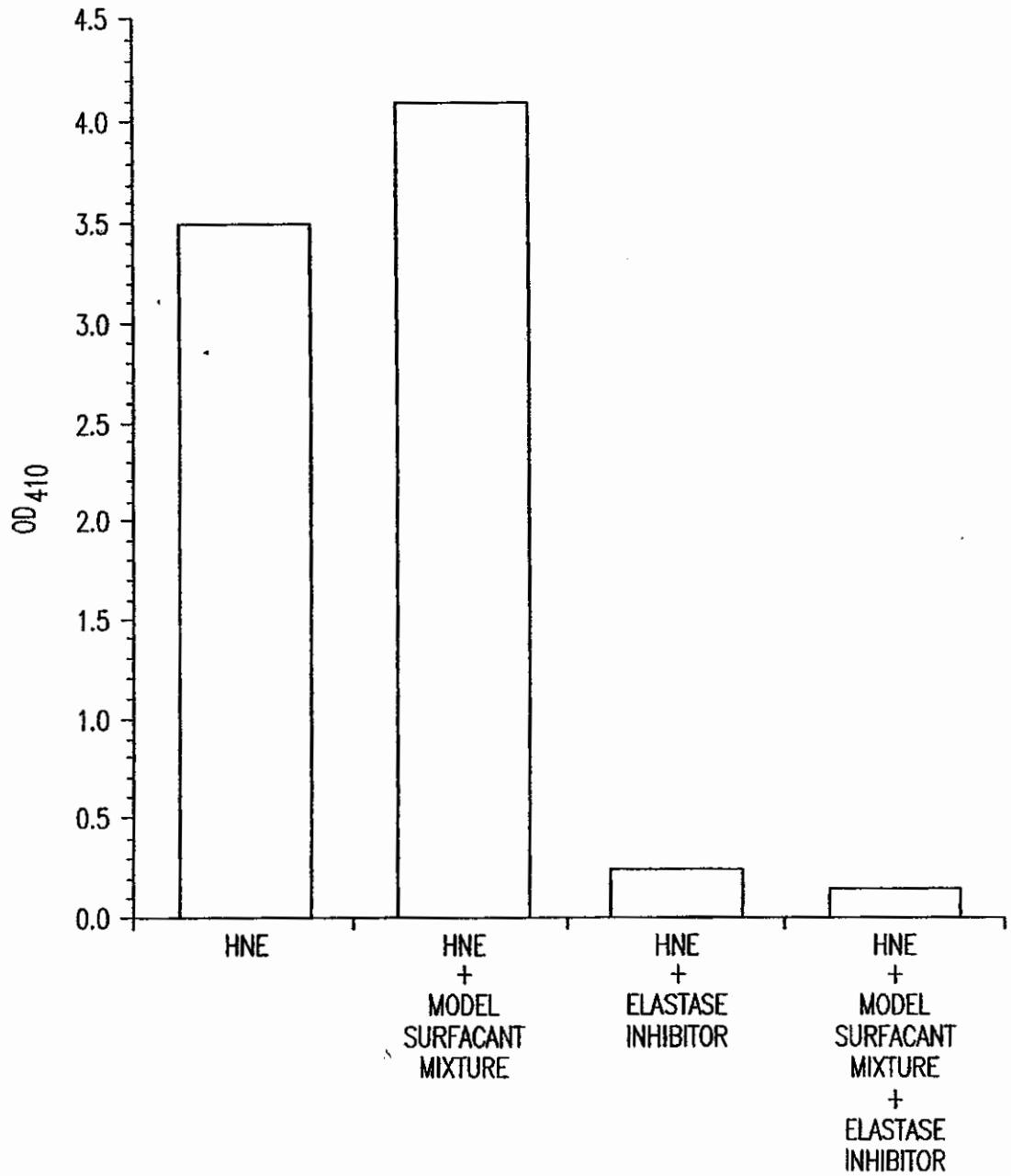
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
OD410
HNE
HNE + MODEL SURFACANT MIXTURE
HNE + ELASTASE INHIBITOR
HNE + MODEL SURFACANT MIXTURE + ELASTASE INHIBITOR

FIG. 8

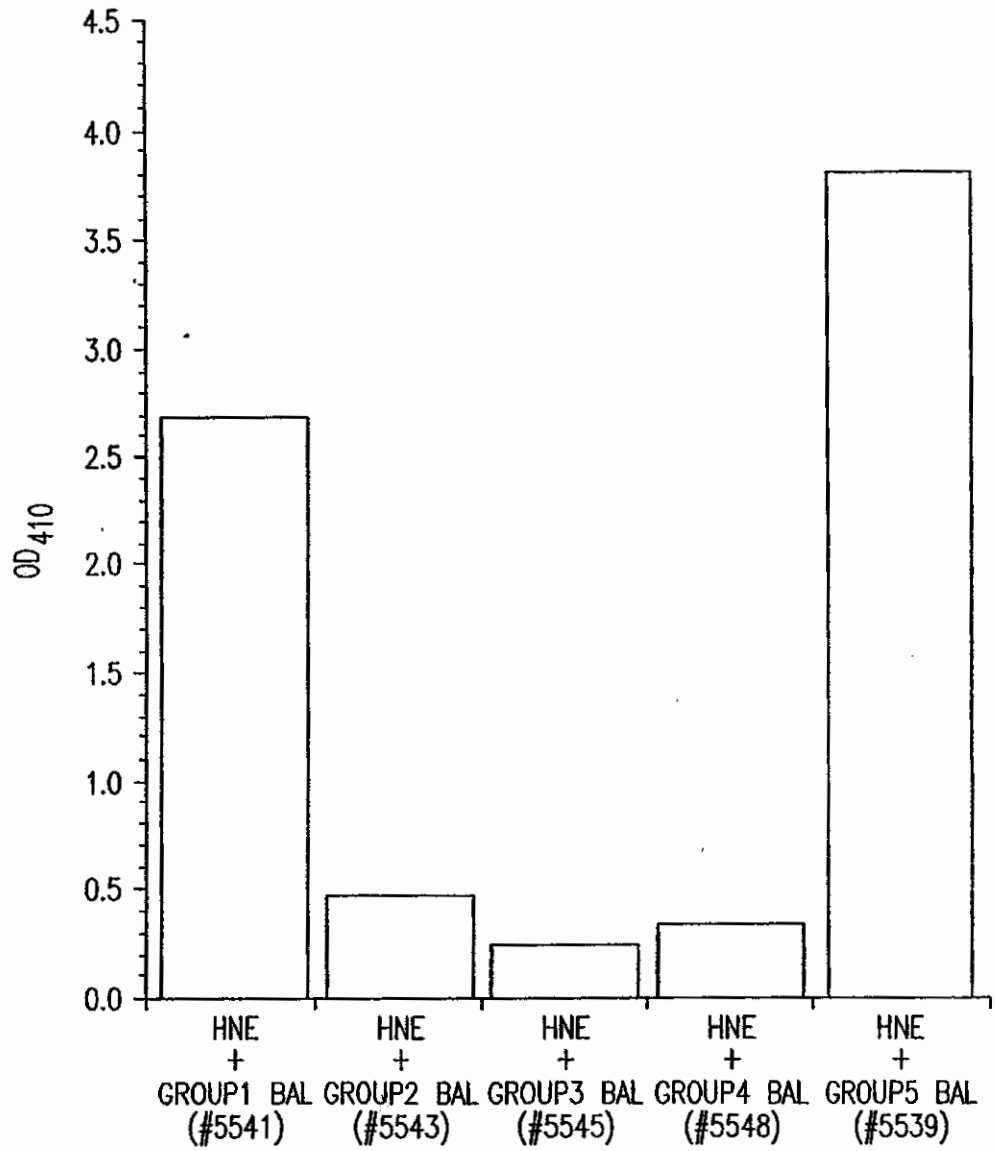
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
OD410
HNE + GROUP1 BAL (#5541)
HNE + GROUP2 BAL (#5543)
HNE + GROUP3 BAL (#5545)
HNE + GROUP4 BAL (#5548)
HNE + GROUP5 BAL (#5539)

FIG. 9

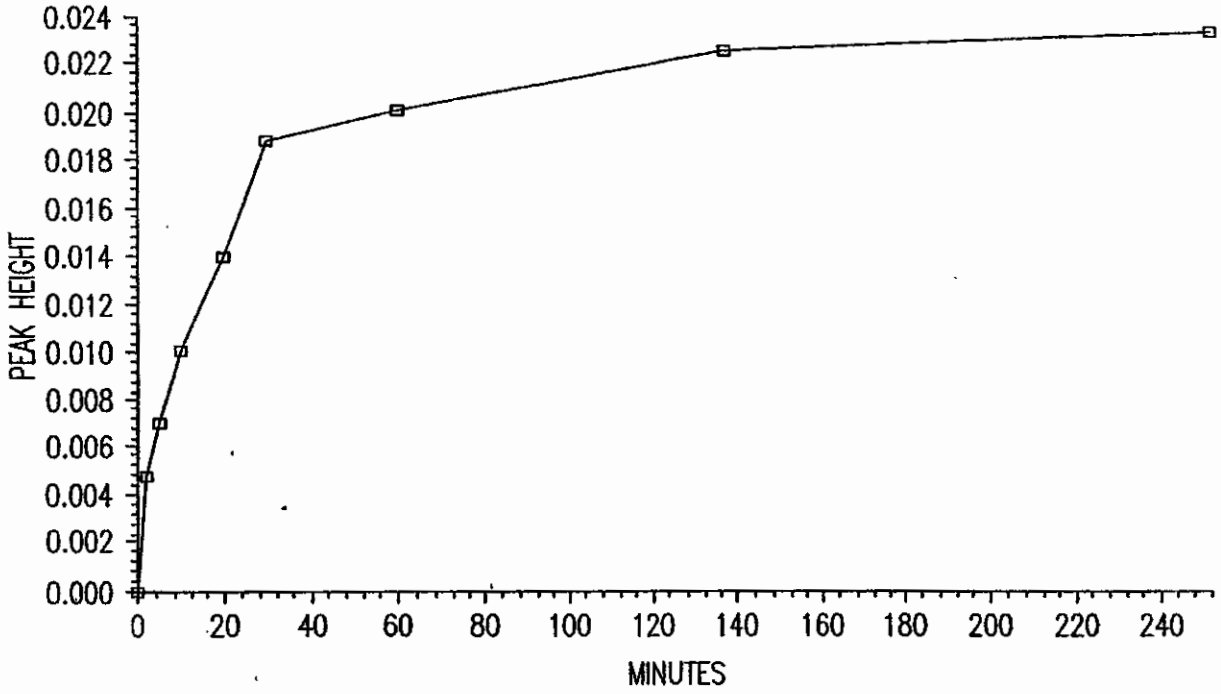
PEAK HEIGHT
0.024
0.022
0.020
0.018
0.016
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
0
20
40
60
80
100
120
140
160
180
200
220
240
MINUTES

FIG. 10

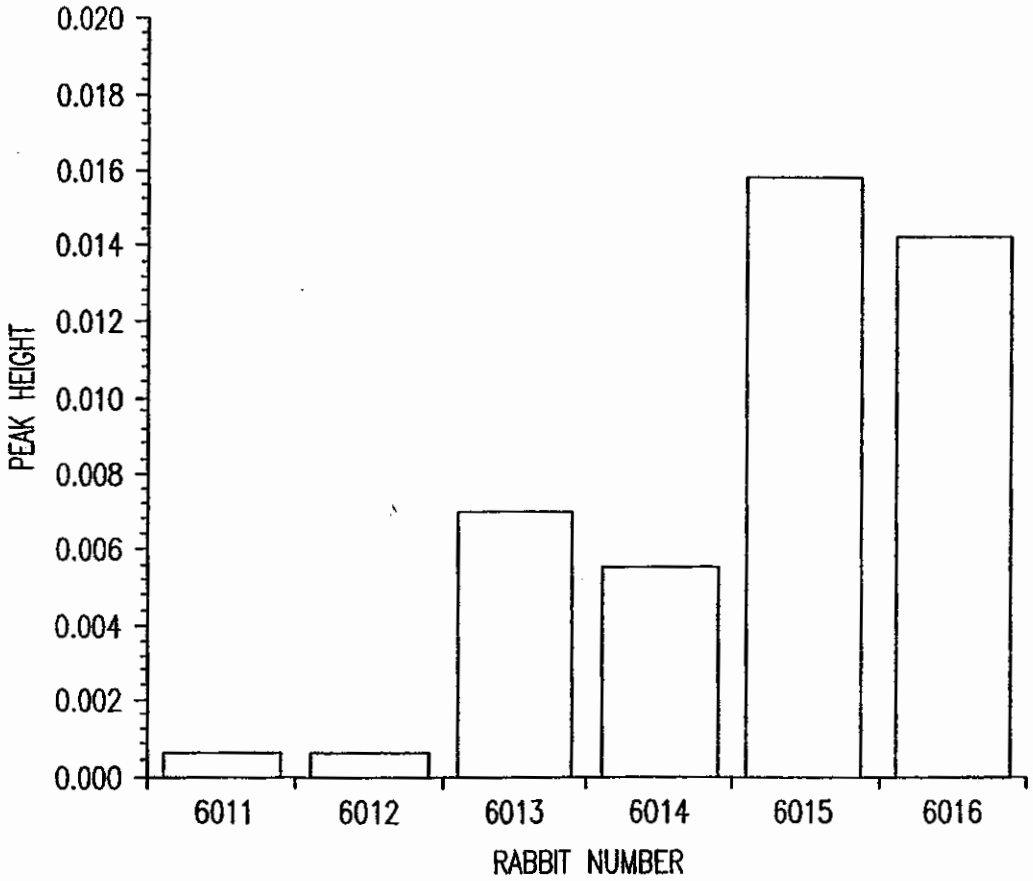
PEAK HEIGHT
0.020
0.018
0.016
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
6011
6012
6013
6014
6015
6016
RABBIT NUMBER

FIG. 11

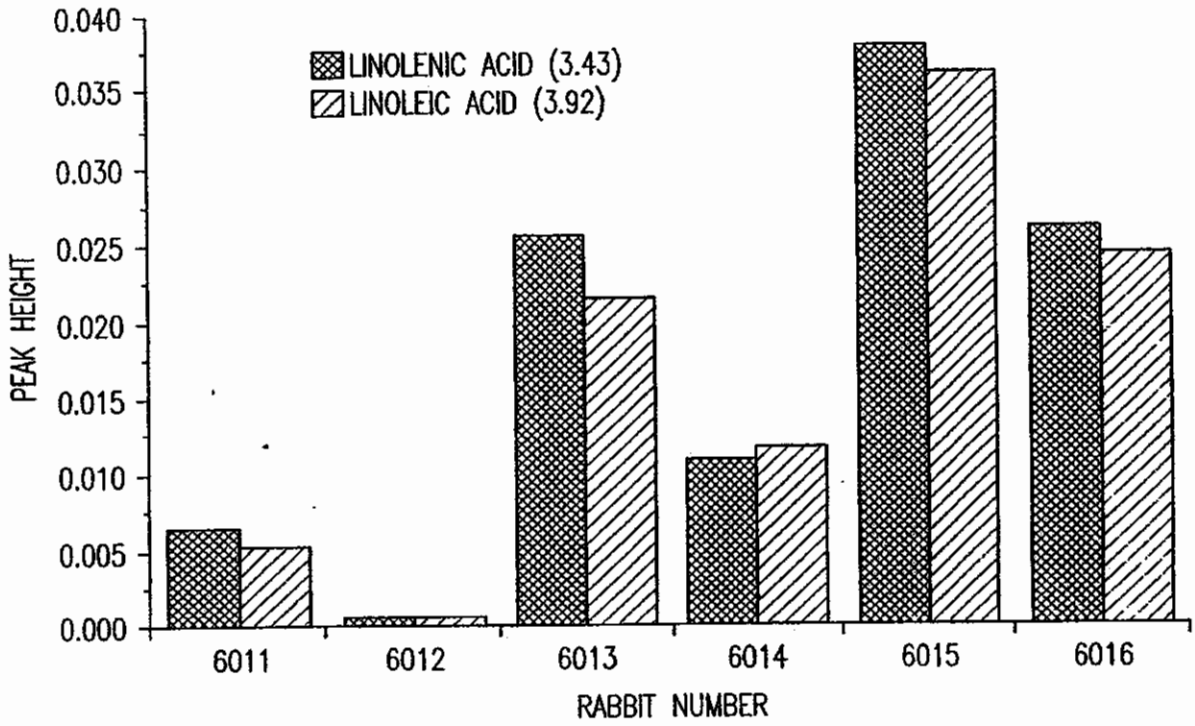
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
PEAK HEIGHT
LINOLENIC ACID (3.43)
LINOLEIC ACID (3.92)
6011
6012
6013
6014
6015
6016
RABBIT NUMBER

FIG. 12

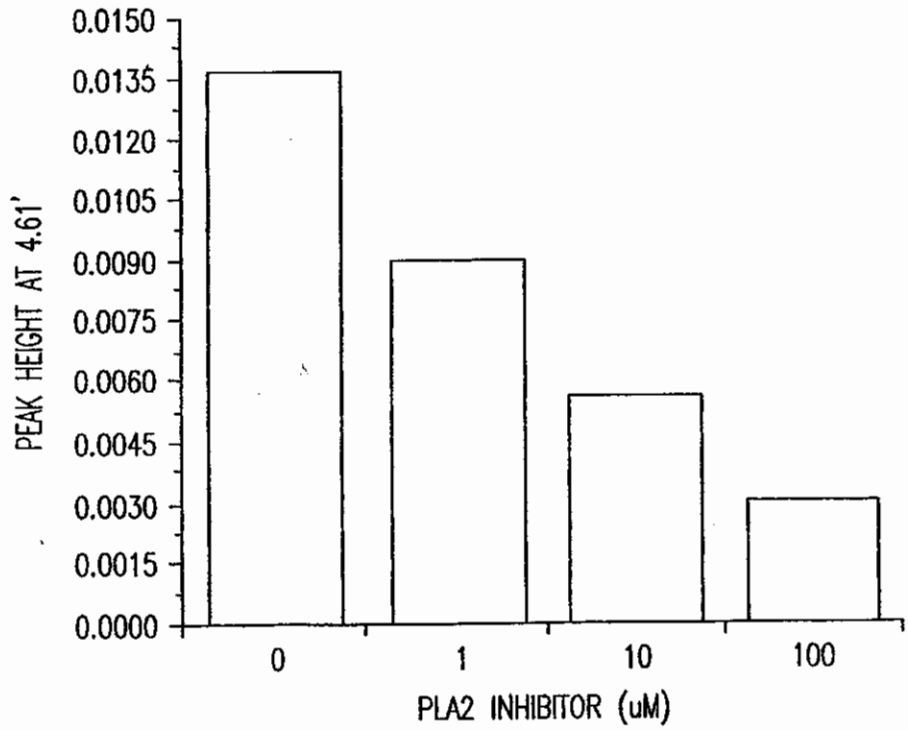
0.0150
0.0135
0.0120
0.0105
0.0090
0.0075
0.0060
0.0045
0.0030
0.0015
0.0000
PEAK HEIGHT AT 4.61'
0
1
10
100
PLA2 INHIBITOR (uM)

FIG. 13

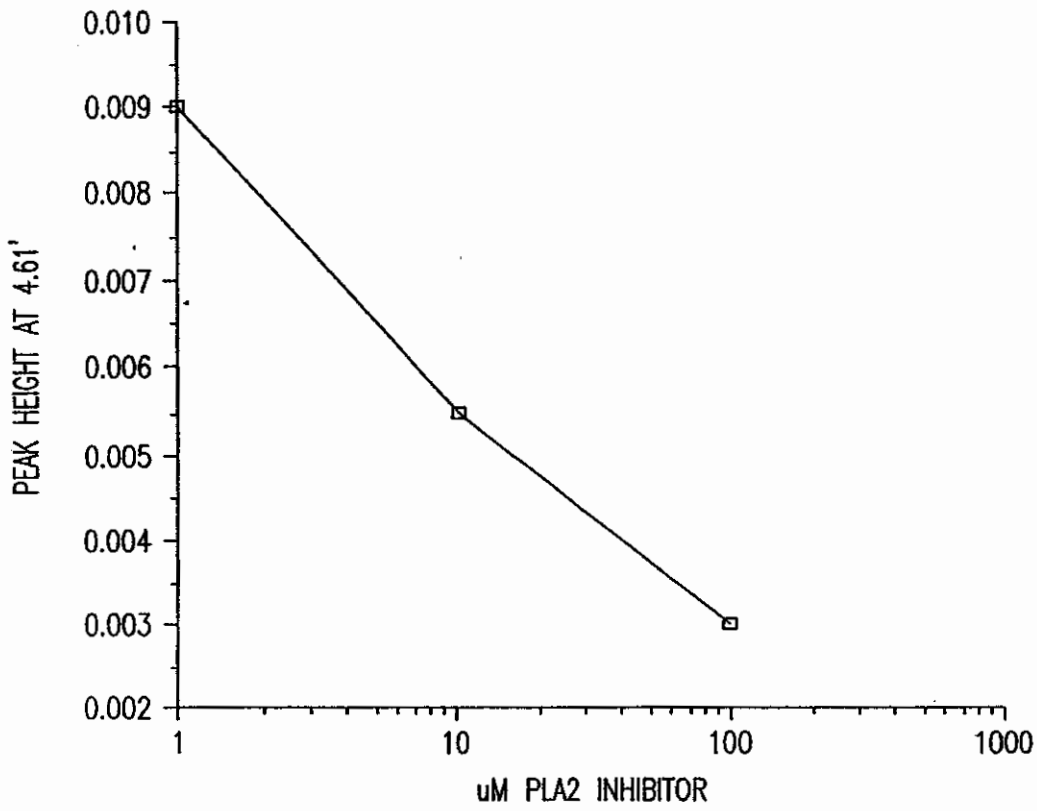
0.010
0.009
0.008
0.007
0.006
0.005
0.004
0.003
0.002
PEAK HEIGHT AT 4.61'
1
10
100
1000
uM PLA2 INHIBITOR

FIG. 14