Fig. 1

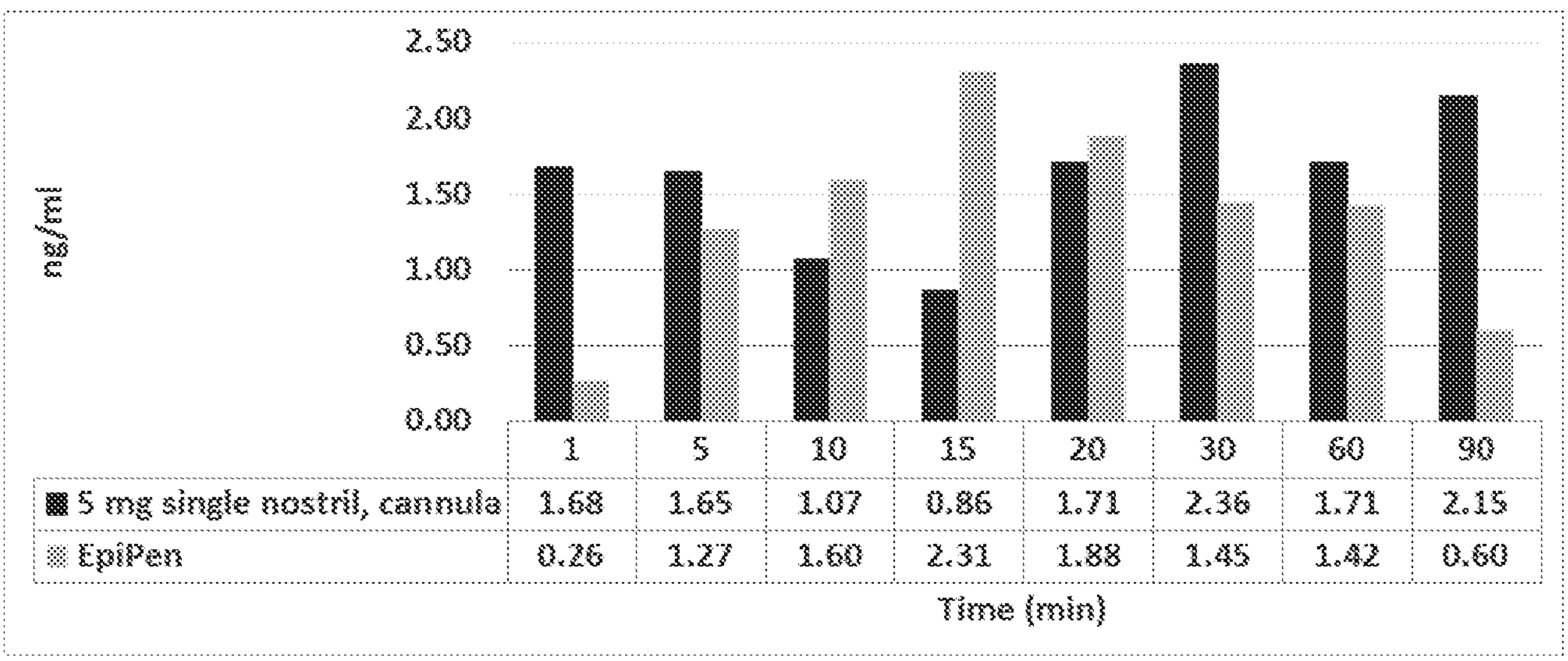

2.50
2.00
1.50
1.00
0.50
0.00
ng/ml
1
5
10
15
20
30
60
90
5 mg single nostril, cannula
1.68
1.65
1.07
0.86
1.71
2.36
1.71
2.15
EpiPen
0.26
1.27
1.60
2.31
1.88
1.45
1.42
0.60
Time (min)

Fig. 2

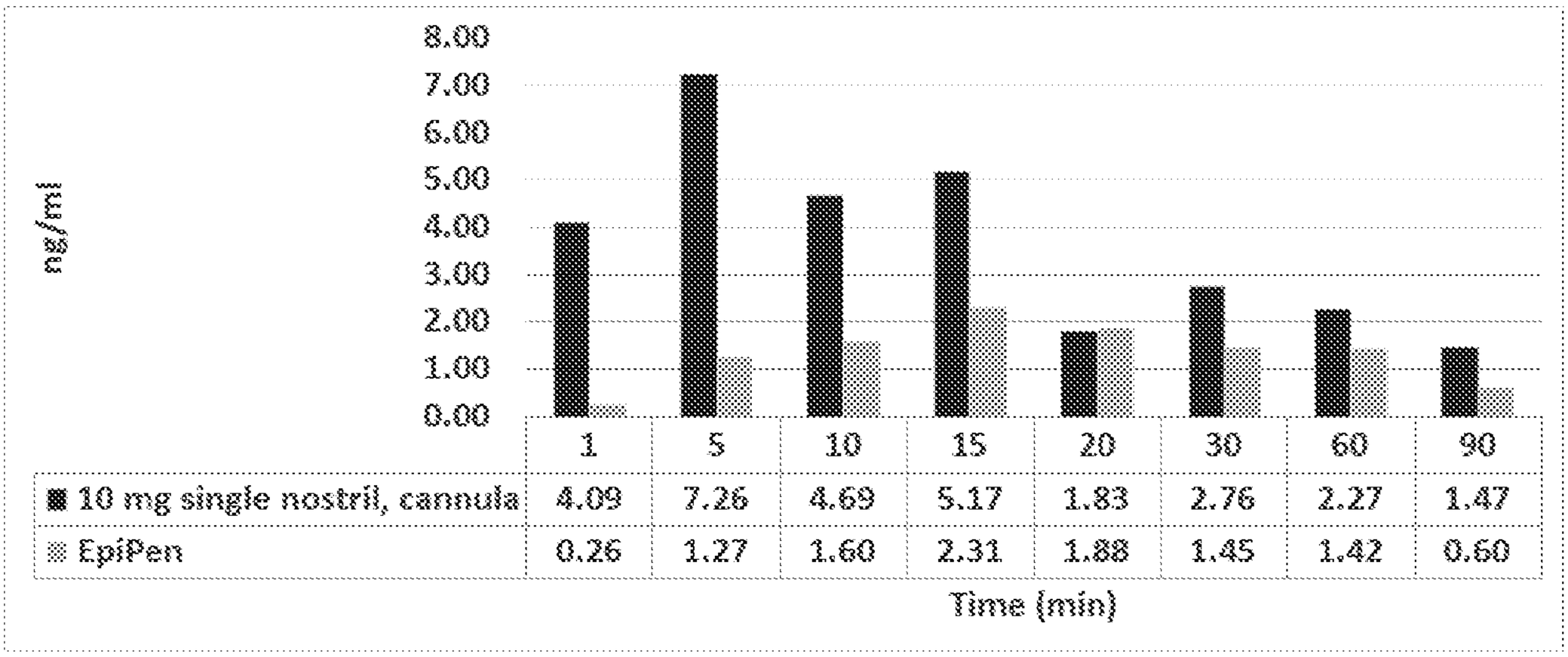

8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
ng/ml
1
5
10
15
20
30
60
90
10 mg single nostril, cannula
4.09
7.26
4.69
5.17
1.83
2.76
2.27
1.47
EpiPen
0.26
1.27
1.60
2.31
1.88
1.45
1.42
0.60
Time (min)

Fig. 3

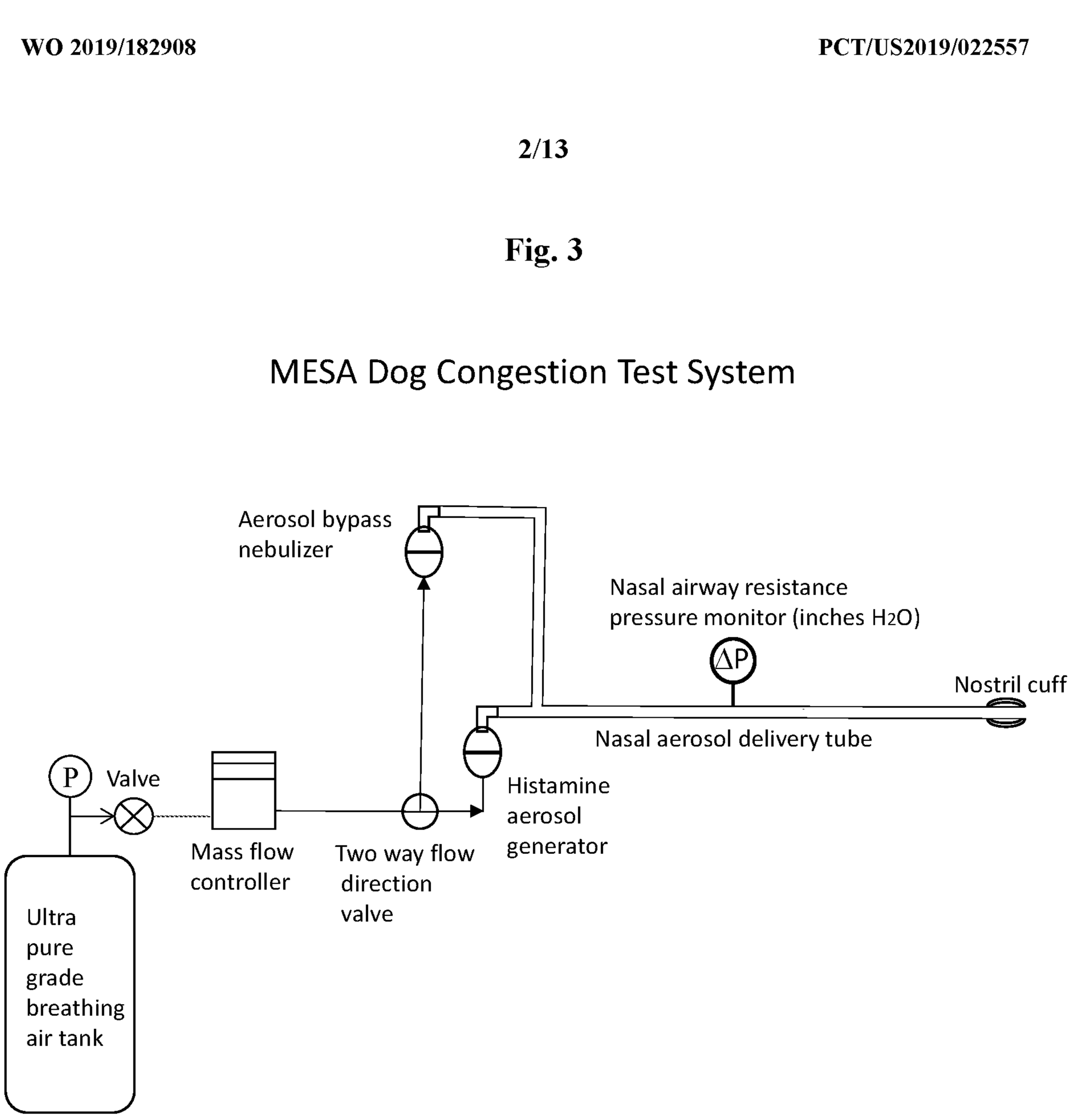

MESA Dog Congestion Test System
Aerosol bypass nebulizer
Nasal airway resistance pressure monitor (inches H2O)
ΔP
Nostril cuff
Nasal aerosol delivery tube
P
Valve
Histamine aerosol generator
Mass flow controller
Two way flow direction valve
Ultra pure grade breathing air tank

Fig. 4

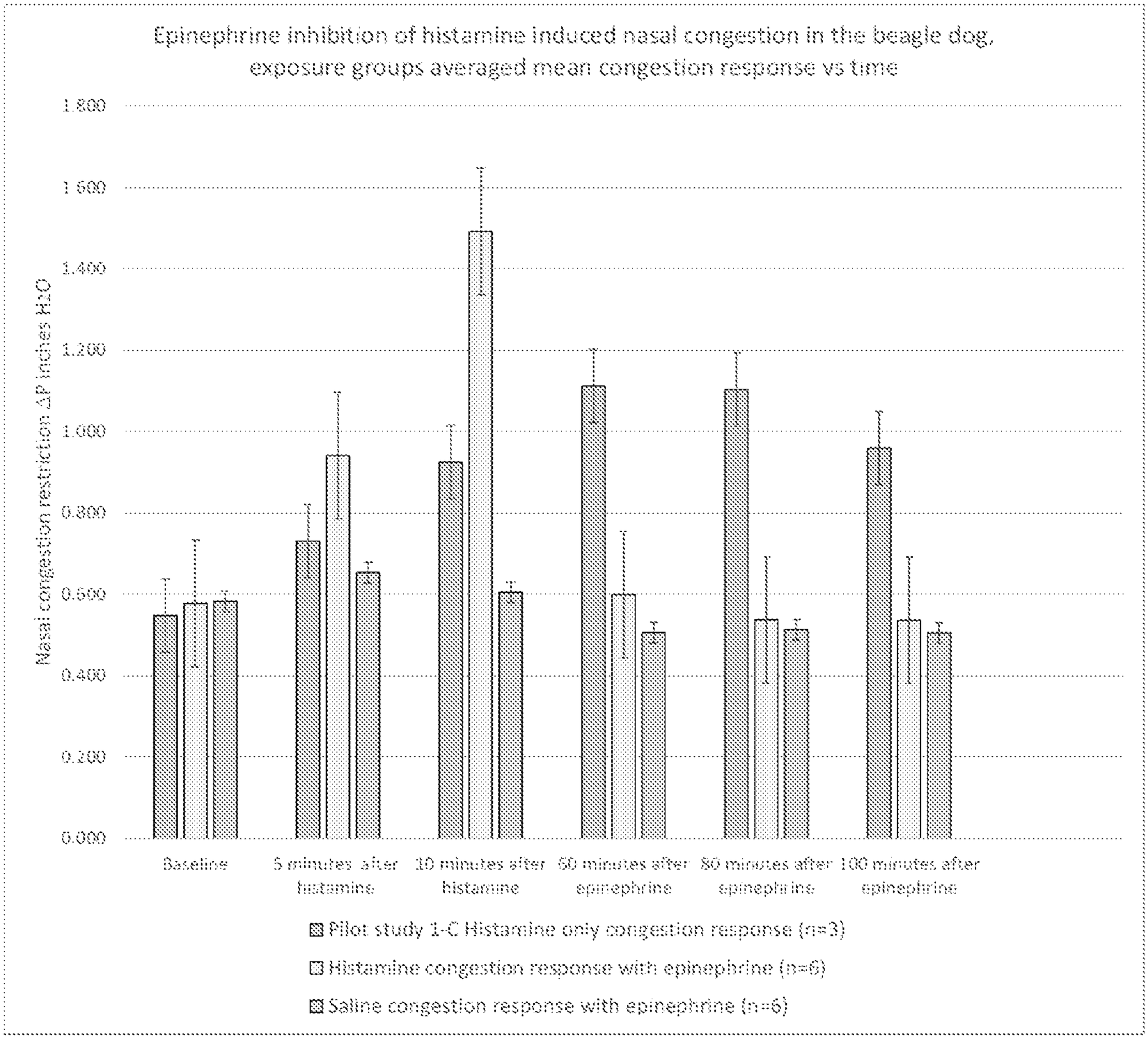

Epinephrine inhibition of histamine induced nasal congestion in the beagle dog,
exposure groups averaged mean congestion response vs time
Nasal congestion restriction ΔP inches H2O
1.800
1.600
1.400
1.200
1.000
0.800
0.600
0.400
0.200
0.000
Baseline
5 minutes after histamine
10 minutes after histamine
60 minutes after epinephrine
80 minutes after epinephrine
100 minutes after epinephrine
Pilot study 1-C Histamine only congestion response (n=3)
Histamine congestion response with epinephrine (n=6)
Saline congestion response with epinephrine (n=6)

Fig. 5

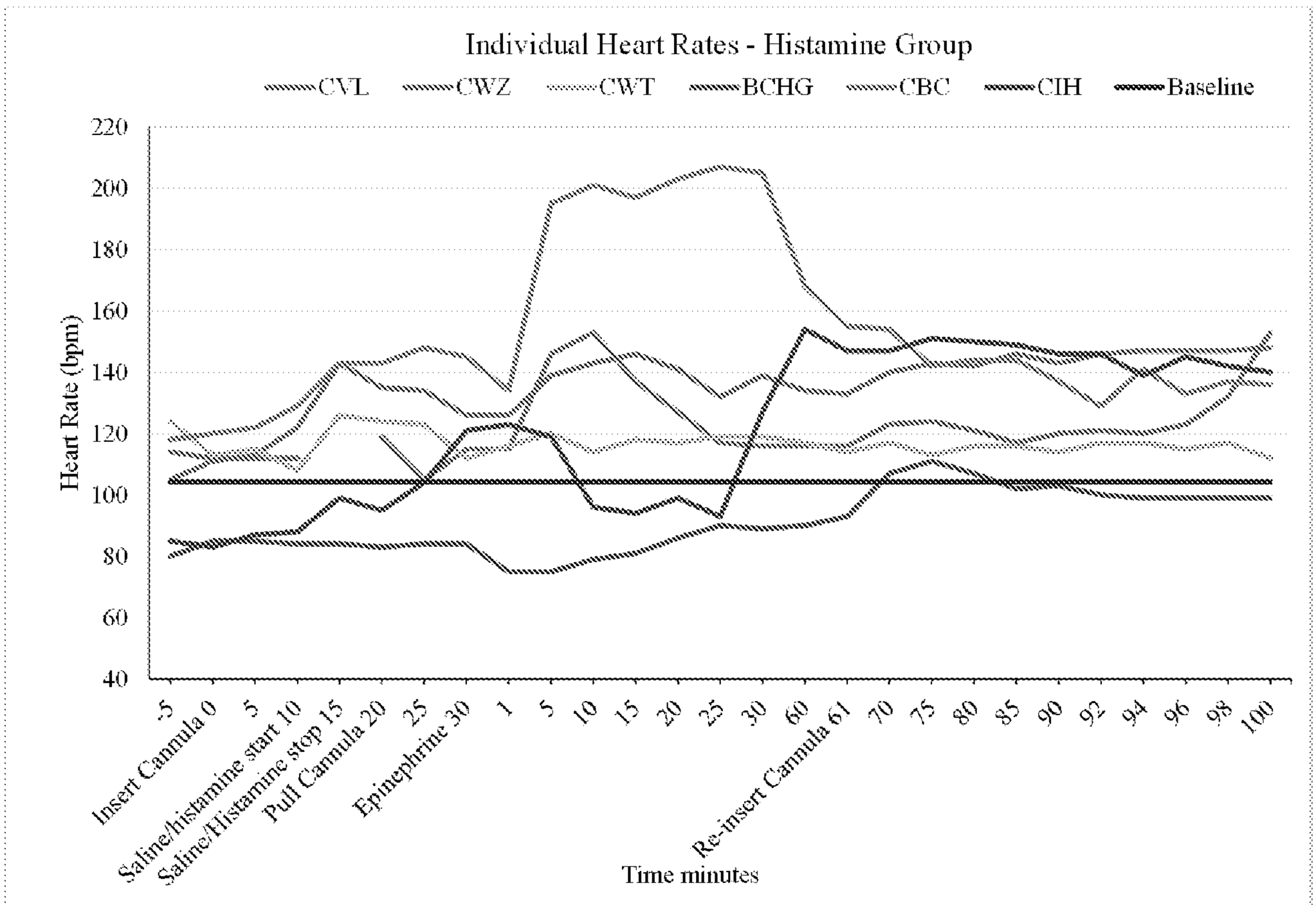

Individual Heart Rates - Histamine Group
CVL
CWZ
CWT
BCHG
CBC
CIH
Baseline
Heart Rate (bpm)
220
200
180
160
140
120
100
80
60
40
-5
Insert Cannula 0
5
Saline/histamine start 10
Saline/Histamine stop 15
Pull Cannula 20
25
Epinephrine 30
1
5
10
15
20
25
30
60
Re-insert Cannula 61
70
75
80
85
90
92
94
96
98
100
Time minutes

Fig. 6

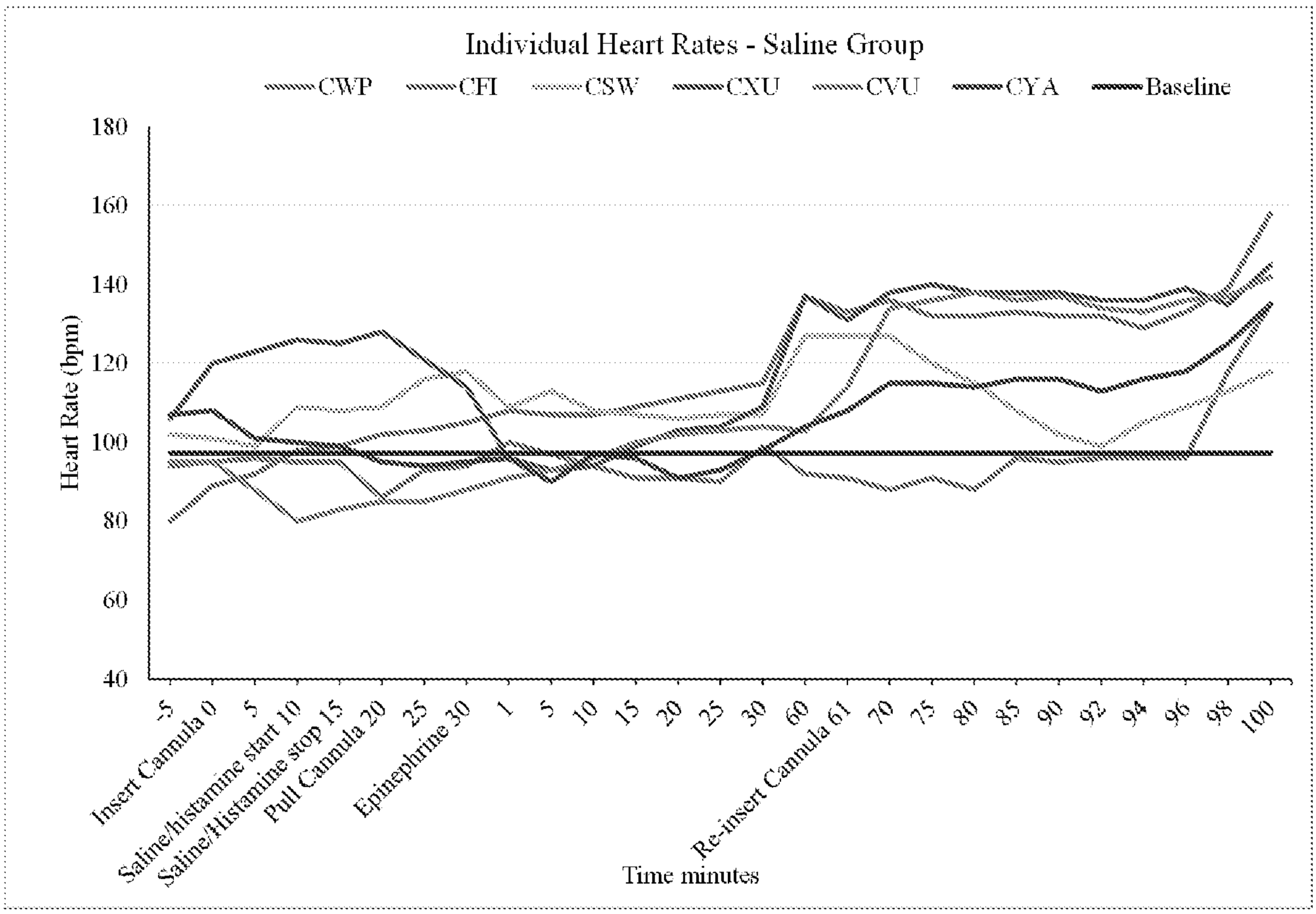

Individual Heart Rates - Saline Group
CWP
CFI
CSW
CXU
CVU
CYA
Baseline
Heart Rate (bpm)
180
160
140
120
100
80
60
40
-5
Insert Cannula 0
5
Saline/histamine start 10
15
Saline/Histamine stop 15
Pull Cannula 20
25
Epinephrine 30
1
5
10
15
20
25
30
60
Re-insert Cannula 61
70
75
80
85
90
92
94
96
98
100
Time minutes

Fig. 7

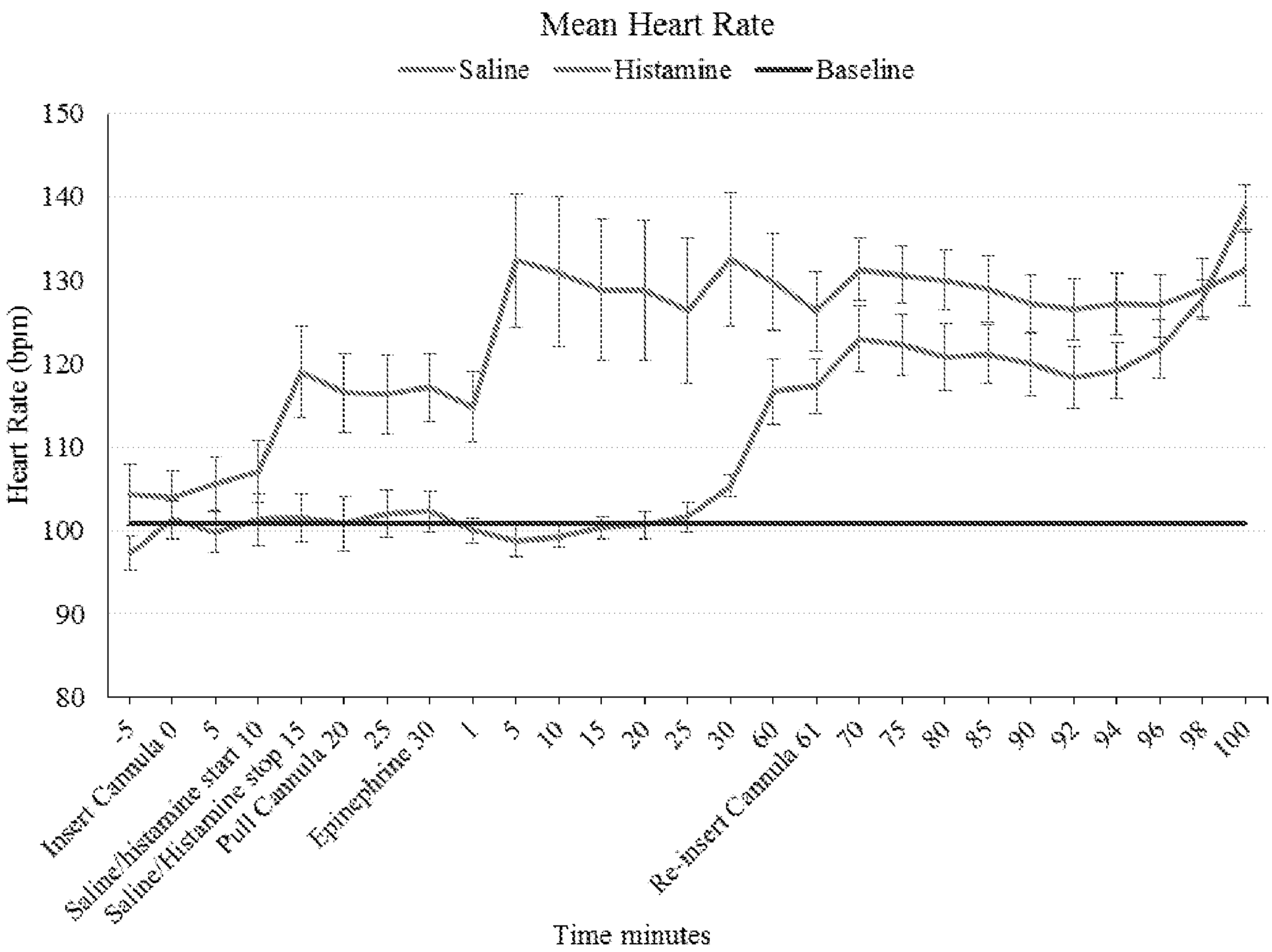

Mean Heart Rate
Saline
Histamine
Baseline
Heart Rate (bpm)
150
140
130
120
110
100
90
80
-5
Insert Cannula 0
5
Saline/histamine start 10
Saline/Histamine stop 15
Pull Cannula 20
25
Epinephrine 30
1
5
10
15
20
25
30
60
Re-insert Cannula 61
70
75
80
85
90
92
94
96
98
100
Time minutes

Fig. 8

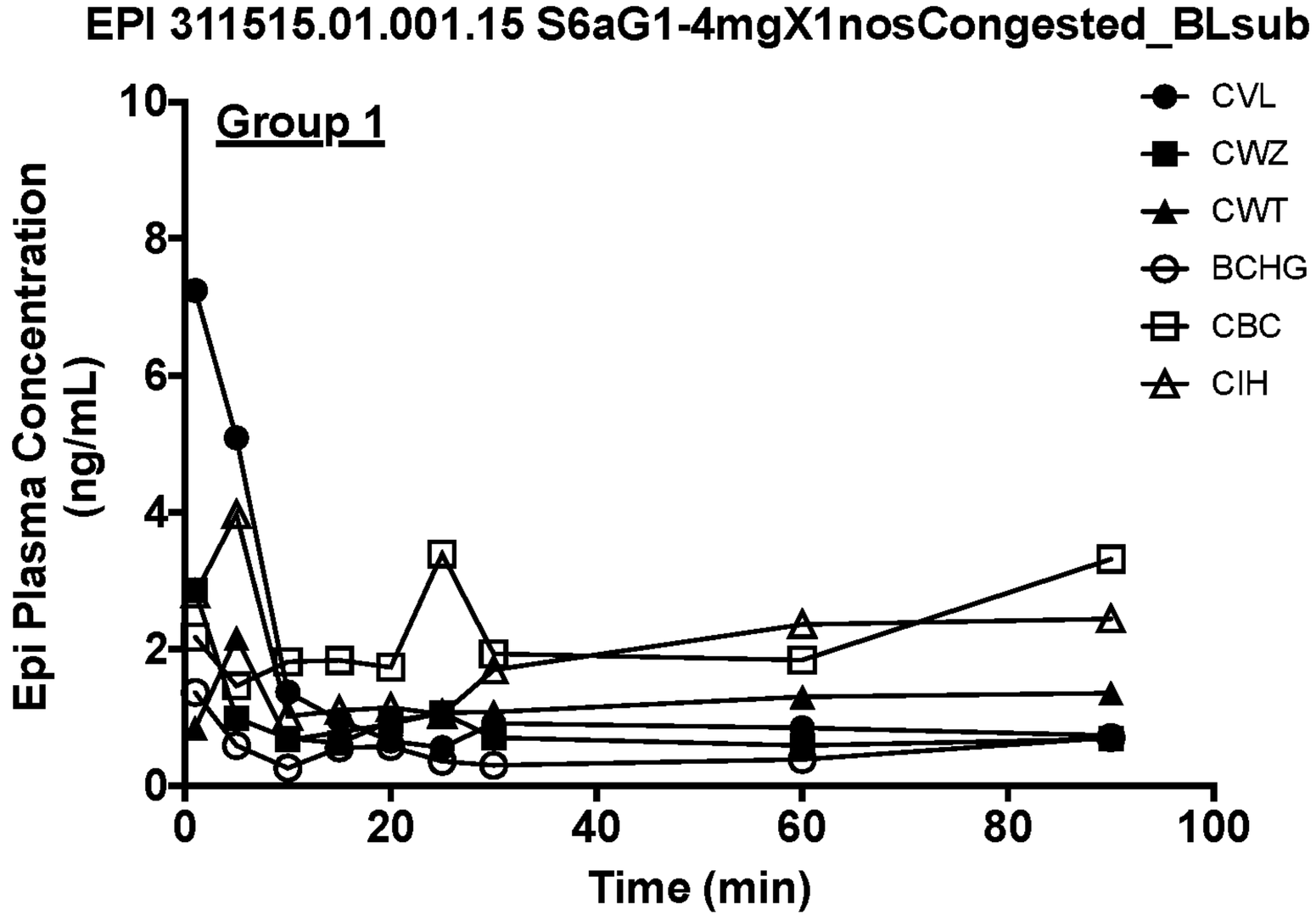

EPI 311515.01.001.15 S6aG1-4mgX1nosCongested_BLsub
Group 1
Epi Plasma Concentration (ng/mL)
Time (min)
0
2
4
6
8
10
0
20
40
60
80
100
CVL
CWZ
CWT
BCHG
CBC
CIH

Fig. 9

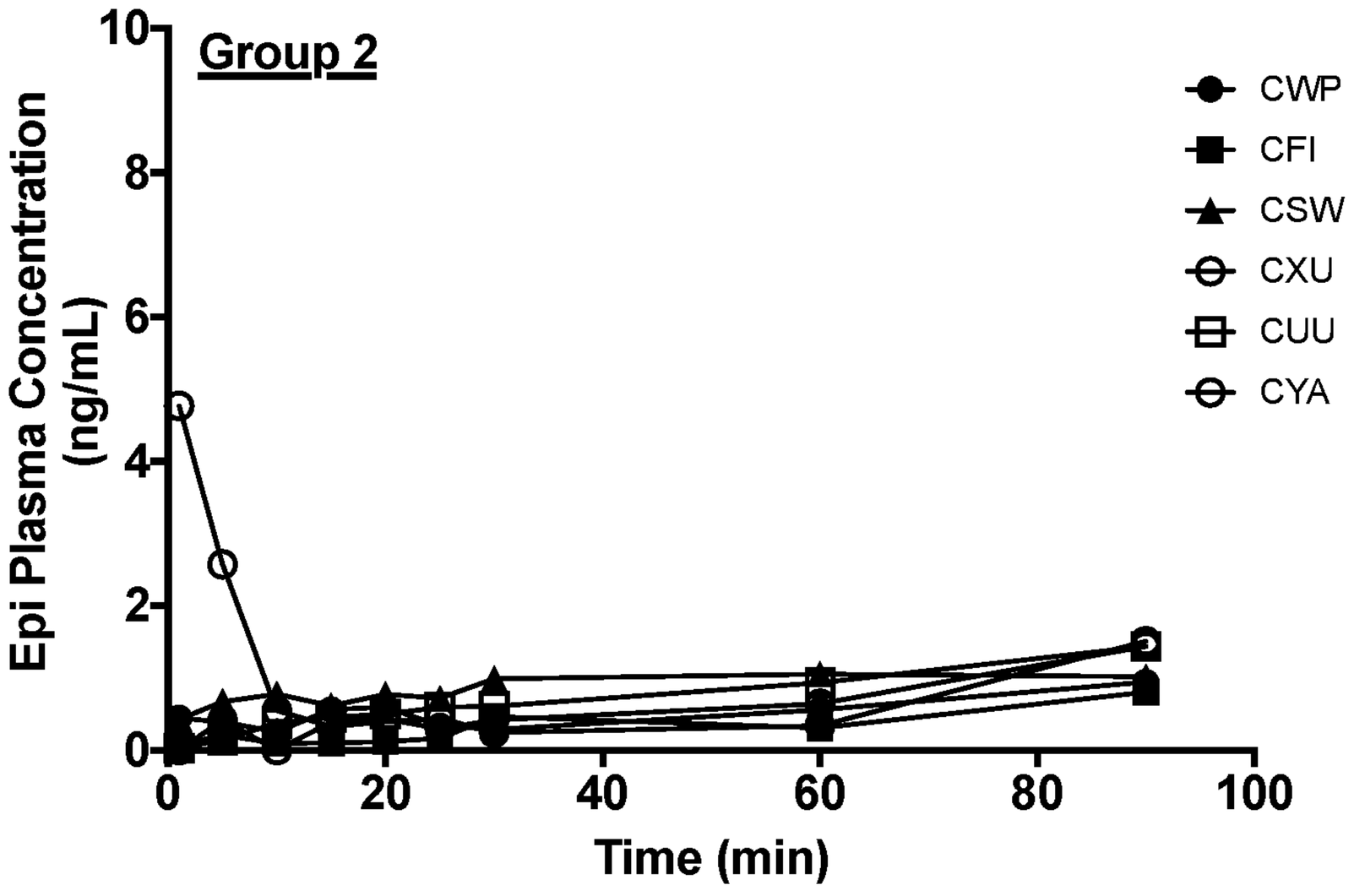

EPI 311515.01.001.15 S6aG2-4mgX1nosSaline_BLsub
Group 2
Epi Plasma Concentration (ng/mL)
Time (min)
0
2
4
6
8
10
0
20
40
60
80
100
CWP
CFI
CSW
CXU
CUU
CYA

Fig. 10

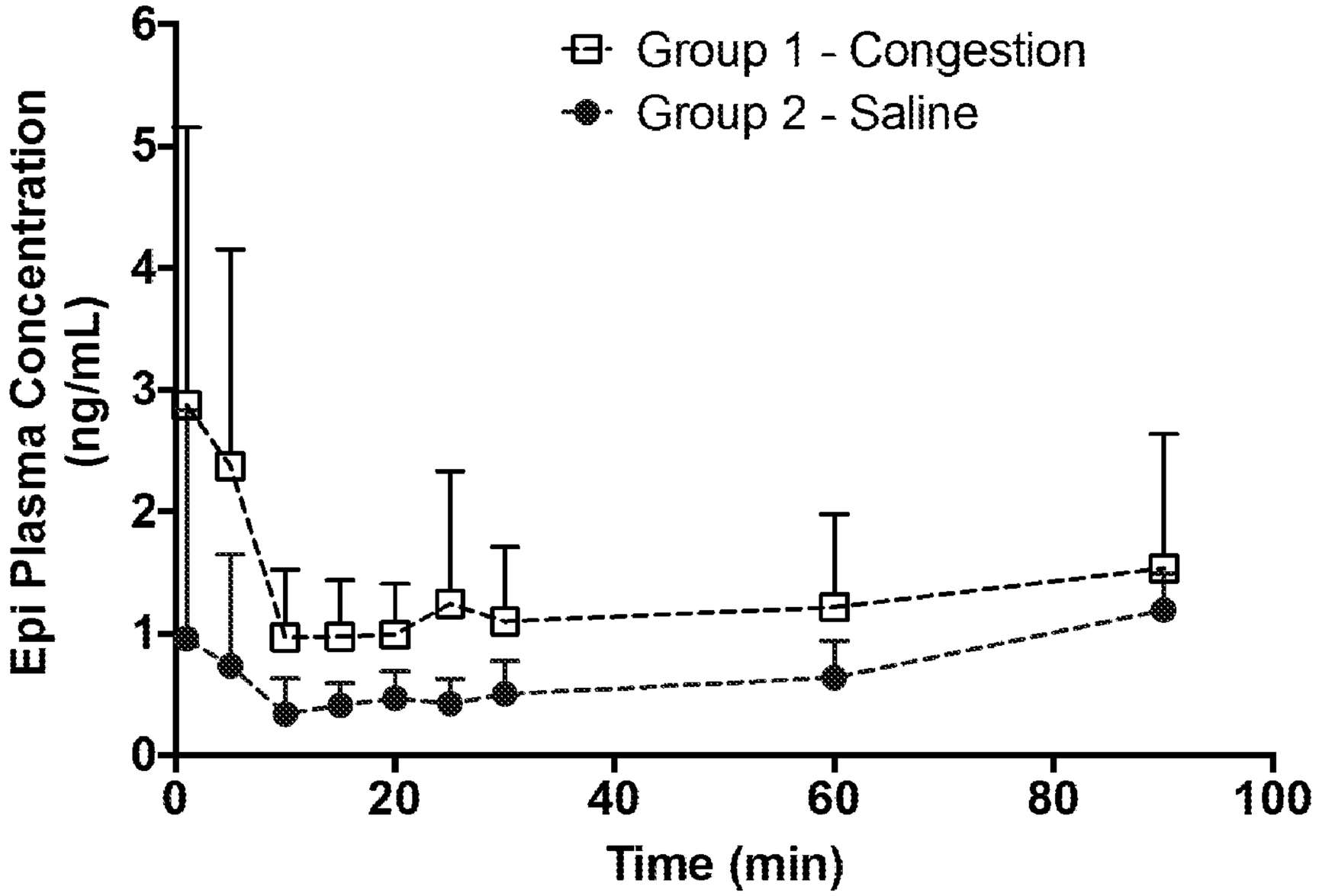
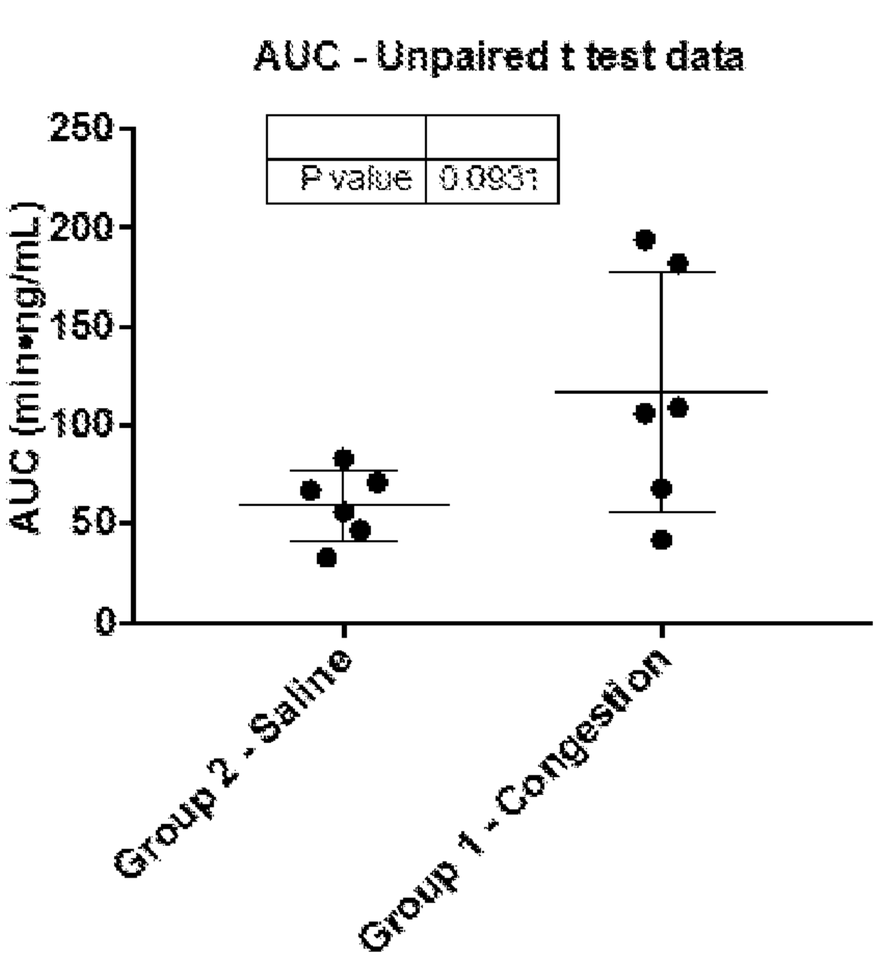
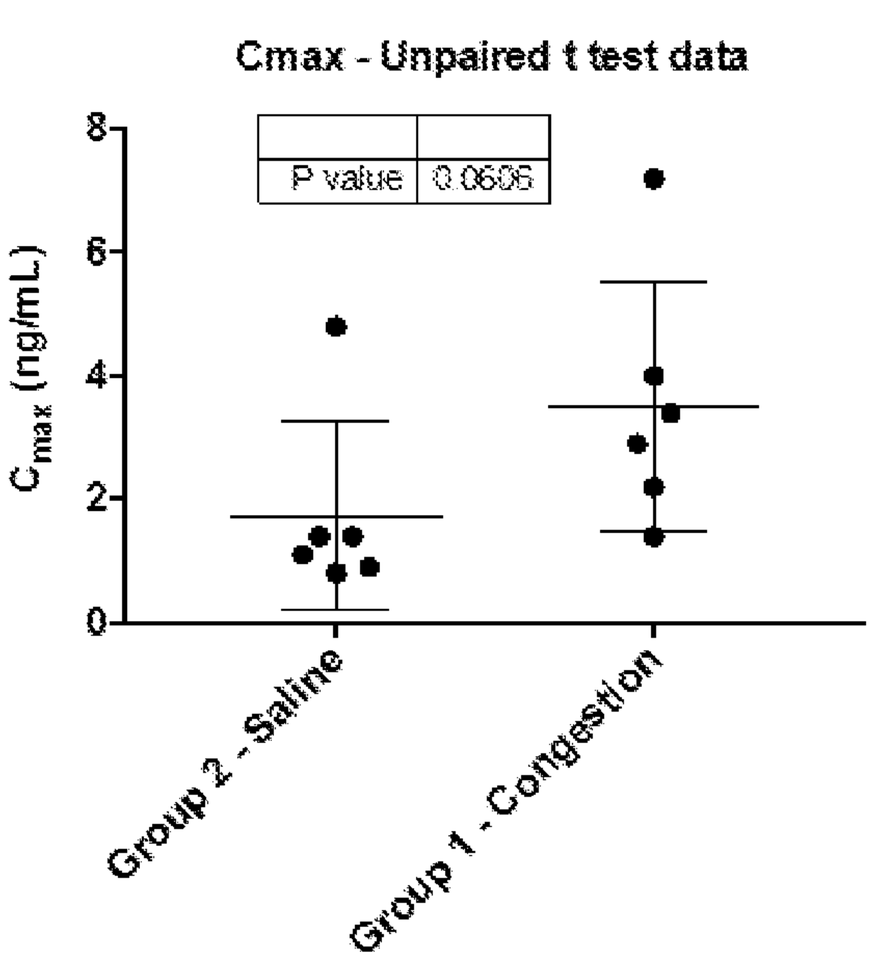

Group 1 - Congestion
Group 2 - Saline
Epi Plasma Concentration (ng/mL)
0
1
2
3
4
5
6
0
20
40
60
80
100
Time (min)

Fig. 11


A)
AUC - Unpaired t test data
P value 0.0931
AUC (min•ng/mL)
250
200
150
100
50
0
Group 2 - Saline
Group 1 - Congestion


B)
Cmax - Unpaired t test data
P value 0.0606
Cmax (ng/mL)
8
6
4
2
0
Group 2 - Saline
Group 1 - Congestion

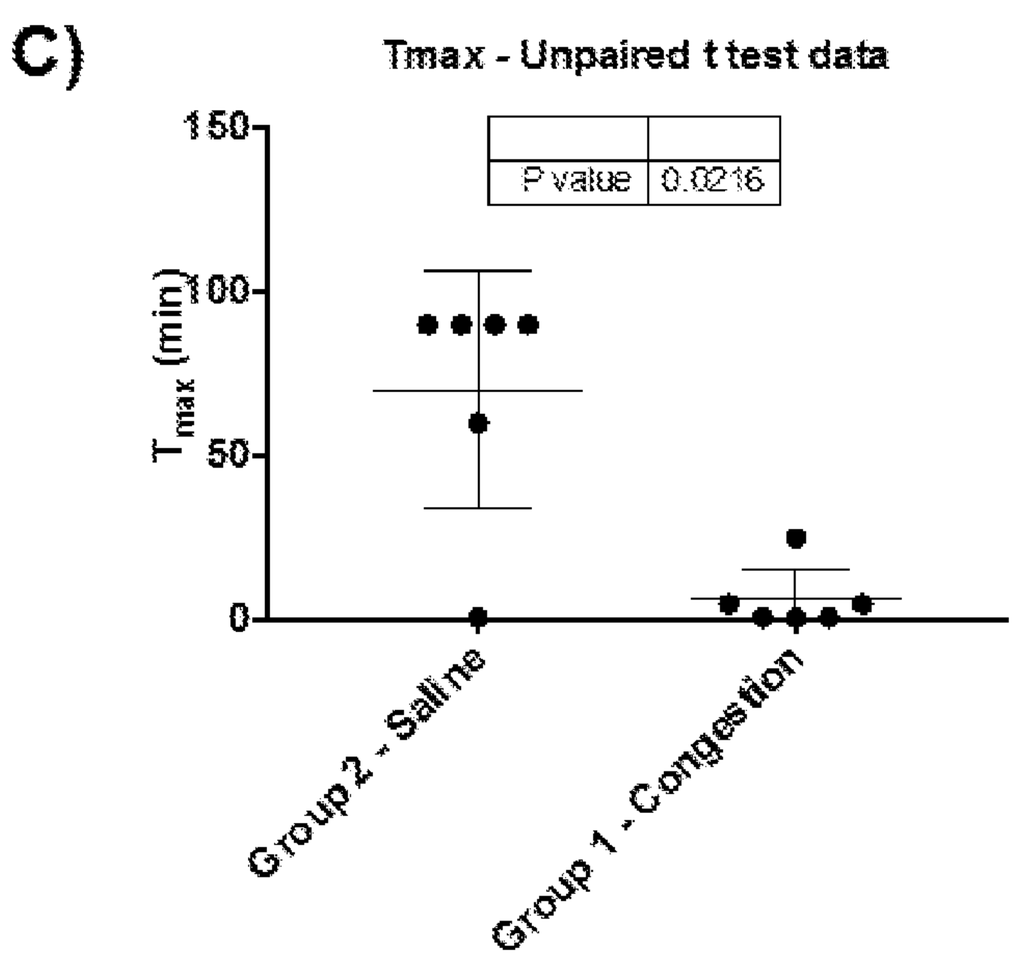

C)
Tmax - Unpaired t test data
P value 0.0216
Tmax (min)
150
100
50
0
Group 2 - Saline
Group 1 - Congestion

Fig. 12

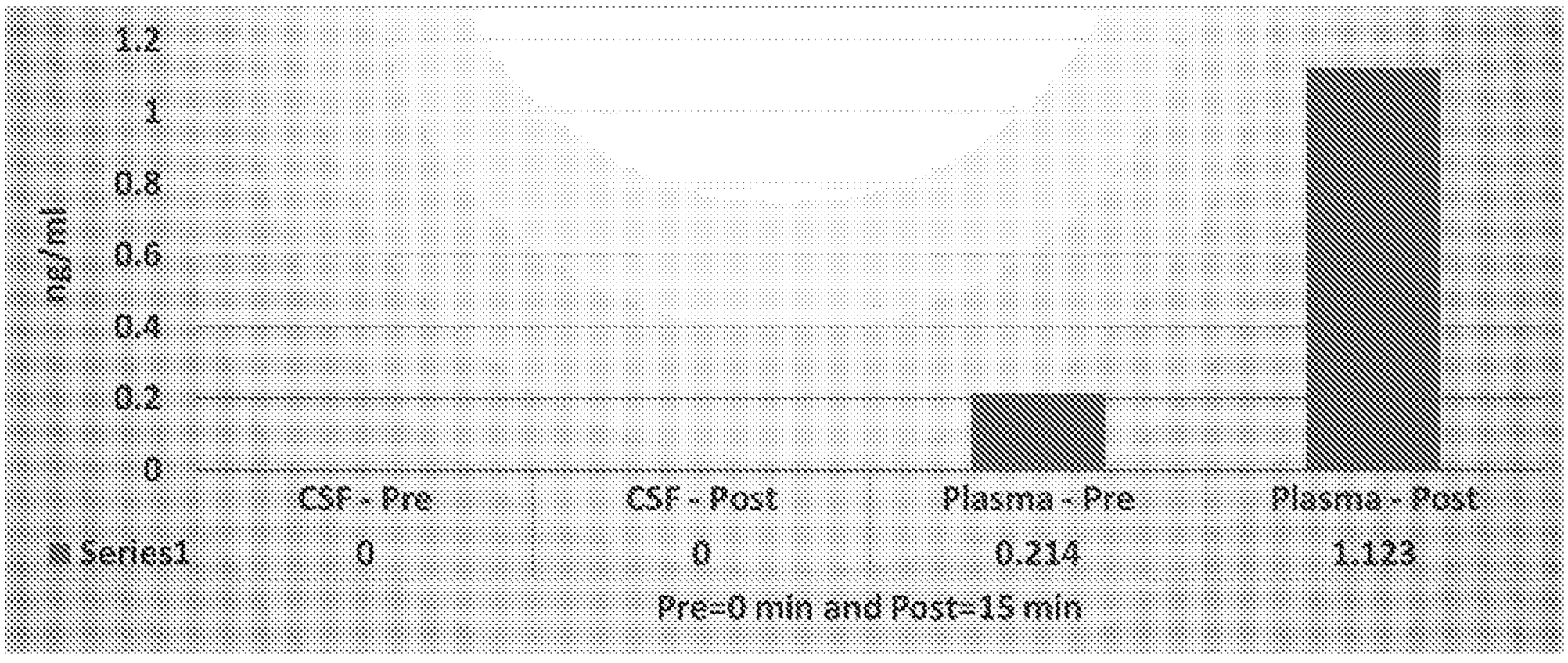

1.2
1
0.8
0.6
0.4
0.2
0
ng/ml
CSF - Pre
CSF - Post
Plasma - Pre
Plasma - Post
Series1
0
0
0.214
1.123
Pre=0 min and Post=15 min

Fig. 13

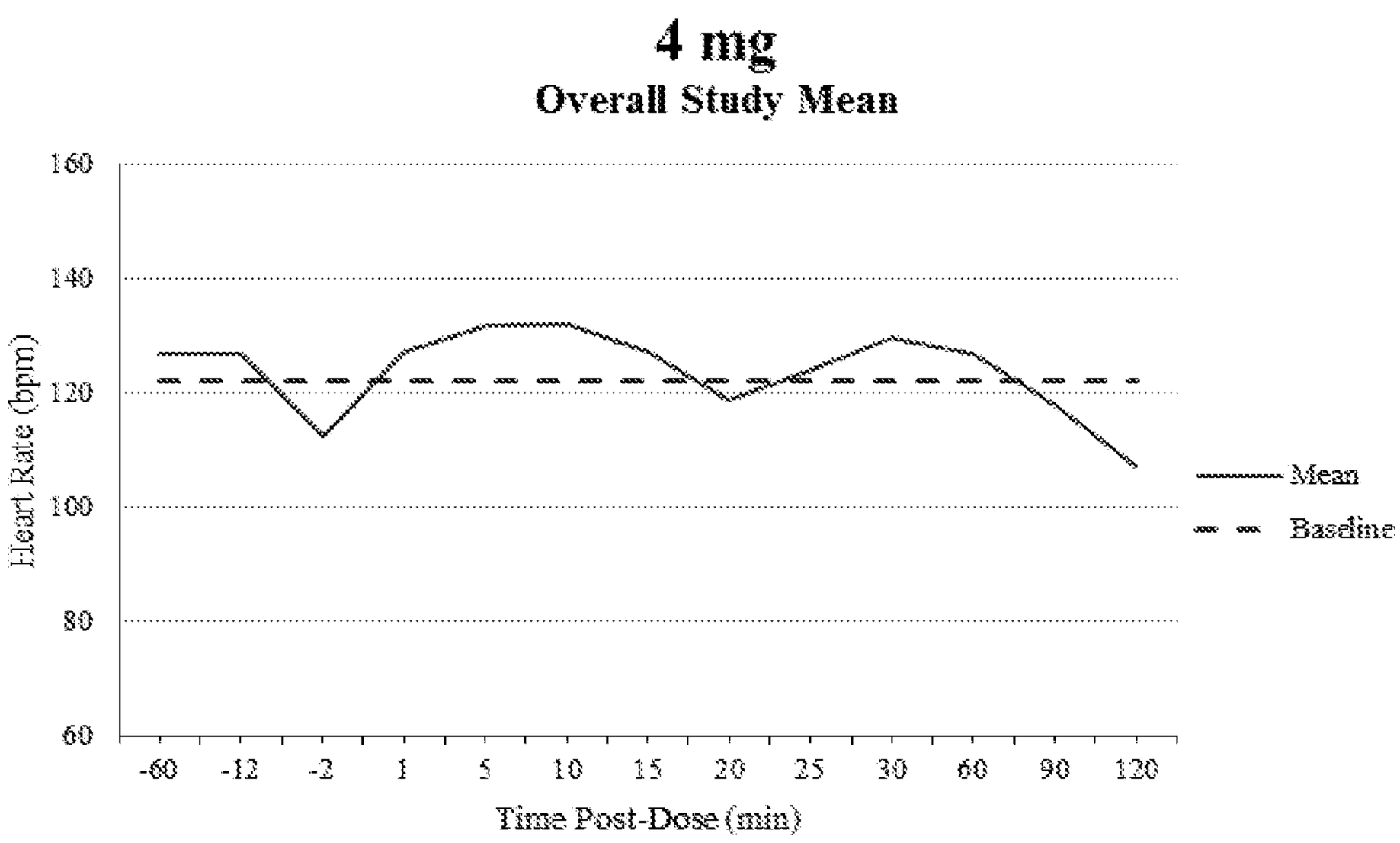

4 mg
Overall Study Mean
Heart Rate (bpm)
160
140
120
100
80
60
-60
-12
-2
1
5
10
15
20
25
30
60
90
120
Time Post-Dose (min)
Mean
Baseline

Fig. 14

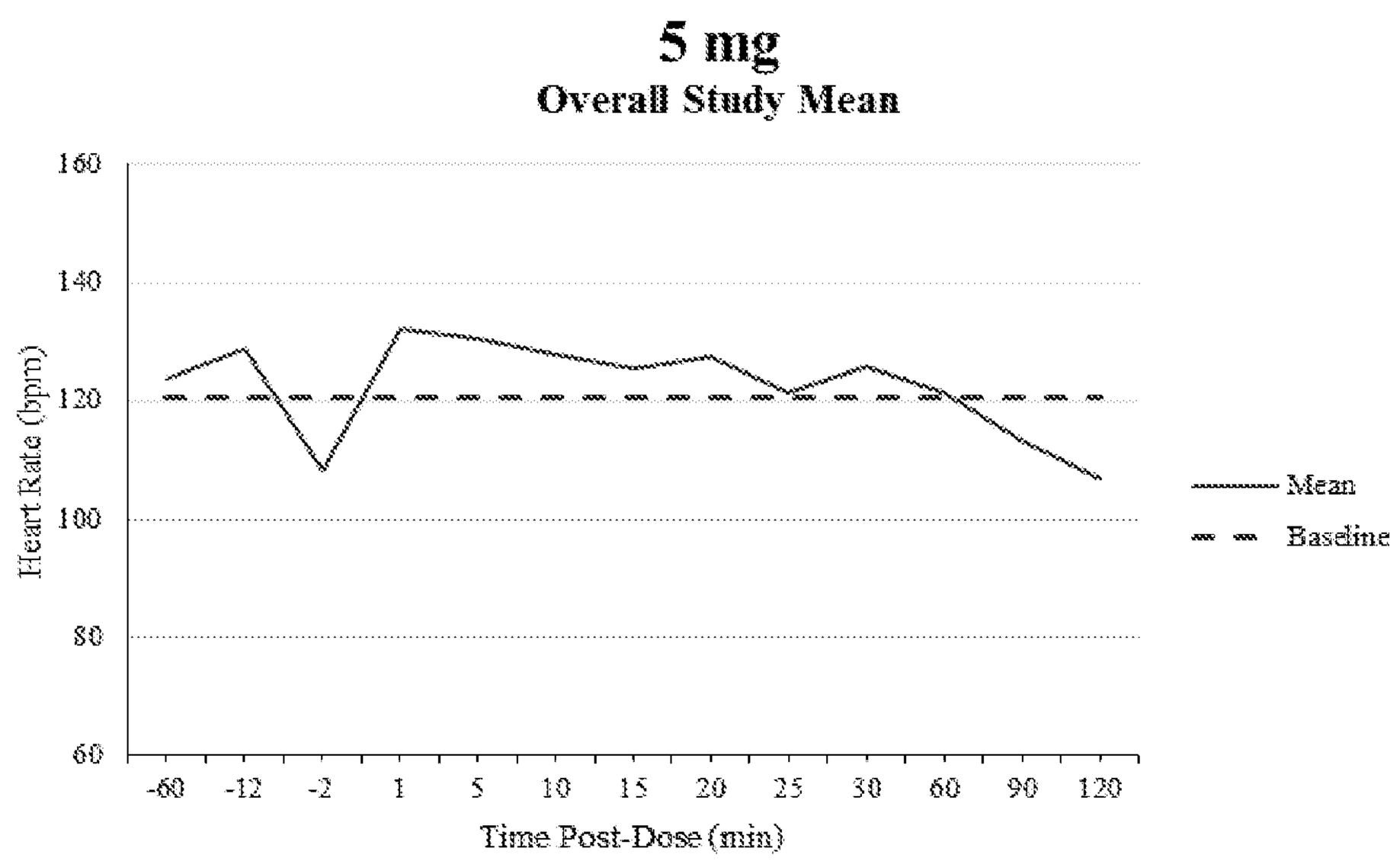

5 mg
Overall Study Mean
Heart Rate (bpm)
160
140
120
100
80
60
-60
-12
-2
1
5
10
15
20
25
30
60
90
120
Time Post-Dose (min)
Mean
Baseline

Fig. 15

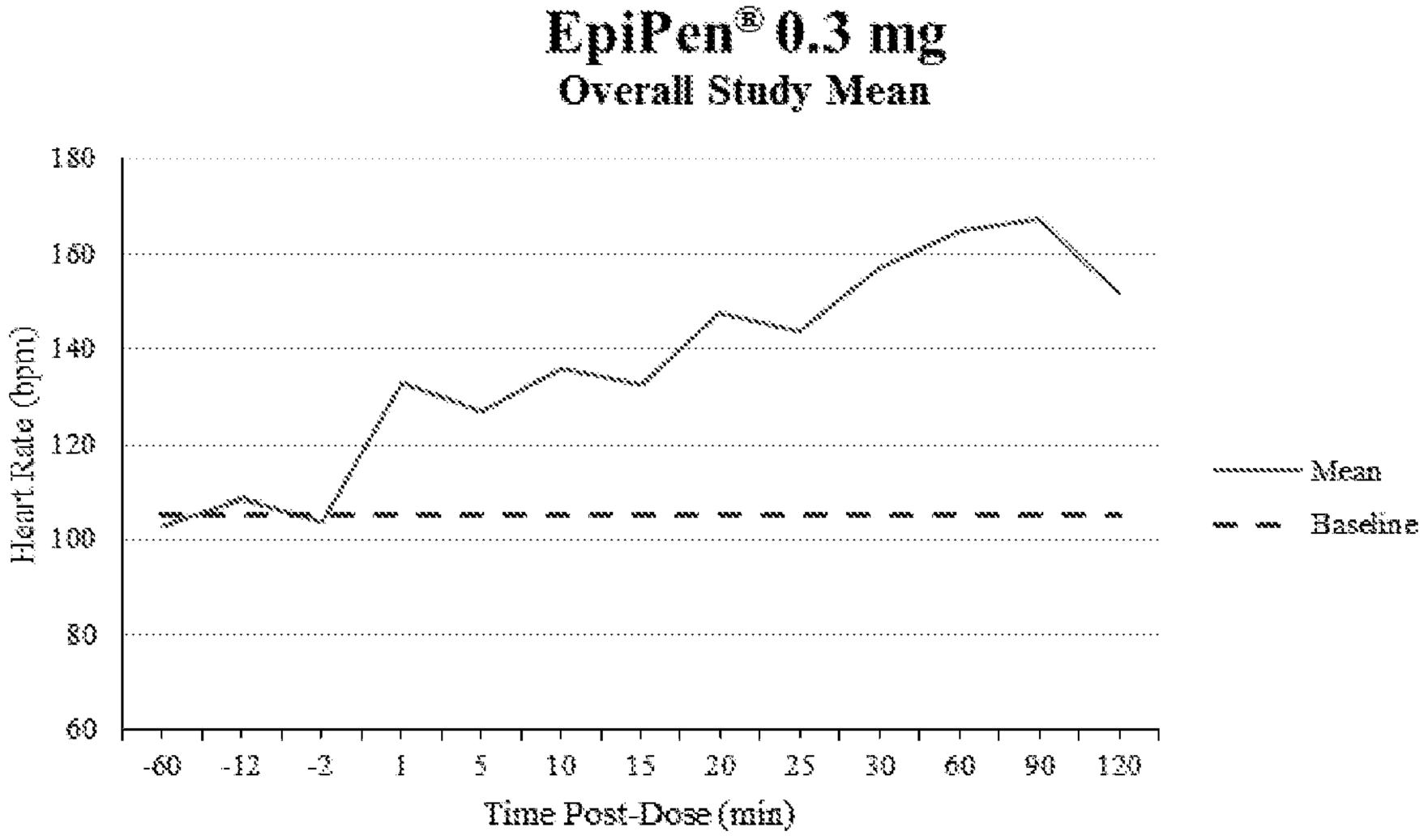

EpiPen® 0.3 mg
Overall Study Mean
Heart Rate (bpm)
180
160
140
120
100
80
60
-60
-12
-3
1
5
10
15
20
25
30
60
90
120
Time Post-Dose (min)
Mean
Baseline

Fig. 16

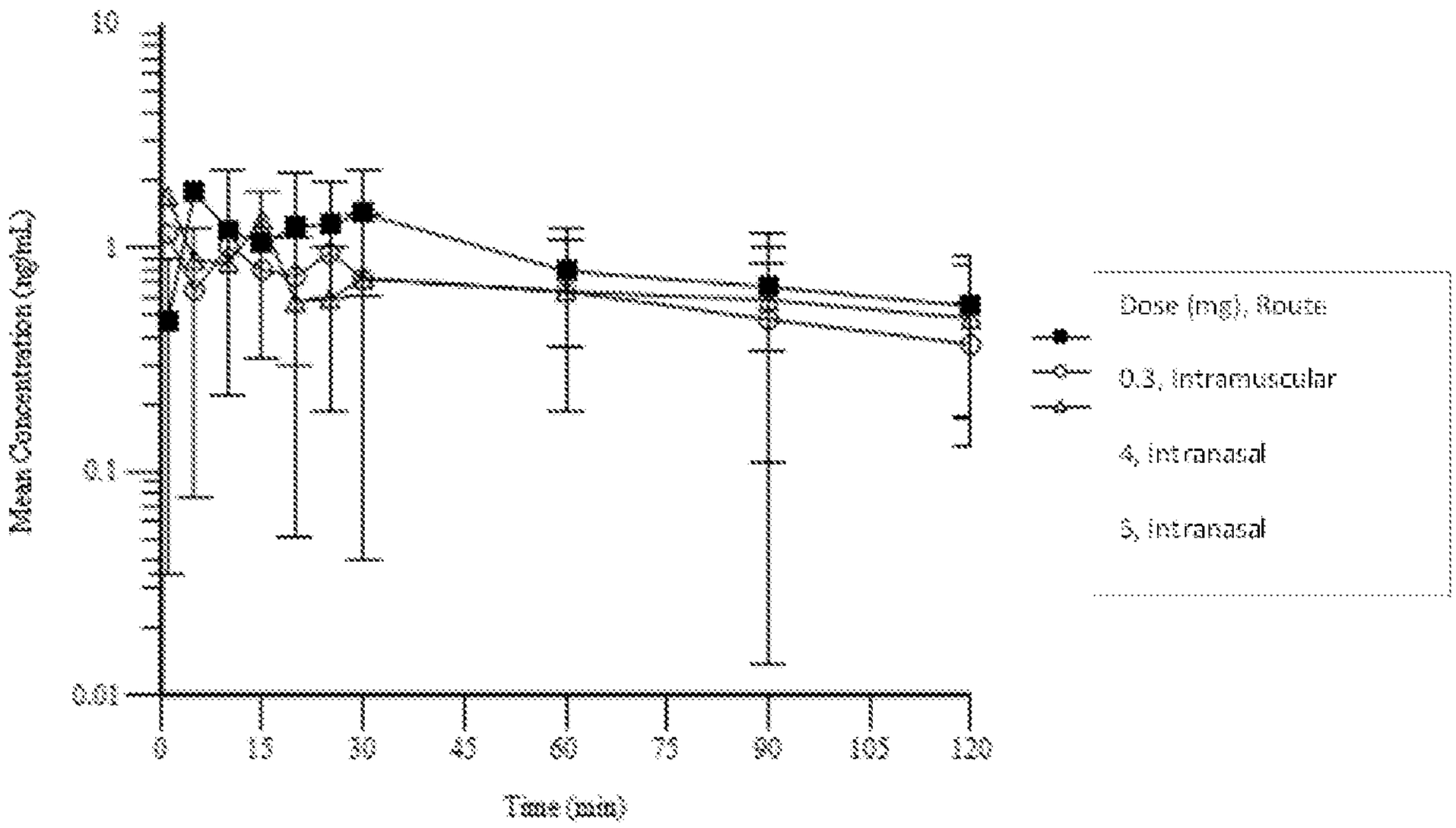

Mean Concentration (ng/mL)
10
1
0.1
0.01
0
15
30
45
60
75
90
105
120
Time (min)
Dose (mg), Route
0.3, Intramuscular
4, Intranasal
8, Intranasal

Fig. 17

