Figure 1

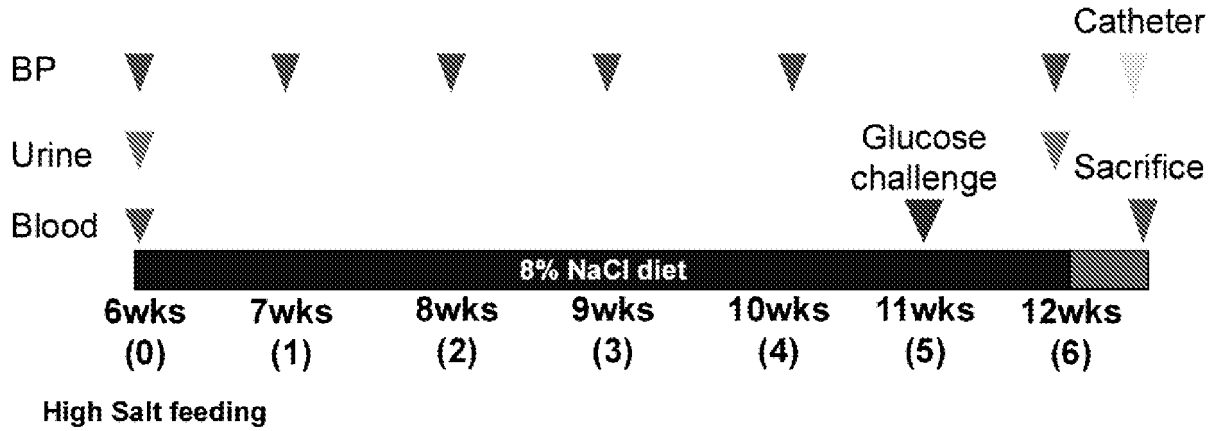

Catheter
BP
Urine
Blood
Glucose challenge
Sacrifice
8% NaCl diet
6wks (0)
7wks (1)
8wks (2)
9wks (3)
10wks (4)
11wks (5)
12wks (6)
High Salt feeding

Figure 2

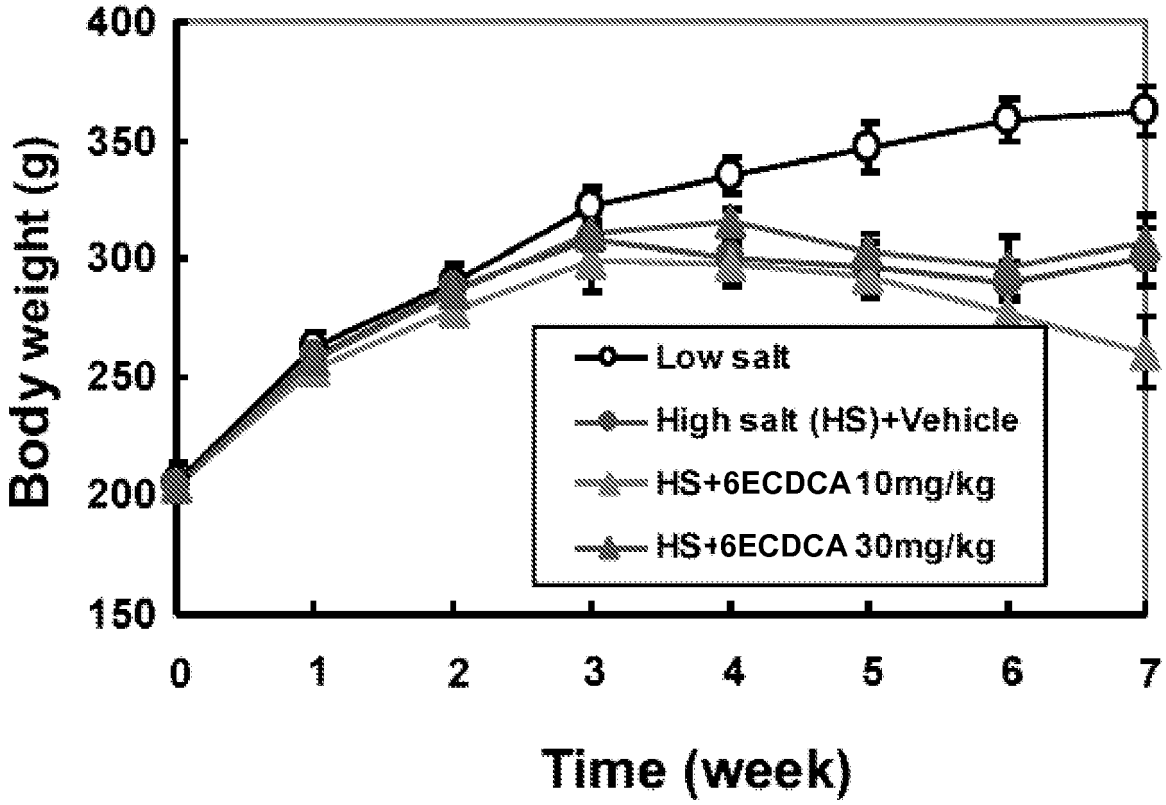

400
350
300
250
200
150
Body weight (g)
0
1
2
3
4
5
6
7
Time (week)
Low salt
High salt (HS)+Vehicle
HS+6ECDCA 10mg/kg
HS+6ECDCA 30mg/kg

Figure 3

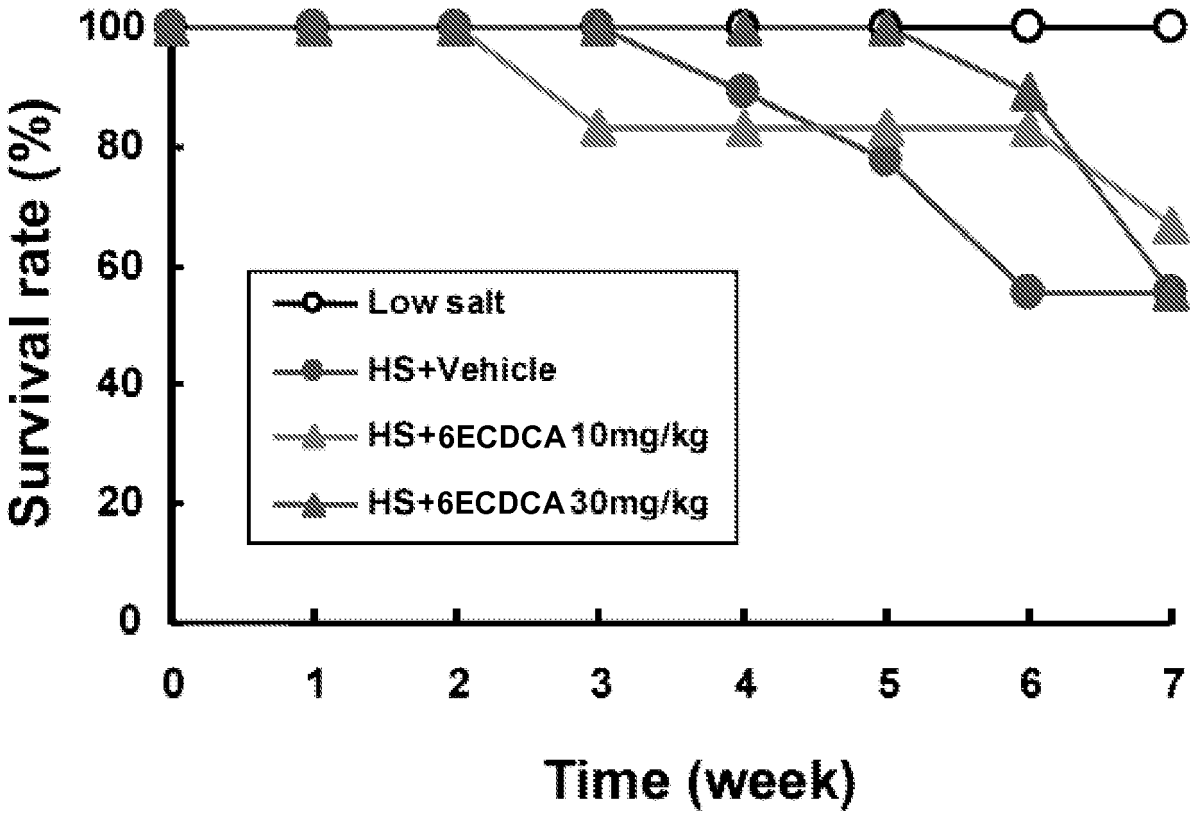

100
80
60
40
20
0
Survival rate (%)
0
1
2
3
4
5
6
7
Time (week)
Low salt
HS+Vehicle
HS+6ECDCA 10mg/kg
HS+6ECDCA 30mg/kg

Figure 4

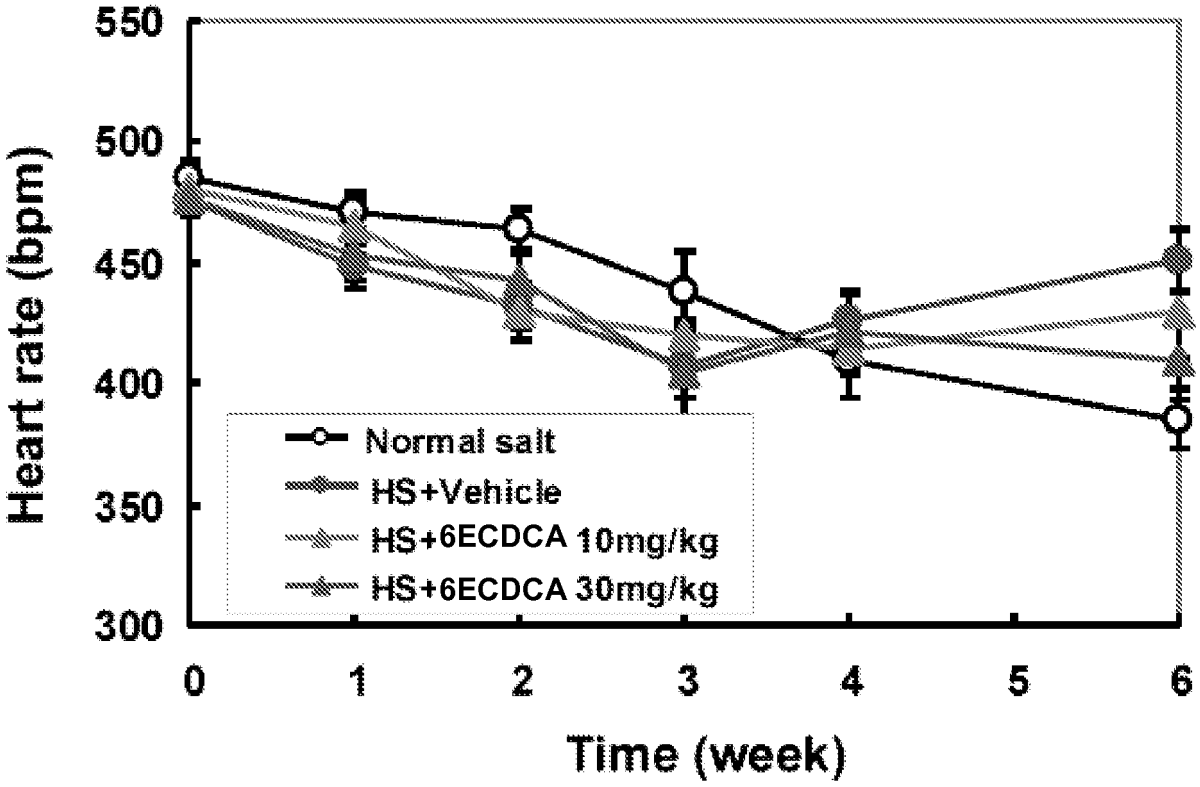

550
500
450
400
350
300
Heart rate (bpm)
0
1
2
3
4
5
6
Time (week)
Normal salt
HS+Vehicle
HS+6ECDCA 10mg/kg
HS+6ECDCA 30mg/kg

Figure 5

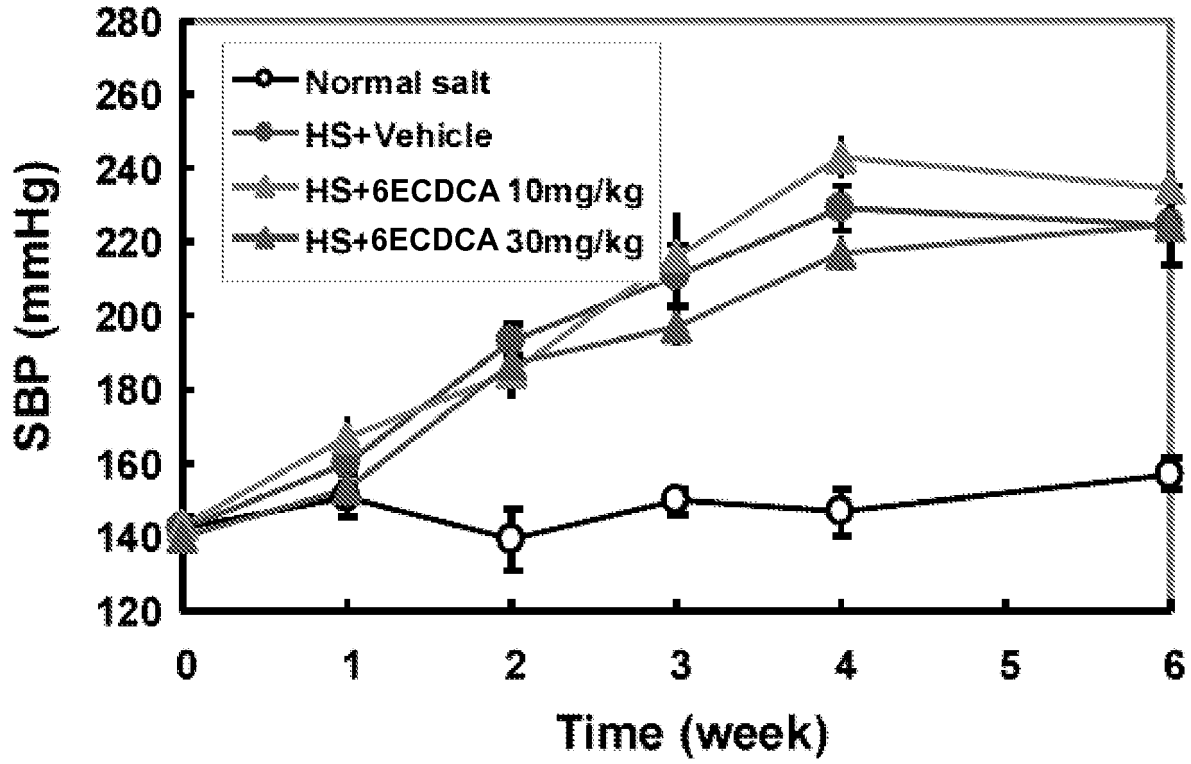

Normal salt
HS+Vehicle
HS+6ECDCA 10mg/kg
HS+6ECDCA 30mg/kg
SBP (mmHg)
280
260
240
220
200
180
160
140
120
0
1
2
3
4
5
6
Time (week)

Figure 6A

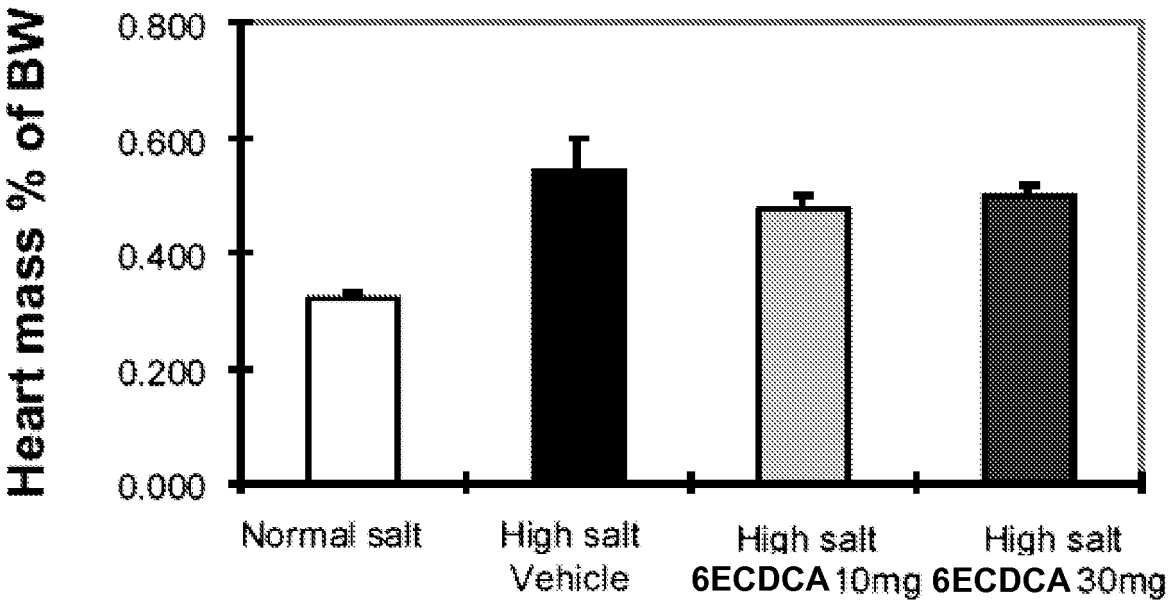

Heart mass % of BW
0.800
0.600
0.400
0.200
0.000
Normal salt
High salt Vehicle
High salt 6ECDCA 10mg
High salt 6ECDCA 30mg

Figure 6B

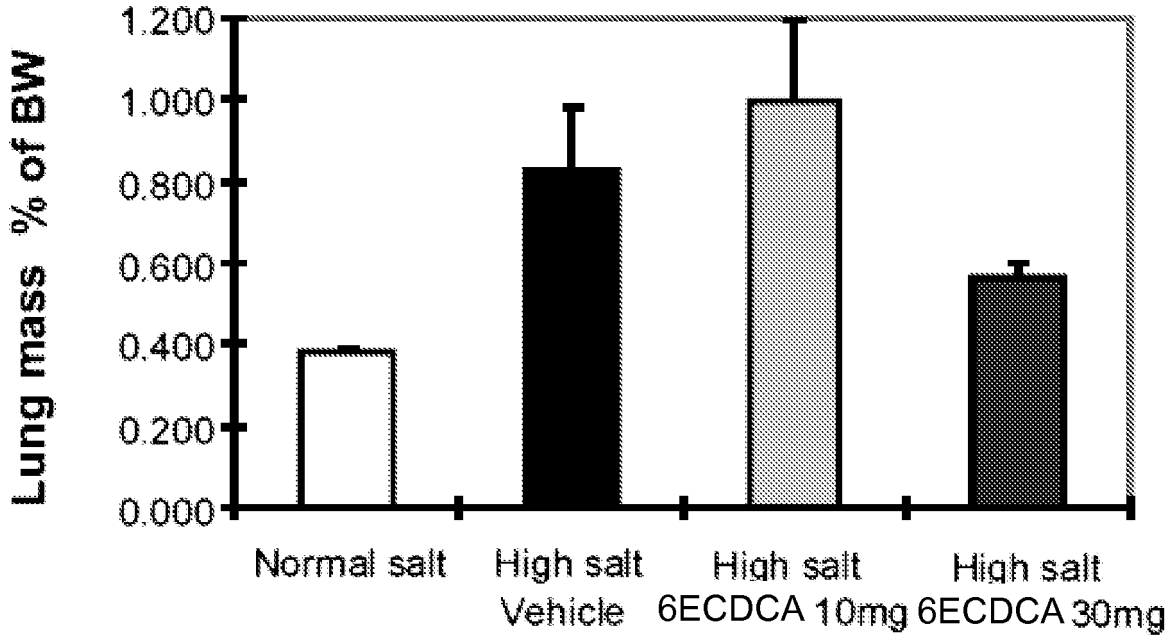

Lung mass % of BW
1.200
1.000
0.800
0.600
0.400
0.200
0.000
Normal salt
High salt Vehicle
High salt 6ECDCA 10mg
High salt 6ECDCA 30mg

Figure 6C

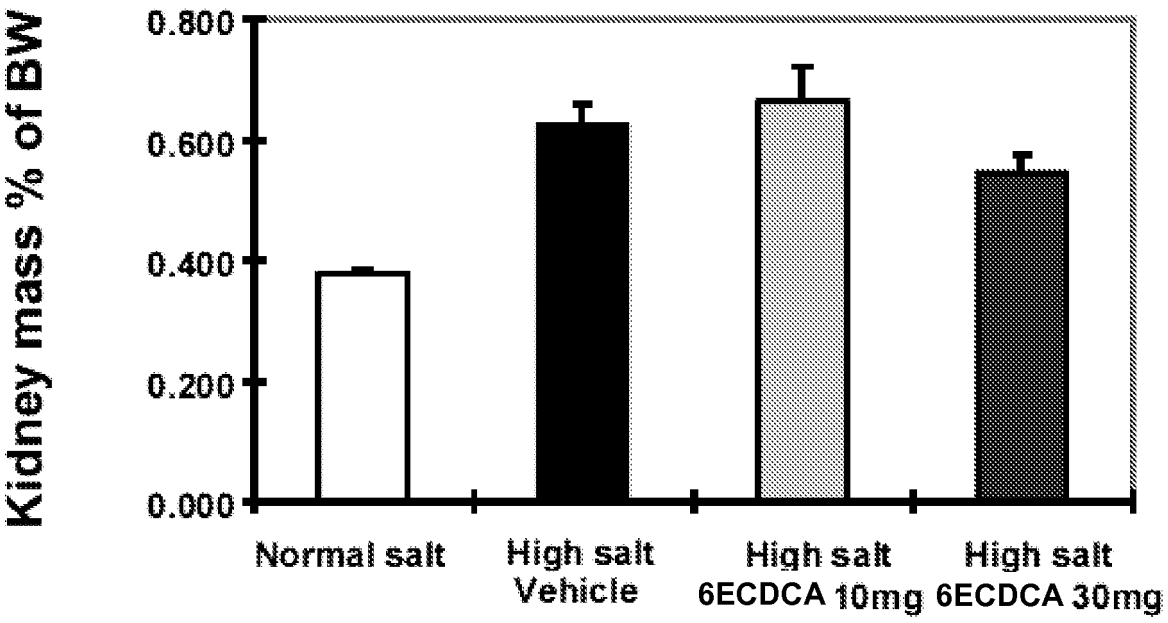

Kidney mass % of BW
0.800
0.600
0.400
0.200
0.000
Normal salt
High salt Vehicle
High salt 6ECDCA 10mg
High salt 6ECDCA 30mg

Figure 7

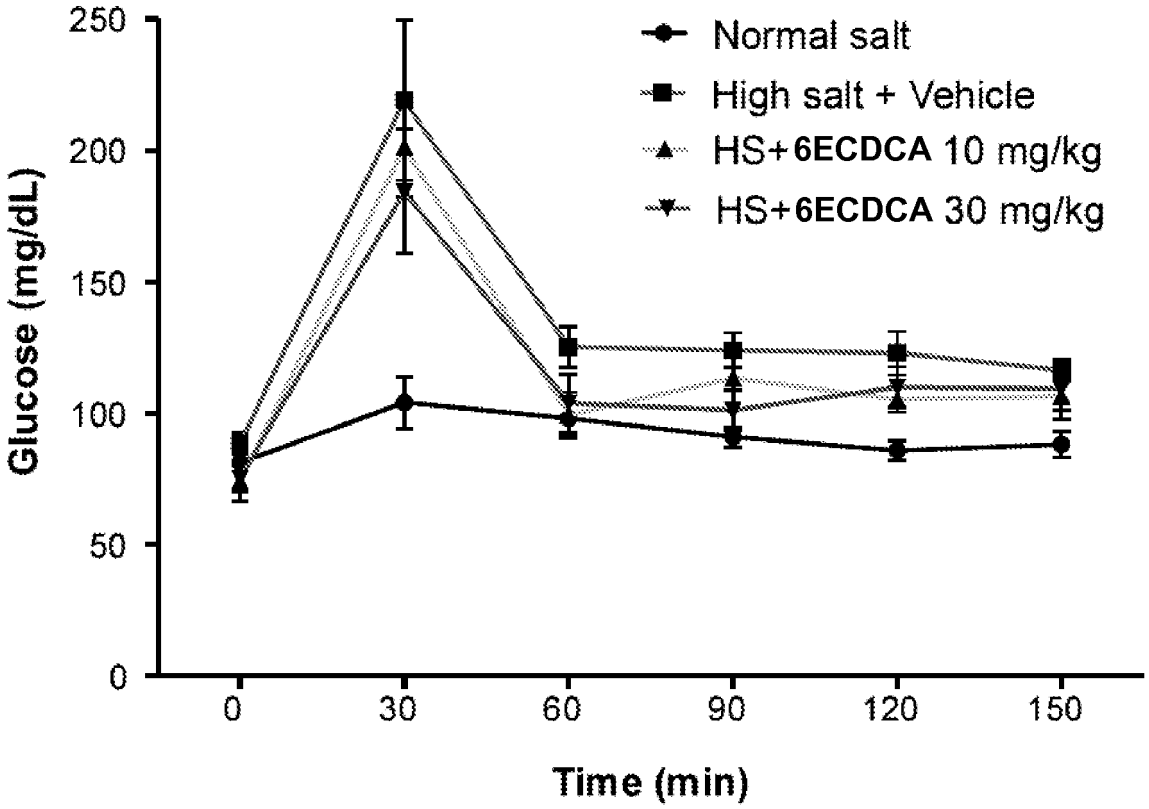

Normal salt
High salt + Vehicle
HS+6ECDCA 10 mg/kg
HS+6ECDCA 30 mg/kg
Glucose (mg/dL)
250
200
150
100
50
0
0
30
60
90
120
150
Time (min)

Figure 8

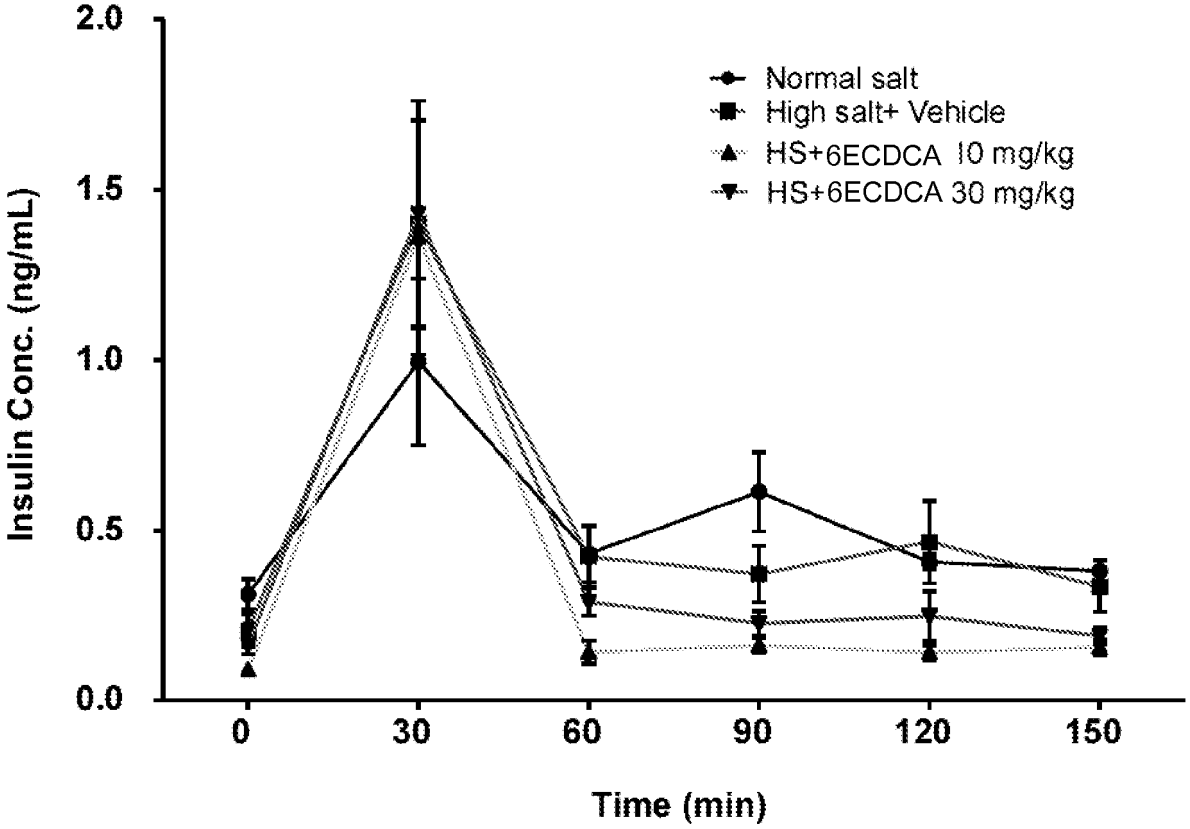

2.0
1.5
1.0
0.5
0.0
Insulin Conc. (ng/mL)
0
30
60
90
120
150
Time (min)
Normal salt
High salt+ Vehicle
HS+6ECDCA 10 mg/kg
HS+6ECDCA 30 mg/kg

Figure 9

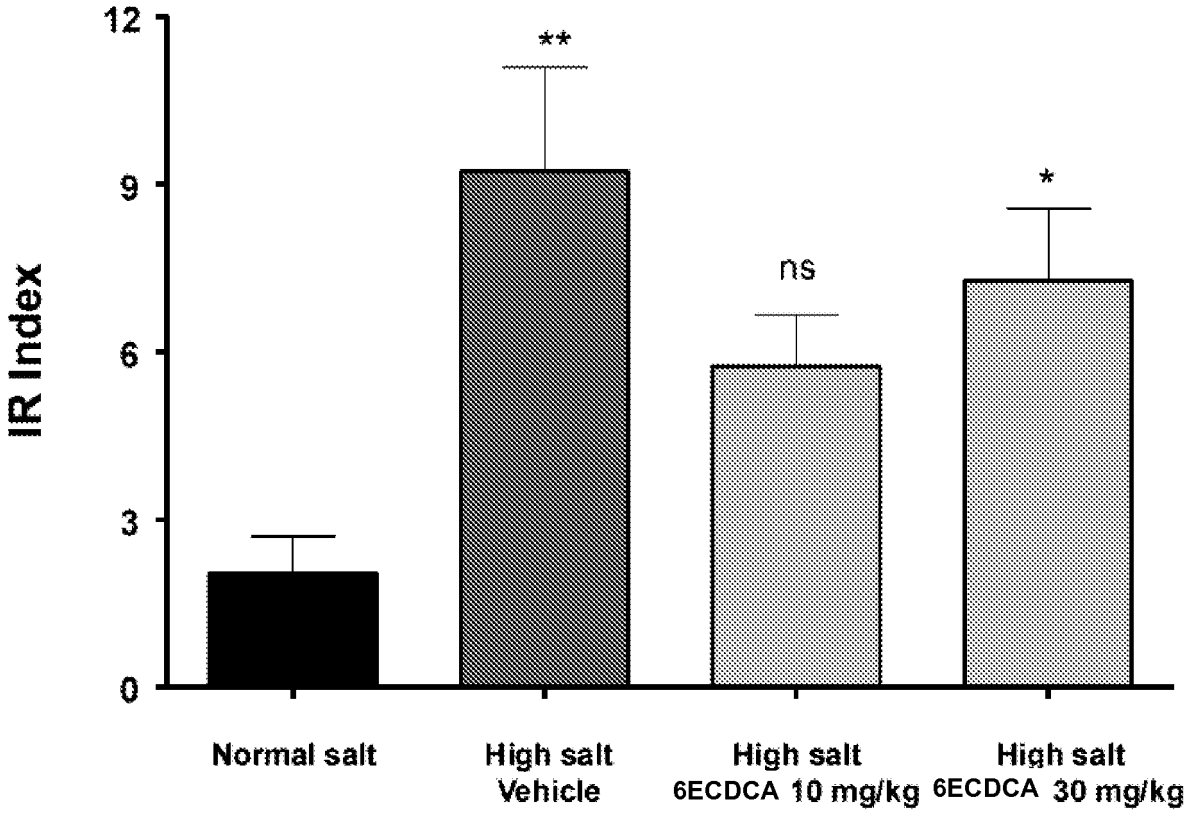

12
9
6
3
0
IR Index
**
ns
*
Normal salt
High salt
Vehicle
High salt
6ECDCA 10 mg/kg
High salt
6ECDCA 30 mg/kg

Figure 10A

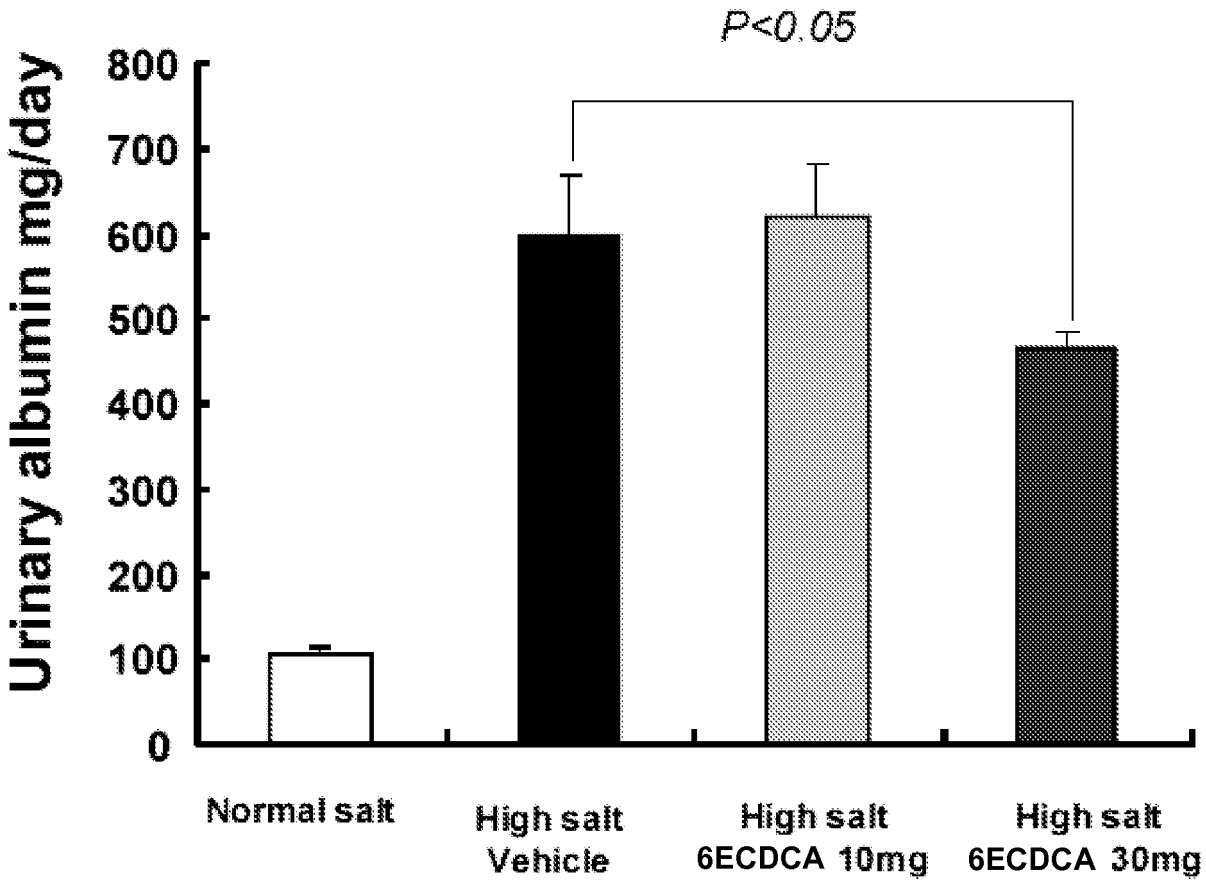

P<0.05
Urinary albumin mg/day
800
700
600
500
400
300
200
100
0
Normal salt
High salt Vehicle
High salt 6ECDCA 10mg
High salt 6ECDCA 30mg

Figure 10B

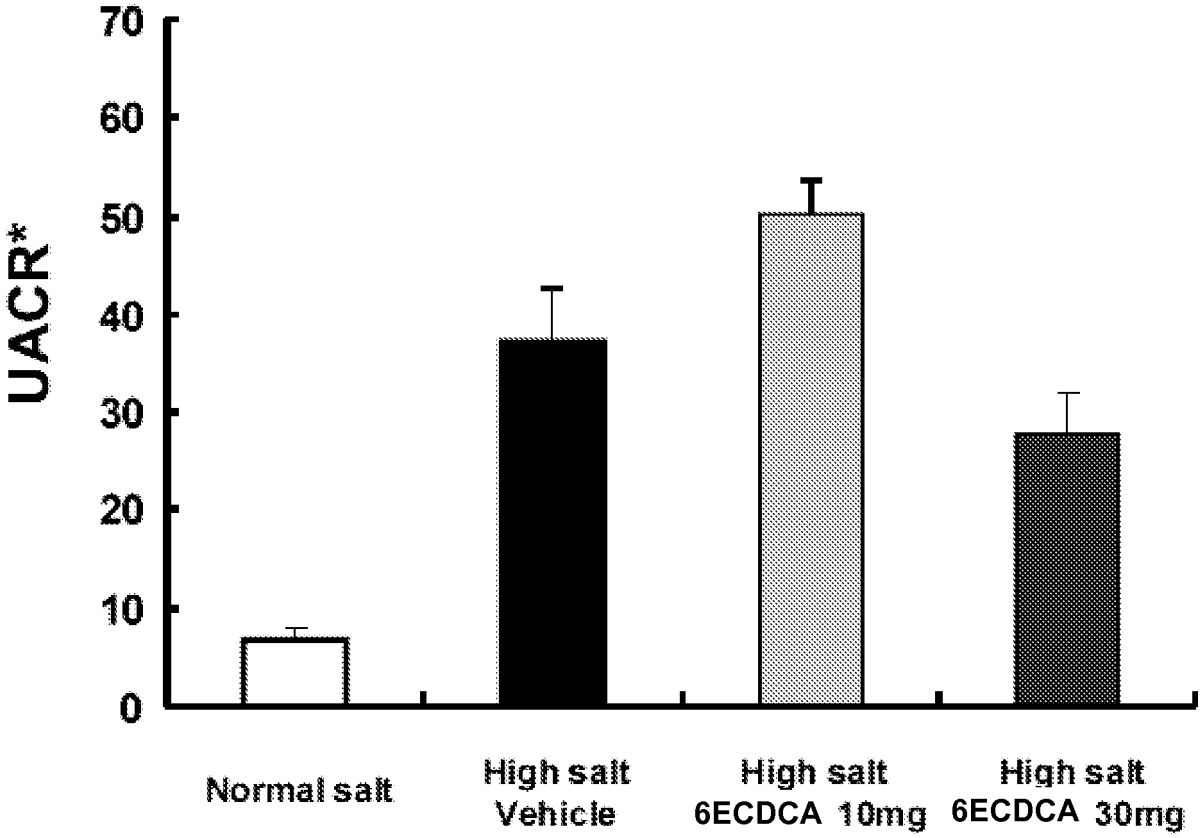

70
60
50
40
30
20
10
0
UACR*
Normal salt
High salt Vehicle
High salt 6ECDCA 10mg
High salt 6ECDCA 30mg

Figure 11A

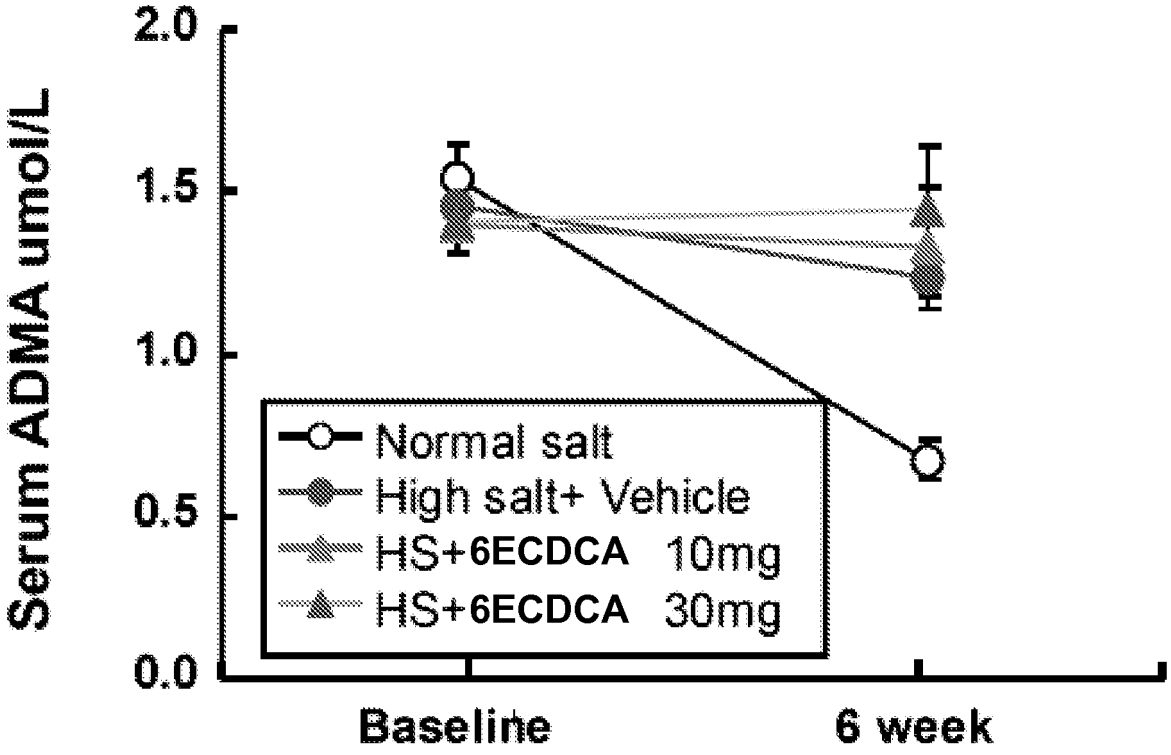

Serum ADMA umol/L
2.0
1.5
1.0
0.5
0.0
Normal salt
High salt+ Vehicle
HS+6ECDCA 10mg
HS+6ECDCA 30mg
Baseline
6 week

Figure 11B

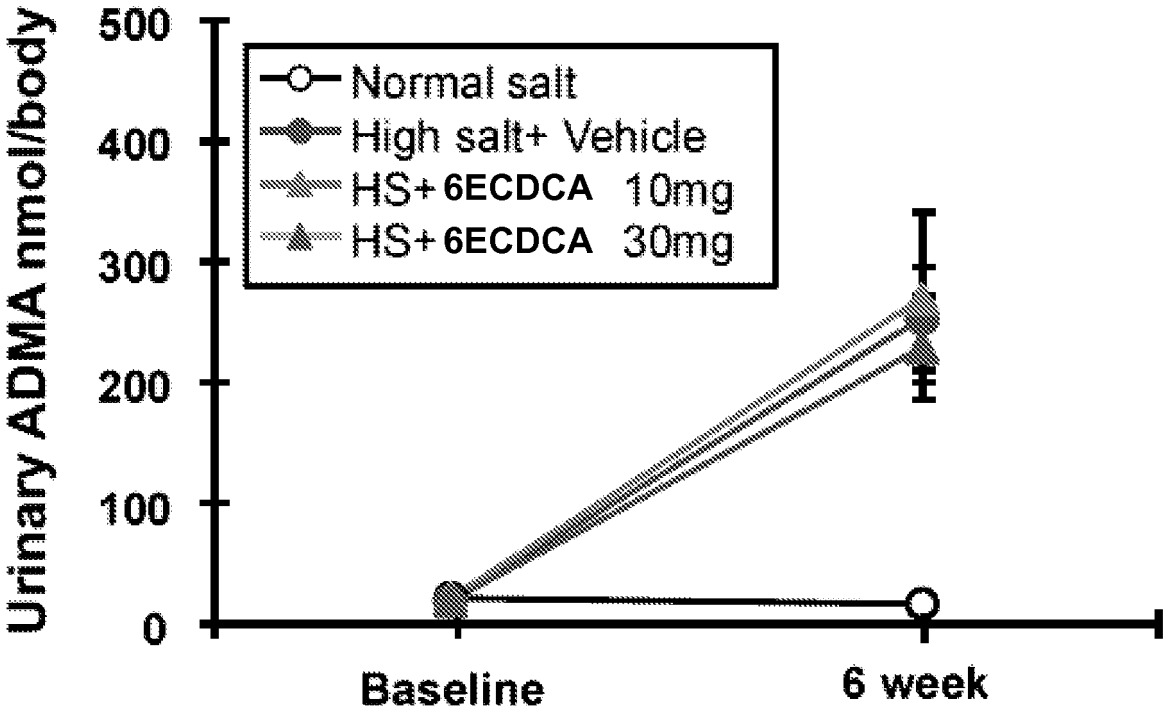

Urinary ADMA nmol/body
500
400
300
200
100
0
Normal salt
High salt+ Vehicle
HS+ 6ECDCA 10mg
HS+ 6ECDCA 30mg
Baseline
6 week

Figure 11C

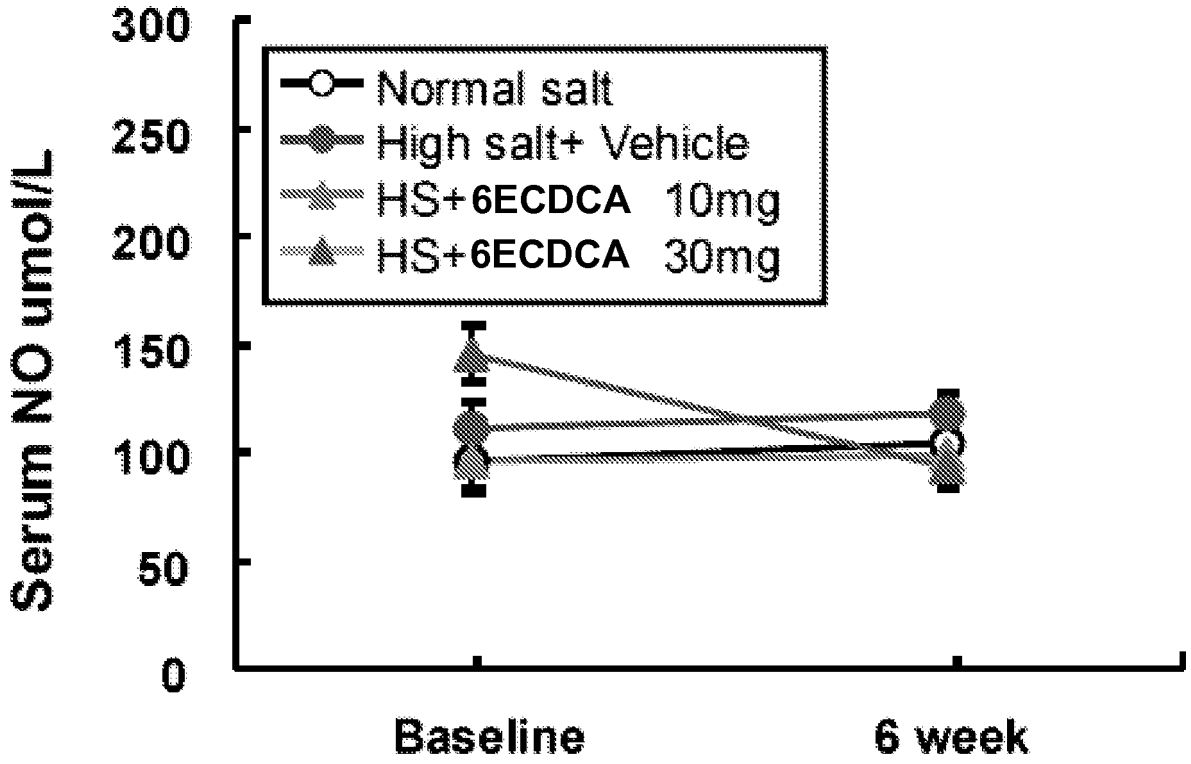

300
250
200
150
100
50
0
Serum NO umol/L
Normal salt
High salt+ Vehicle
HS+6ECDCA 10mg
HS+6ECDCA 30mg
Baseline
6 week

Figure 11D

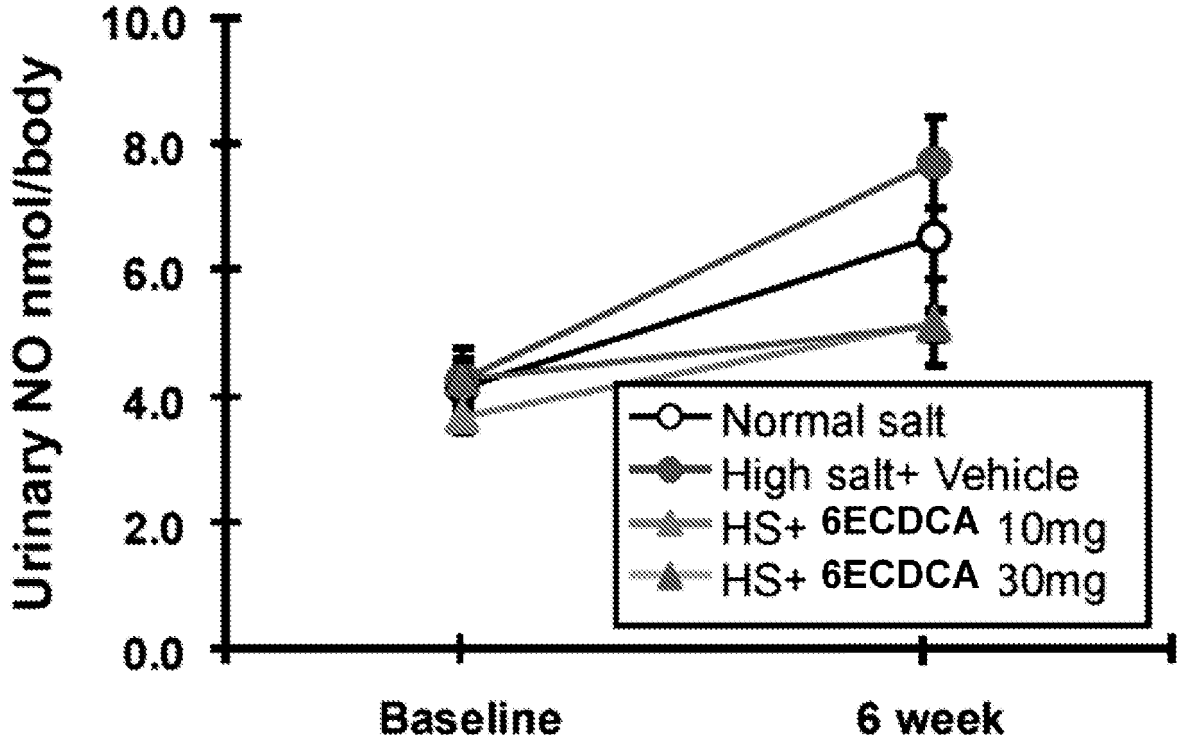
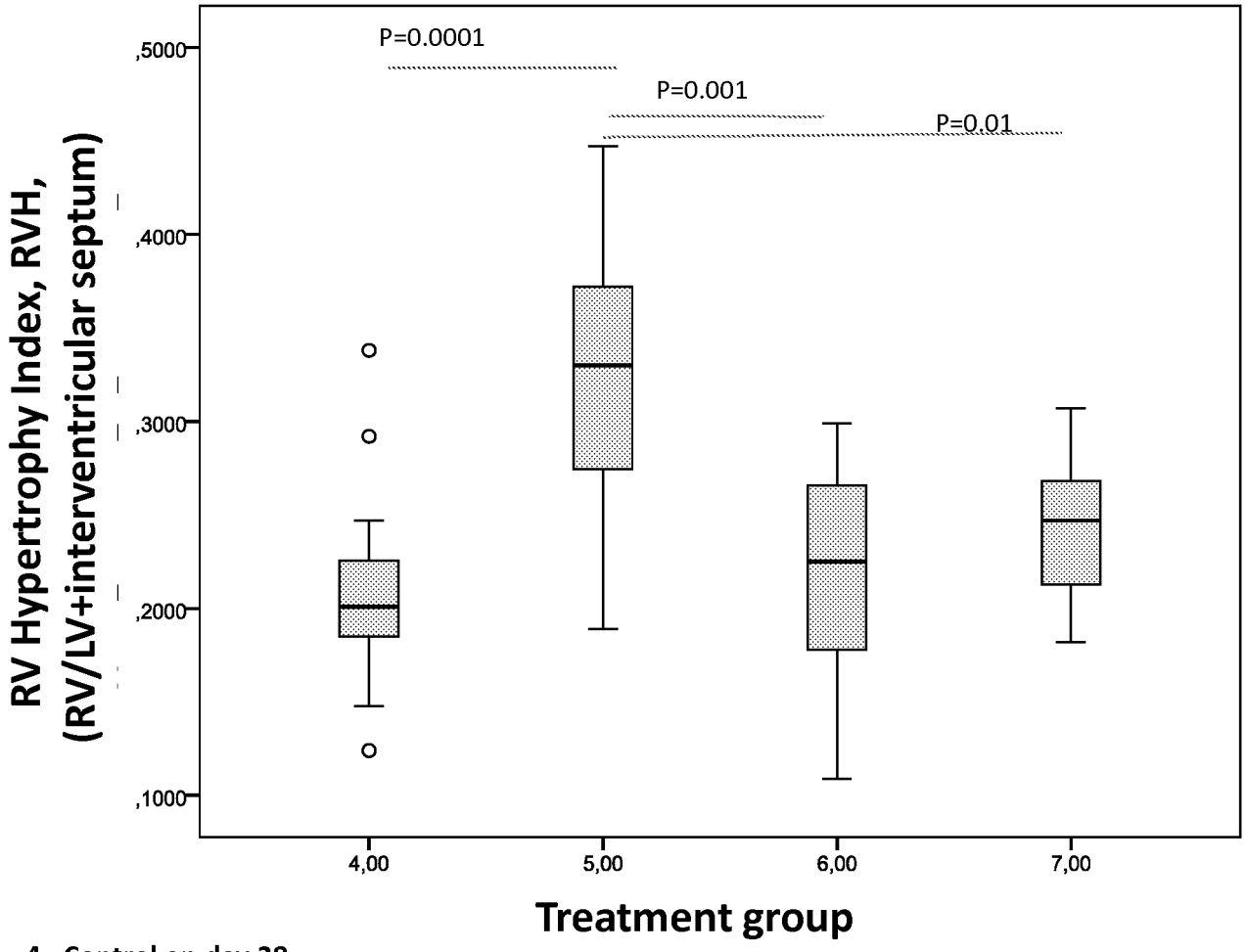

Urinary NO nmol/body
10.0
8.0
6.0
4.0
2.0
0.0
Baseline
6 week
Normal salt
High salt+ Vehicle
HS+ 6ECDCA 10mg
HS+ 6ECDCA 30mg

Fig. 12 OCA normalizes MCT-induced right ventricular hypertrophy (RVH)



4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28

Fig. 13 Hematoxylin-Eosin staining of lung sections on day 7

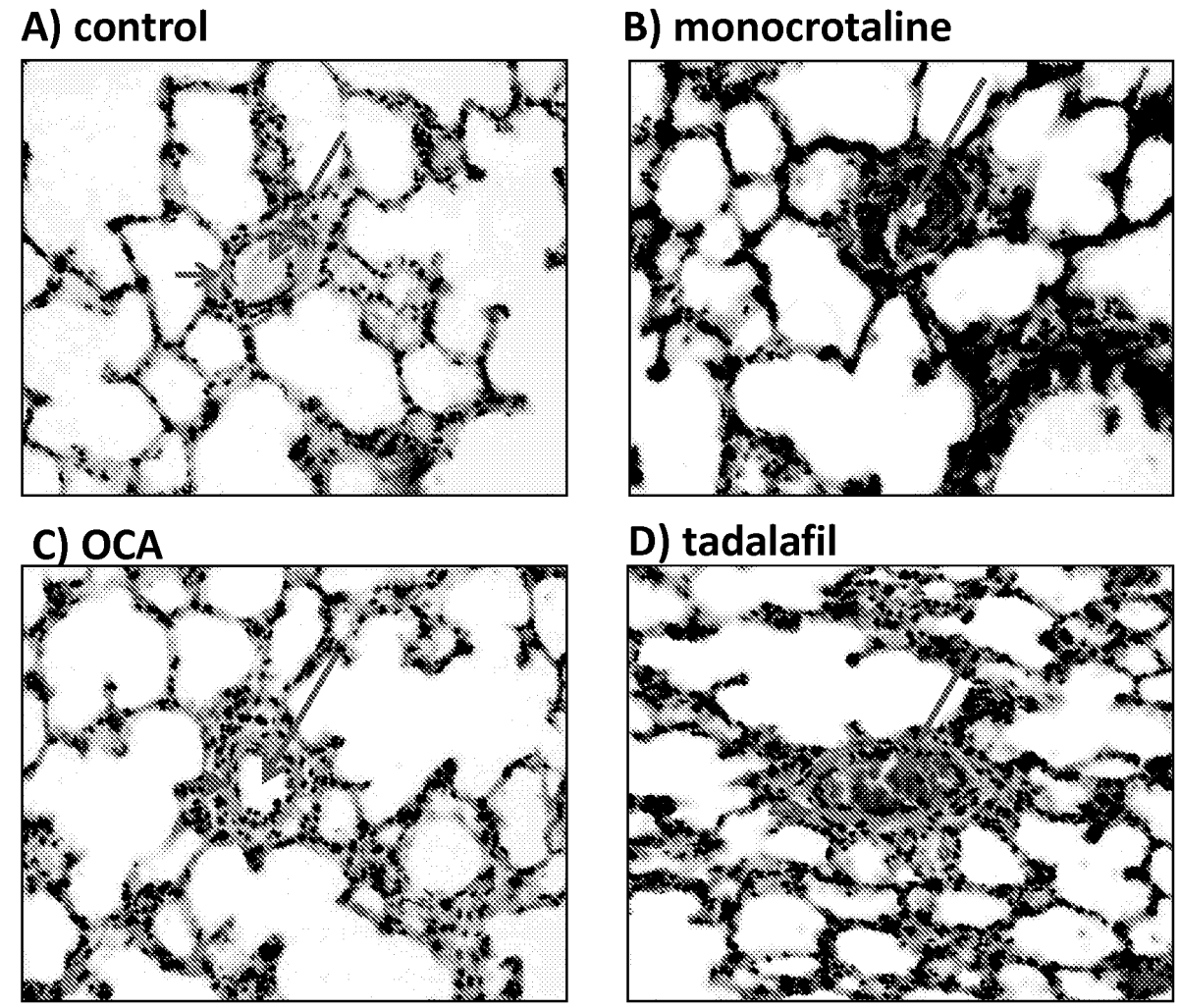


Fig. 14 Hematoxylin-Eosin staining of lung sections on day 28

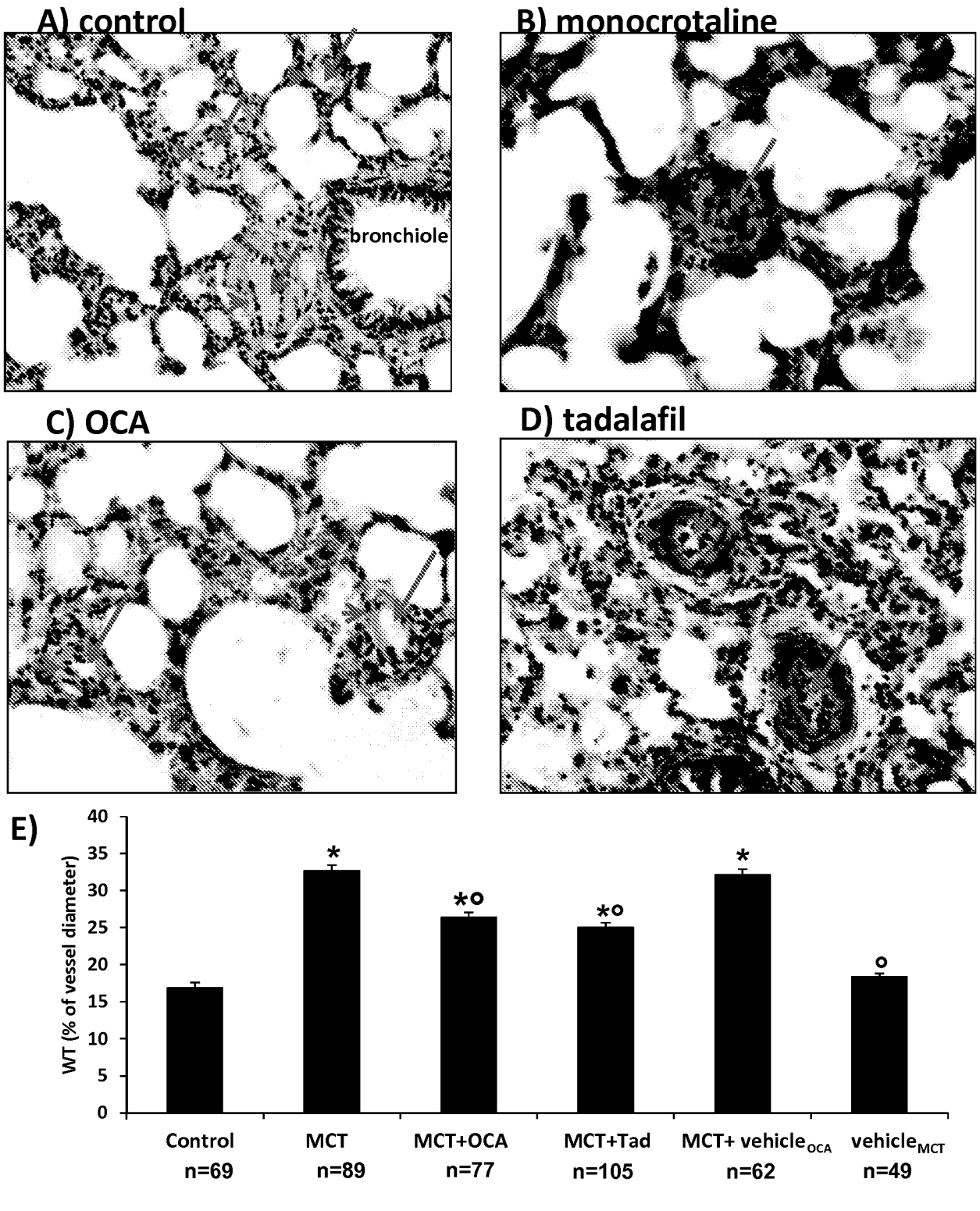
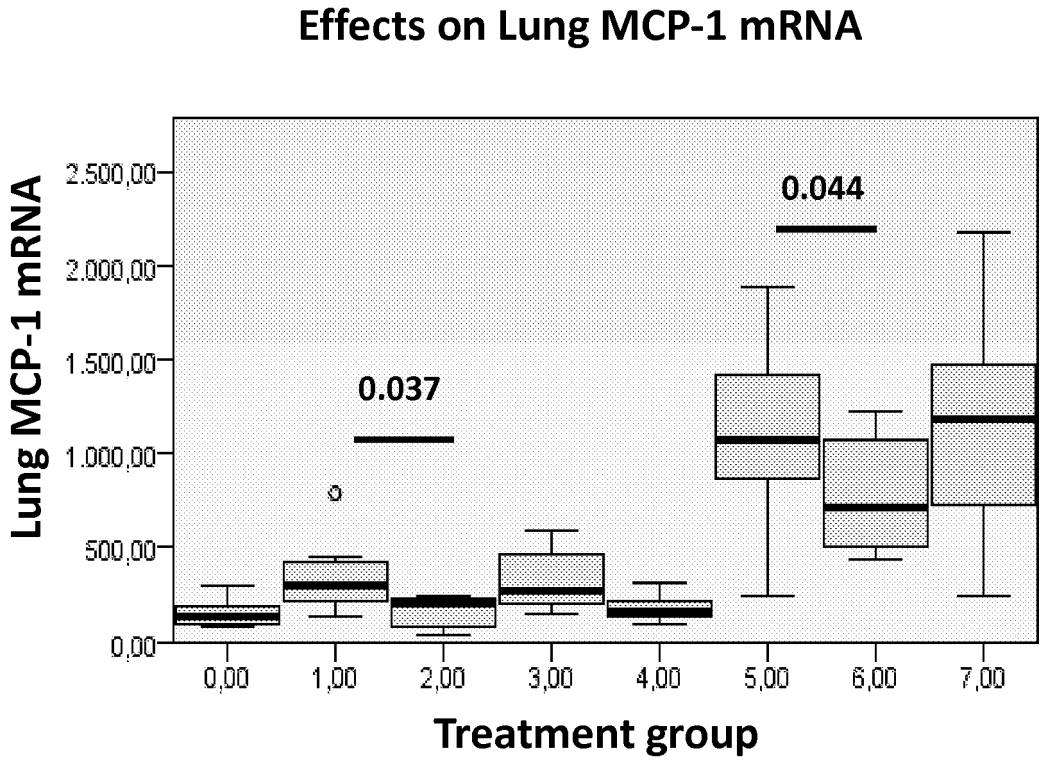
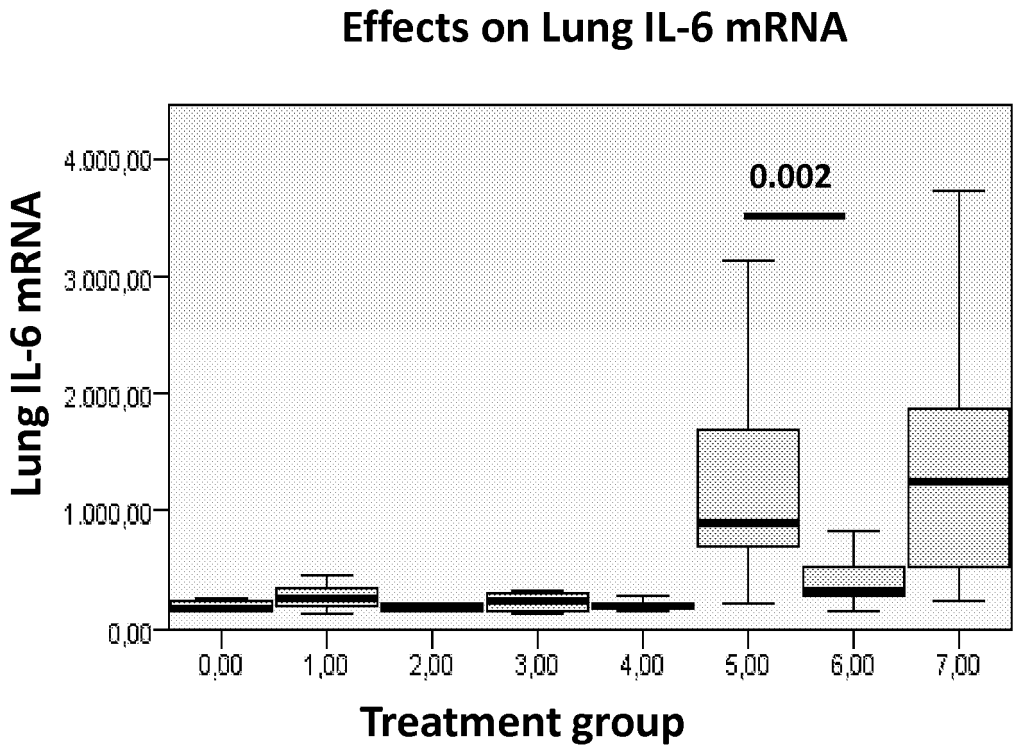


Fig. 15



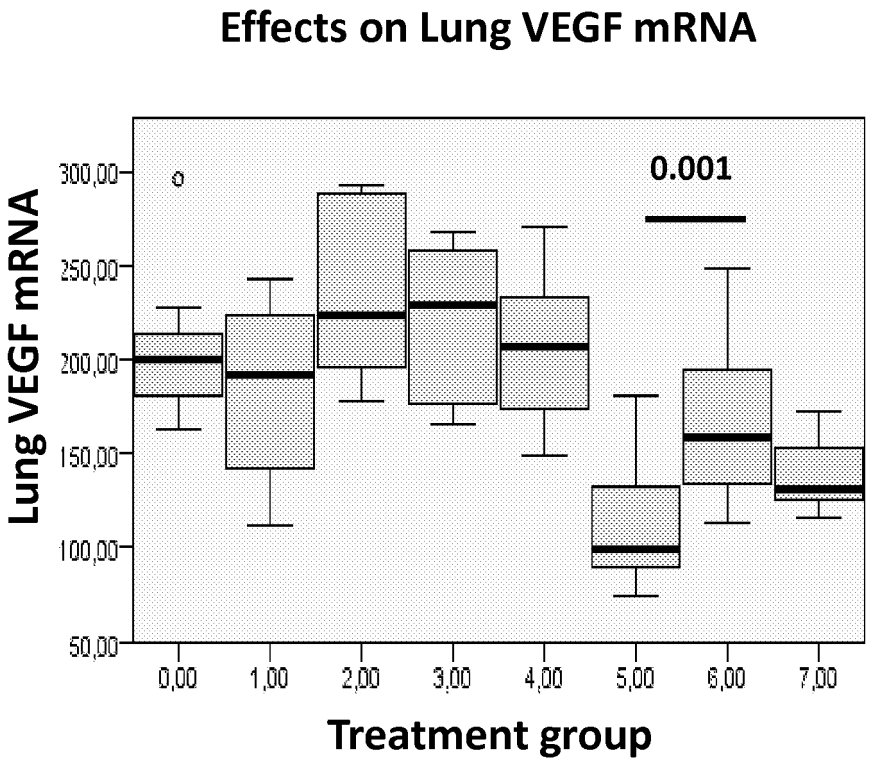
0= Control on day 7
1= MCT on day 7
2= MCT+OCA on day 7
3= MCT+Tadalafil on day 7
4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28

Fig. 16



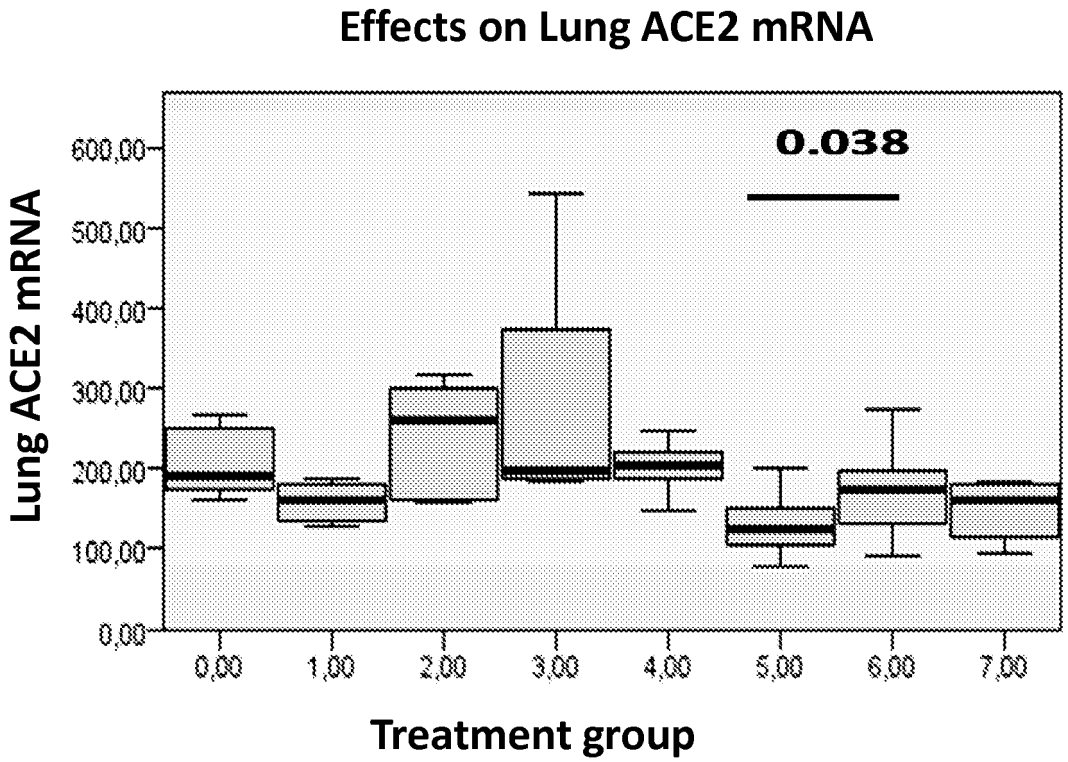
0= Control on day 7
1= MCT on day 7
2= MCT+OCA on day 7
3= MCT+Tadalafil on day 7
4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28

Fig. 17



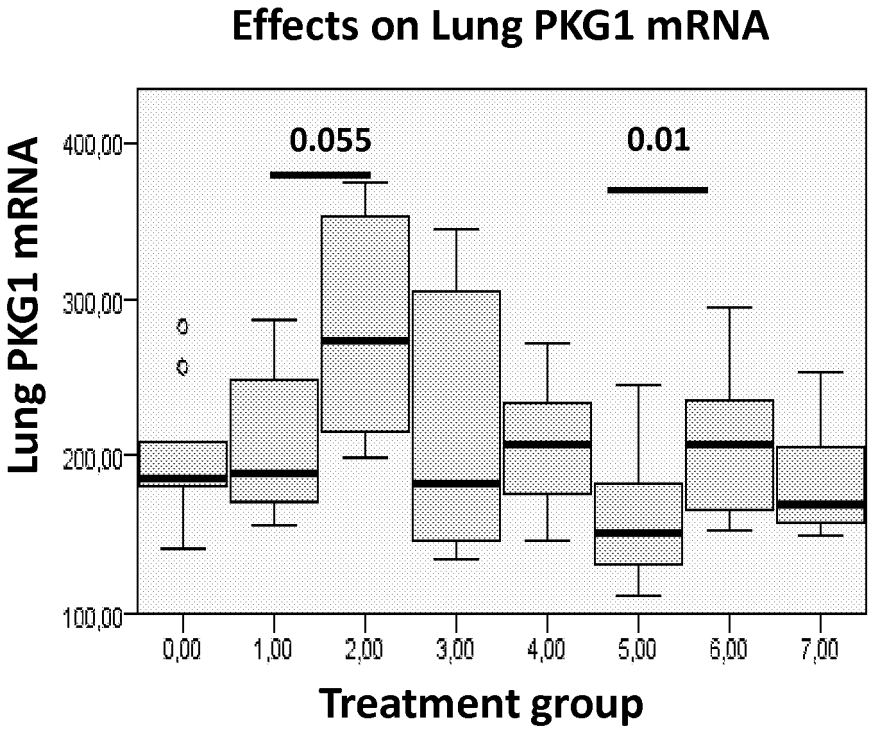
0= Control on day 7
1= MCT on day 7
2= MCT+OCA on day 7
3= MCT+Tadalafil on day 7
4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28

Fig. 18



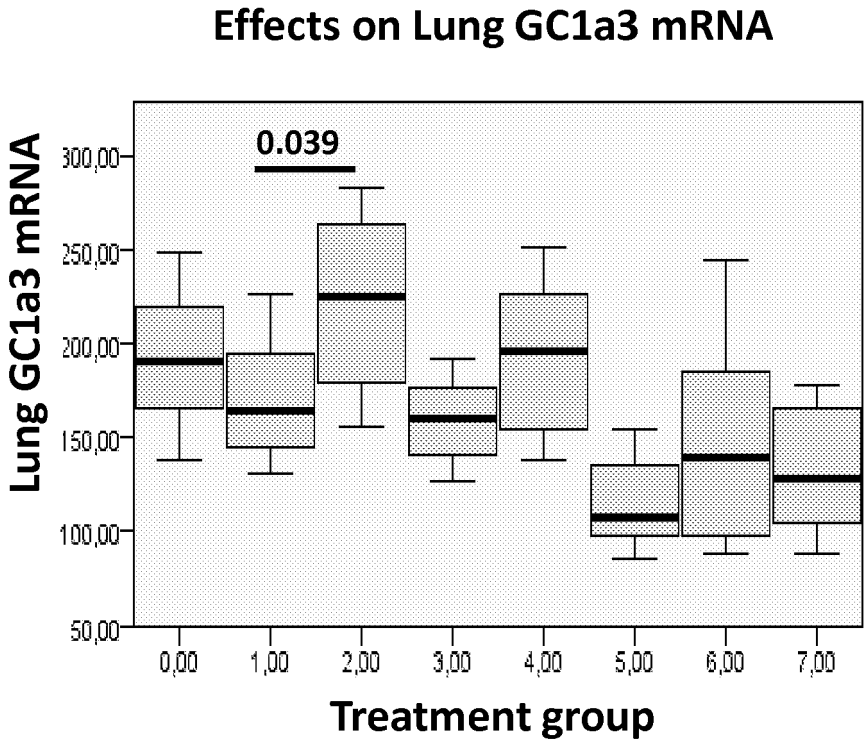
0= Control on day 7
1= MCT on day 7
2= MCT+OCA on day 7
3= MCT+Tadalafil on day 7
4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28

Fig. 19



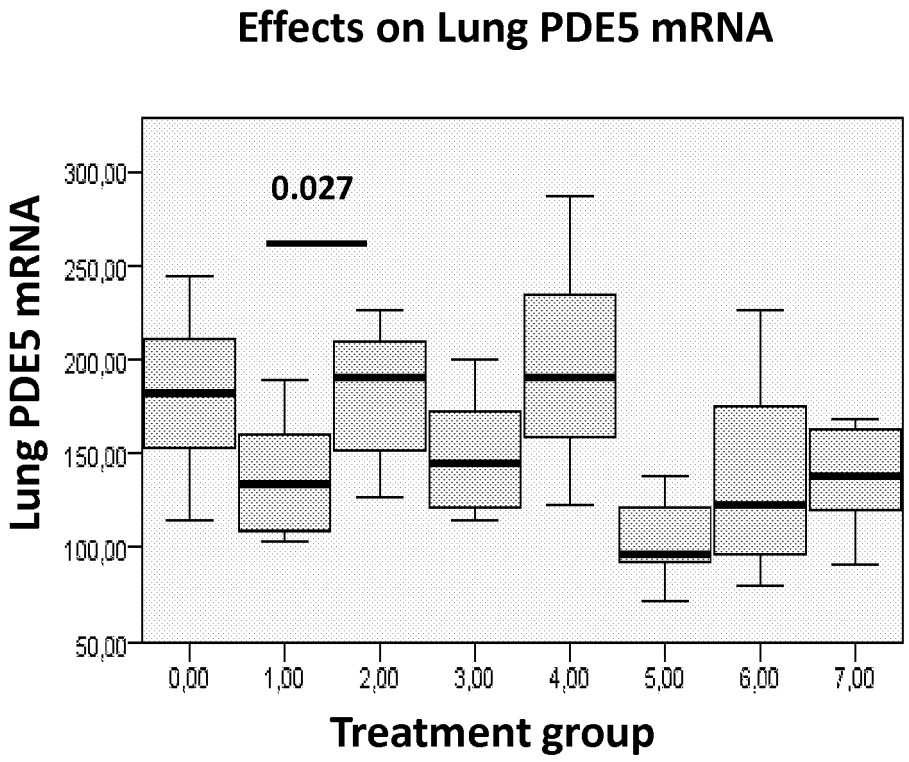
0= Control on day 7
1= MCT on day 7
2= MCT+OCA on day 7
3= MCT+Tadalafil on day 7
4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28

Fig. 20



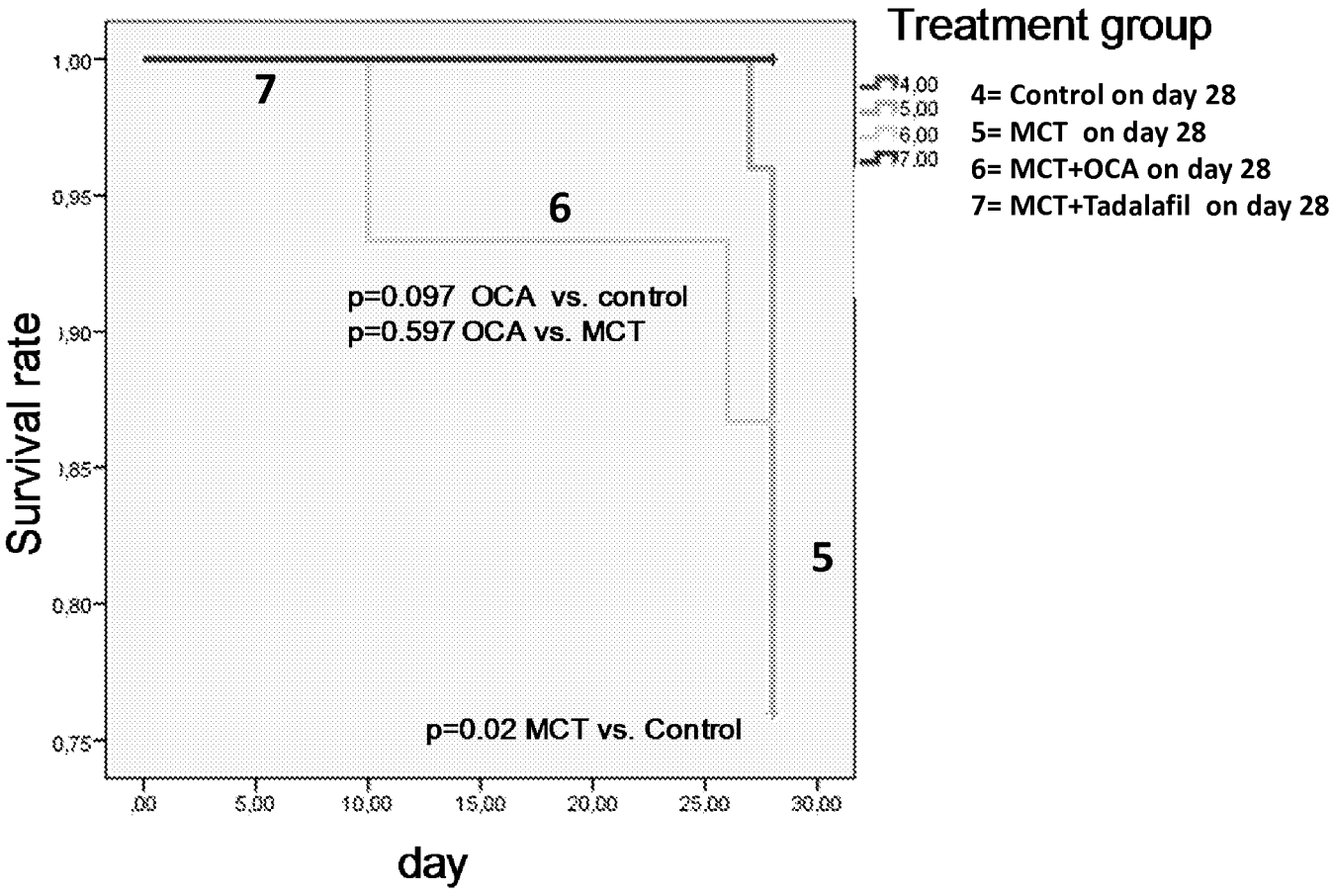
0= Control on day 7
1= MCT on day 7
2= MCT+OCA on day 7
3= MCT+Tadalafil on day 7
4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28

Fig. 21



0= Control on day 7
1= MCT on day 7
2= MCT+OCA on day 7
3= MCT+Tadalafil on day 7
4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28

Fig. 22


Treatment group
4,00
5,00
6,00
7,00
4= Control on day 28
5= MCT on day 28
6= MCT+OCA on day 28
7= MCT+Tadalafil on day 28
Survival rate
1,00
0,95
0,90
0,85
0,80
0,75
7
6
5
p=0.097 OCA vs. control
p=0.597 OCA vs. MCT
p=0.02 MCT vs. Control
,00
5,00
10,00
15,00
20,00
25,00
30,00
day