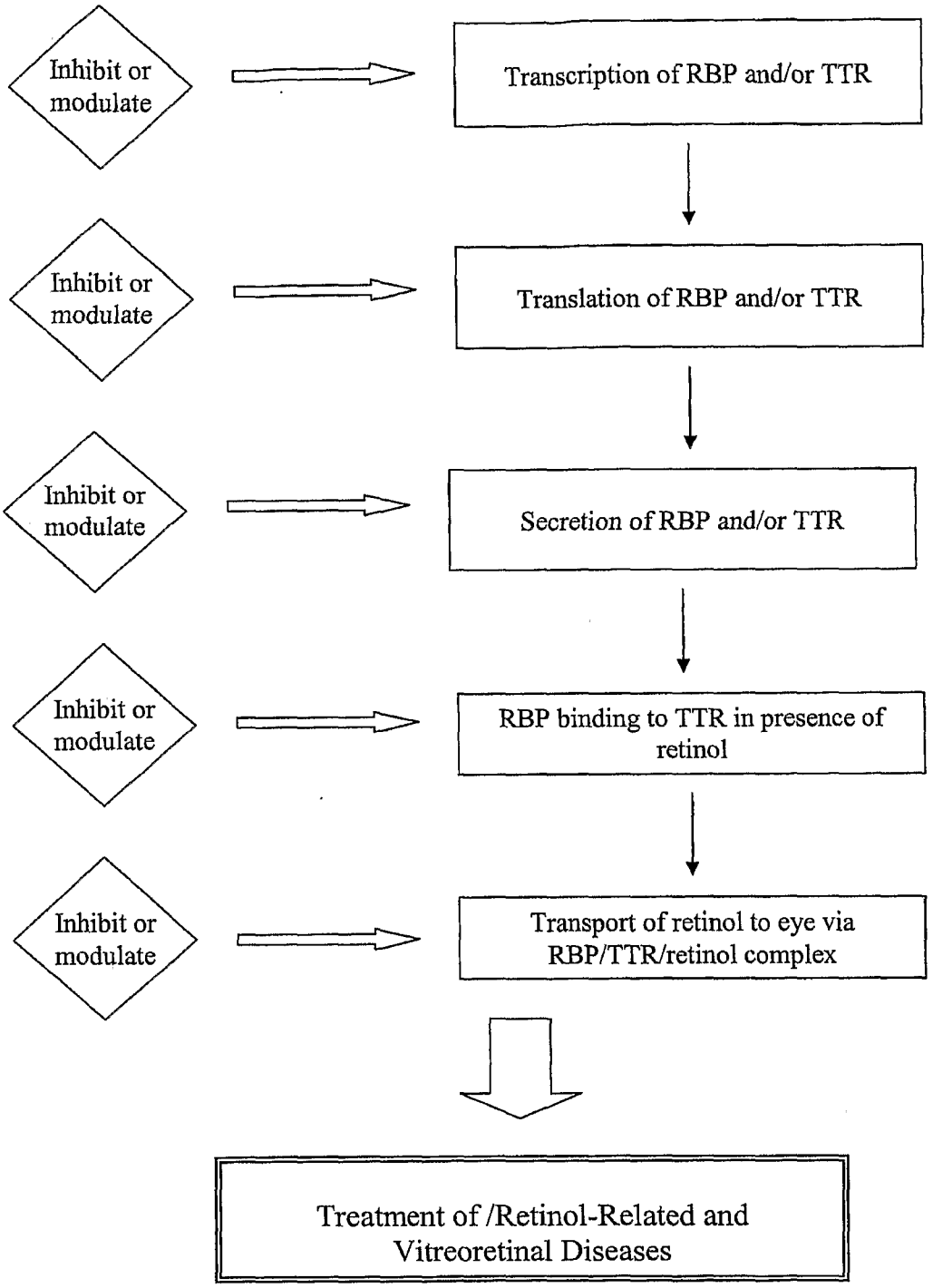


Figure 1. Flowchart of Treatment Methodology

FIGURE 1

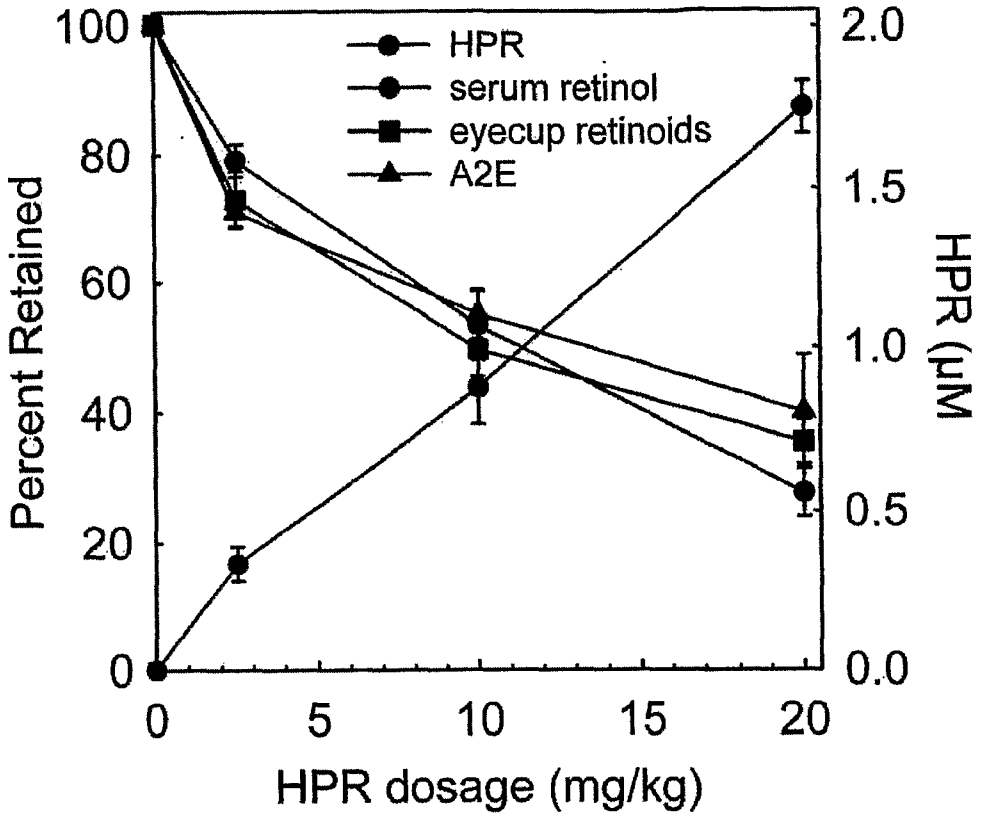

HPR
serum retinol
eyecup retinoids
A2E
Percent Retained
HPR (μM
HPR dosage (mg/kg)
100
80
60
40
20
0
2.0
1.5
1.0
0.5
0.0
0
5
10
15
20

FIGURE 2

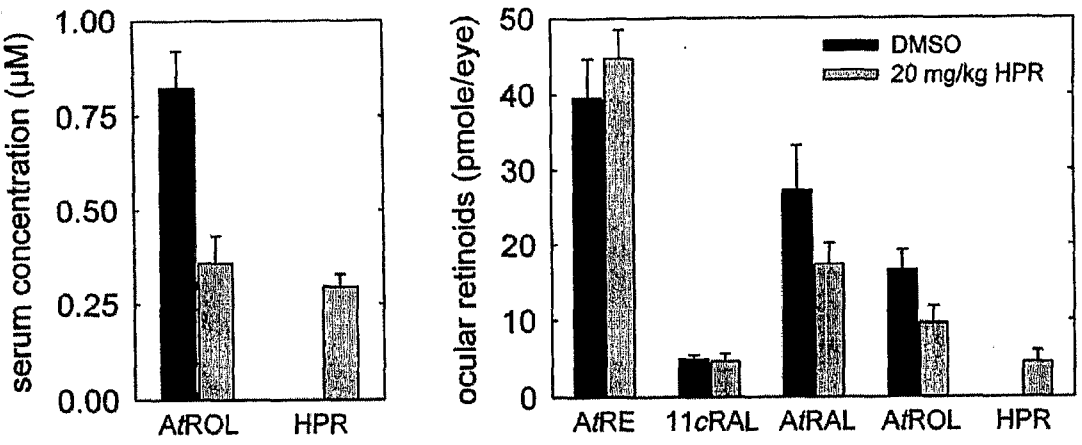

serum concentration (μM)
1.00
0.75
0.50
0.25
0.00
AtROL
HPR
ocular retinoids (pmole/eye)
50
40
30
20
10
0
DMSO
20 mg/kg HPR
AtRE
11cRAL
AtRAL
AtROL
HPR

FIGURE 3

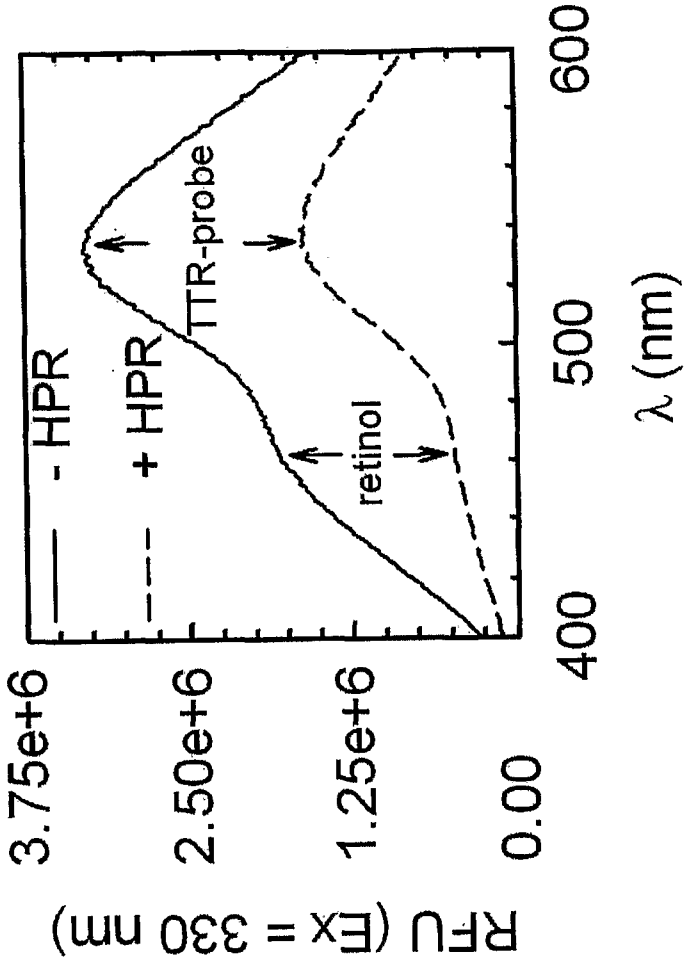

RFU (Ex = 330 nm)
3.75e+6
2.50e+6
1.25e+6
0.00
400
500
600
λ (nm)
- HPR
+ HPR
TTR-probe
retinol

FIGURE 4

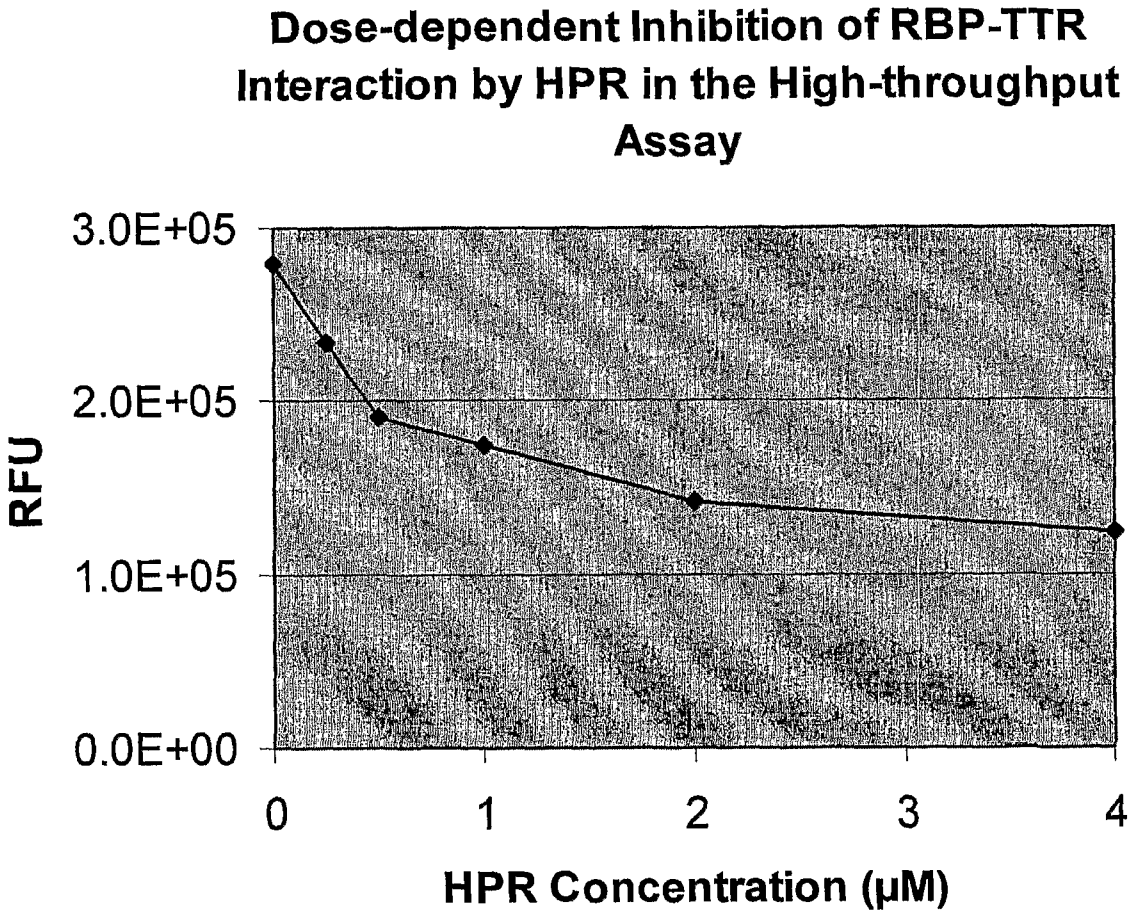

Dose-dependent Inhibition of RBP-TTR Interaction by HPR in the High-throughput Assay
3.0E+05
2.0E+05
1.0E+05
0.0E+00
RFU
0
1
2
3
4
HPR Concentration (µM)

FIGURE 5

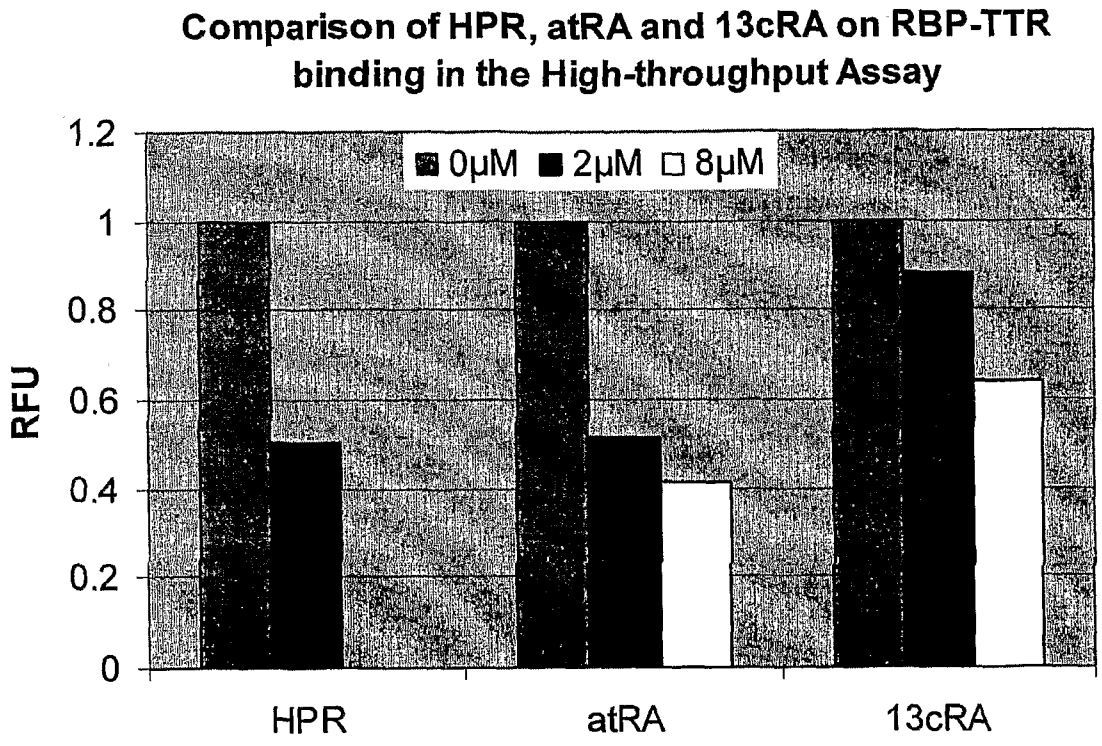

Comparison of HPR, atRA and 13cRA on RBP-TTR binding in the High-throughput Assay
0μM
2μM
8μM
RFU
1.2
1
0.8
0.6
0.4
0.2
0
HPR
atRA
13cRA

FIGURE 6

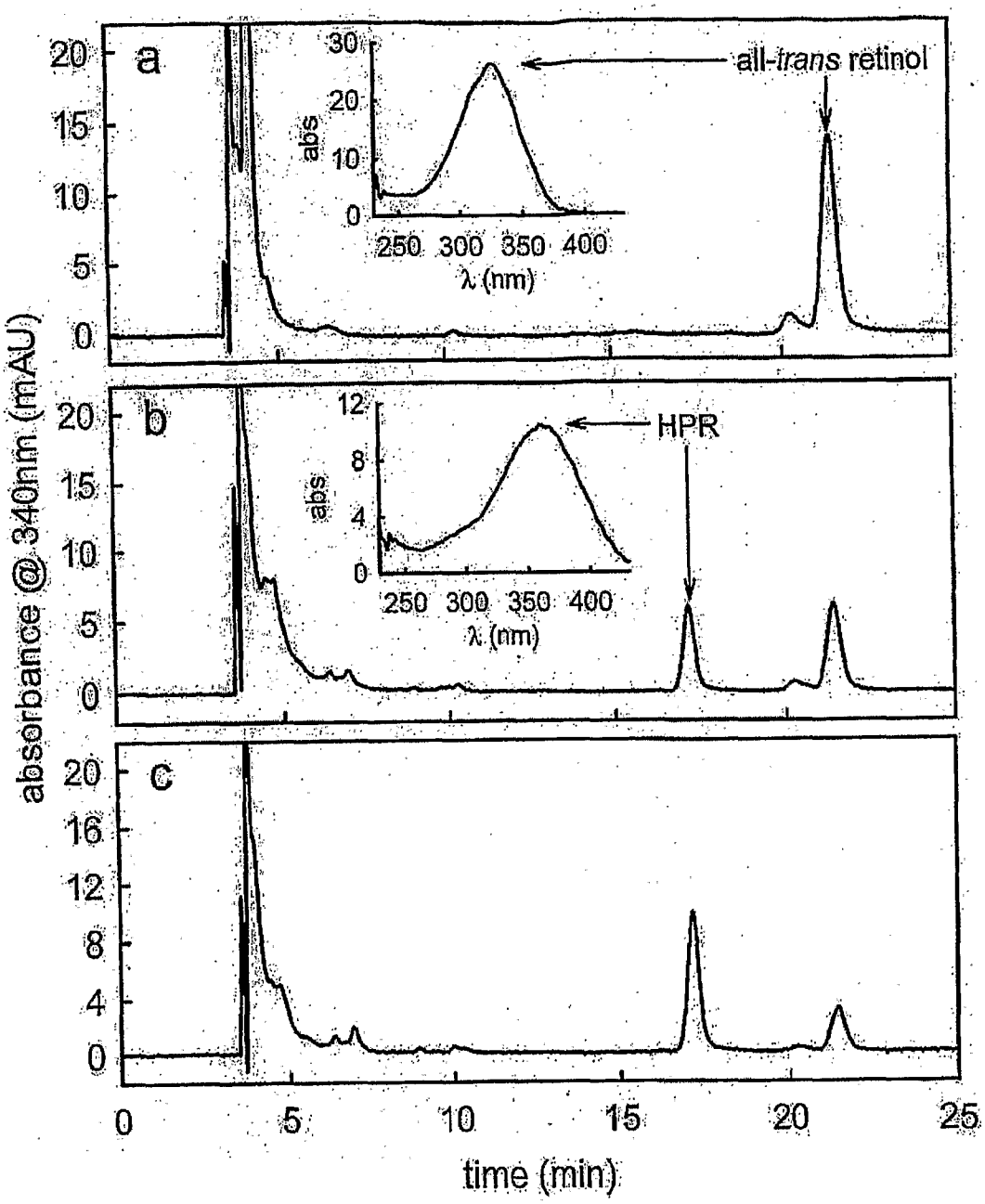

a
all-trans retinol
abs
λ (nm)
b
HPR
c
absorbance @ 340nm (mAU)
time (min)

FIGURE 7A-C

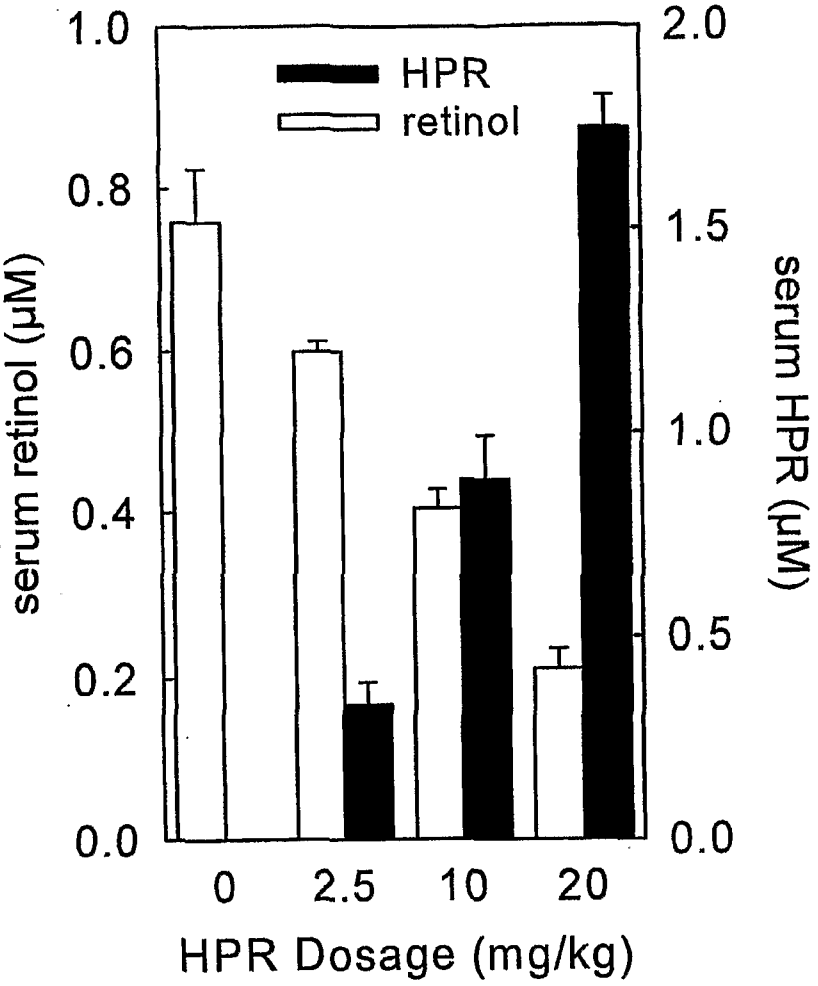

1.0
0.8
0.6
0.4
0.2
0.0
serum retinol (μM)
2.0
1.5
1.0
0.5
0.0
serum HPR (μM)
HPR
retinol
0
2.5
10
20
HPR Dosage (mg/kg)

FIGURE 8

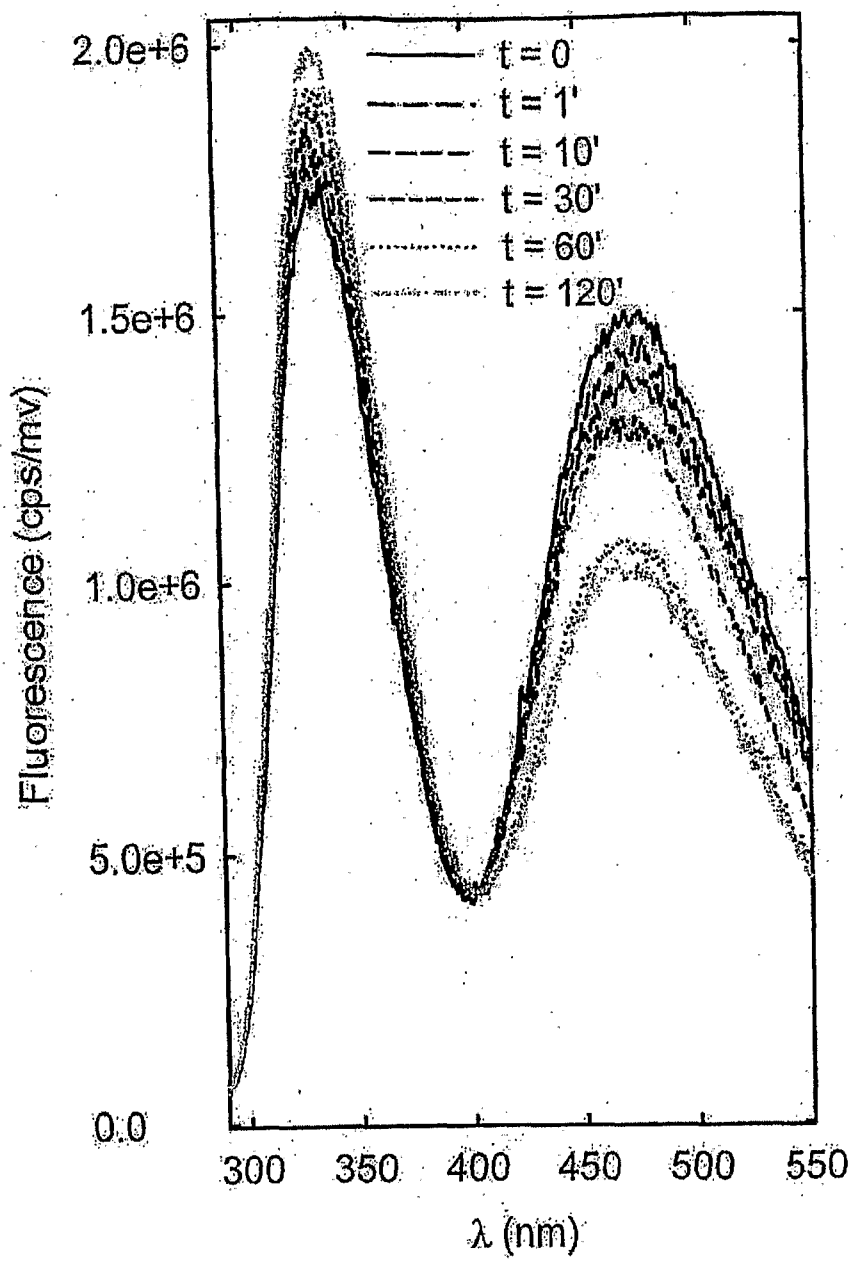

2.0e+6
1.5e+6
1.0e+6
5.0e+5
0.0
Fluorescence (cps/mv)
t = 0
t = 1'
t = 10'
t = 30'
t = 60'
t = 120'
300
350
400
450
500
550
λ (nm)

FIGURE 9A

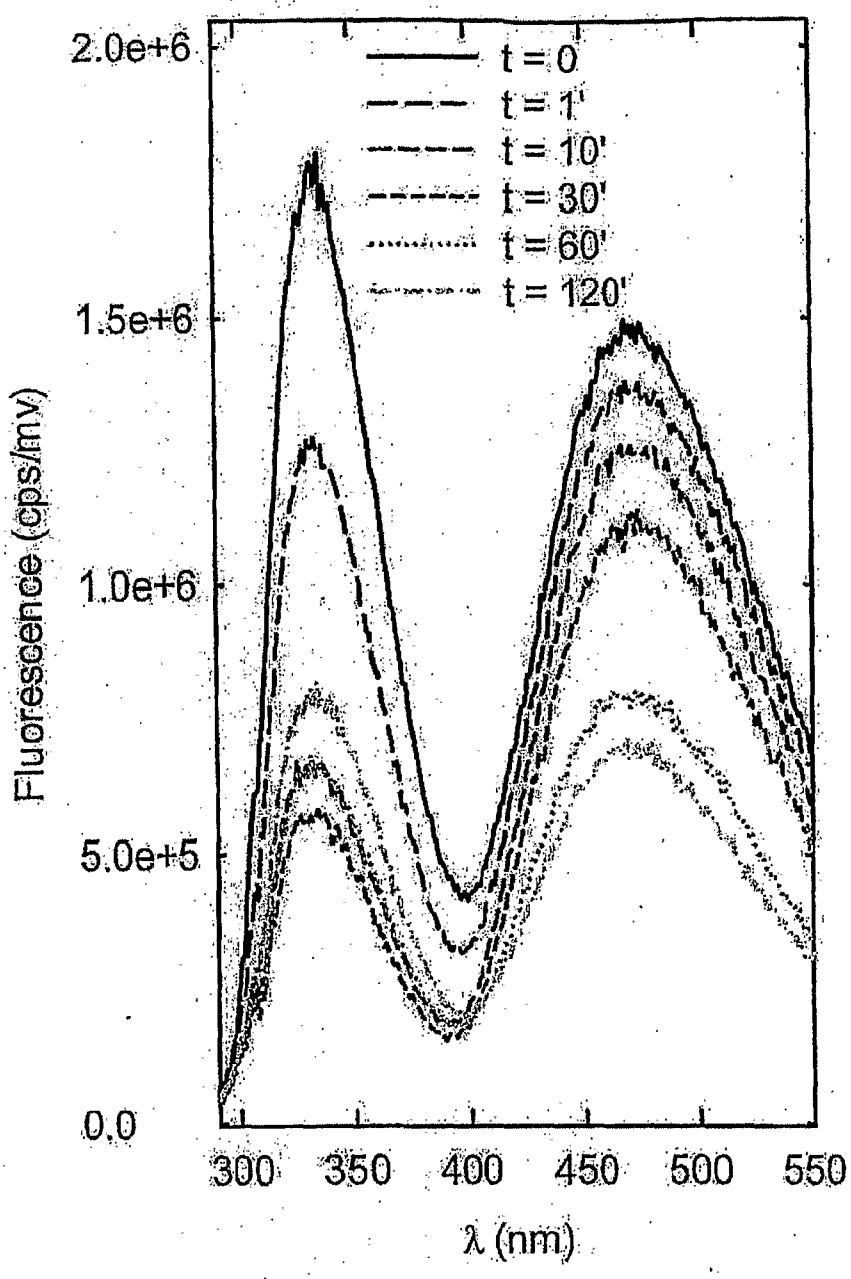

2.0e+6
1.5e+6
1.0e+6
5.0e+5
0.0
Fluorescence (cps/mv)
t = 0
t = 1'
t = 10'
t = 30'
t = 60'
t = 120'
300
350
400
450
500
550
λ (nm)

FIGURE 9B

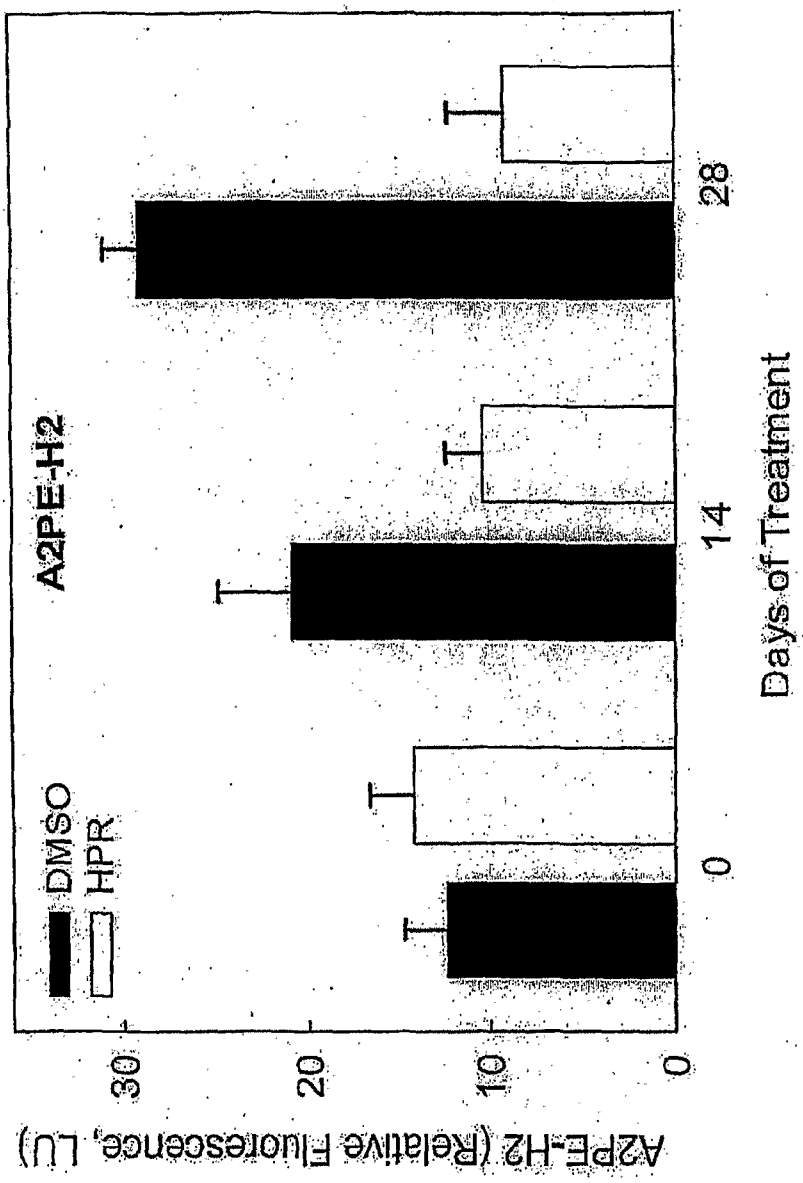

A2PE-H2 (Relative Fluorescence, LU)
0
10
20
30
A2PE-H2
DMSO
HPR
0
14
28
Days of Treatment

FIGURE 10A

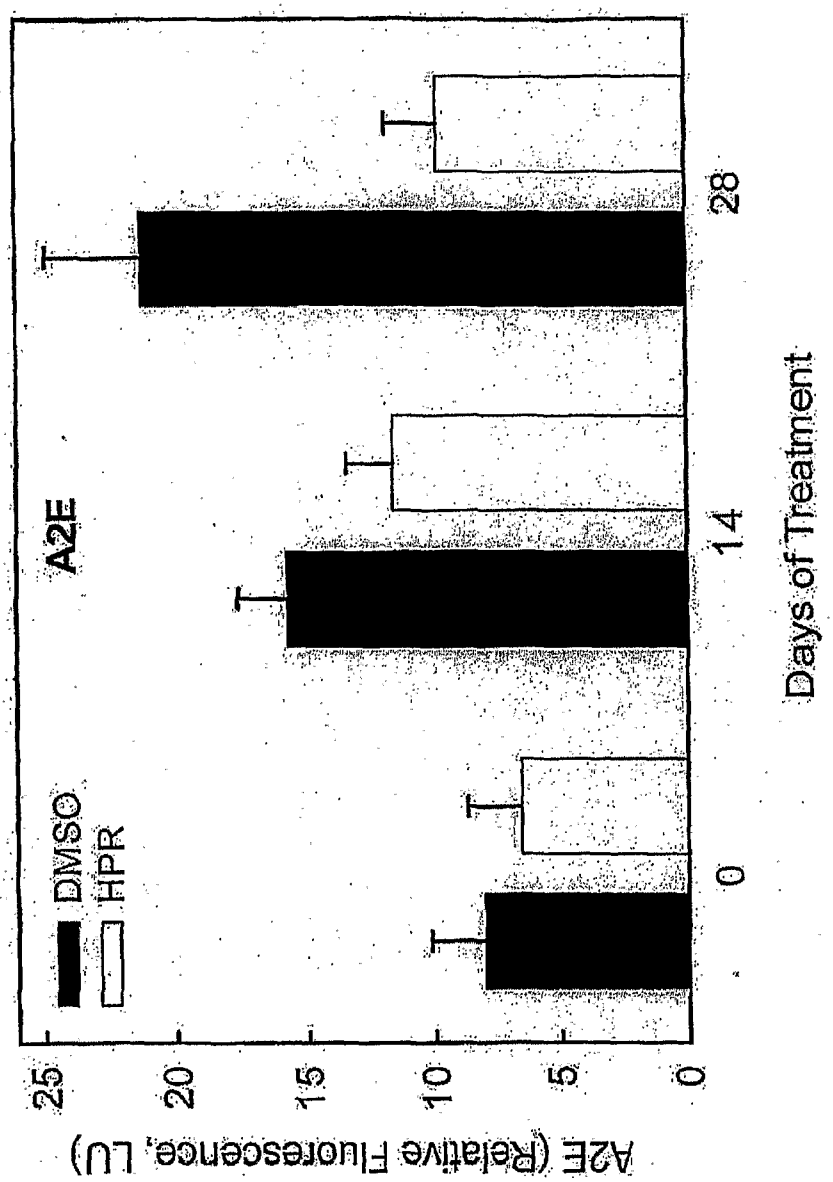

A2E (Relative Fluorescence, LU)
25
20
15
10
5
0
DMSO
HPR
A2E
0
14
28
Days of Treatment

FIGURE 10B

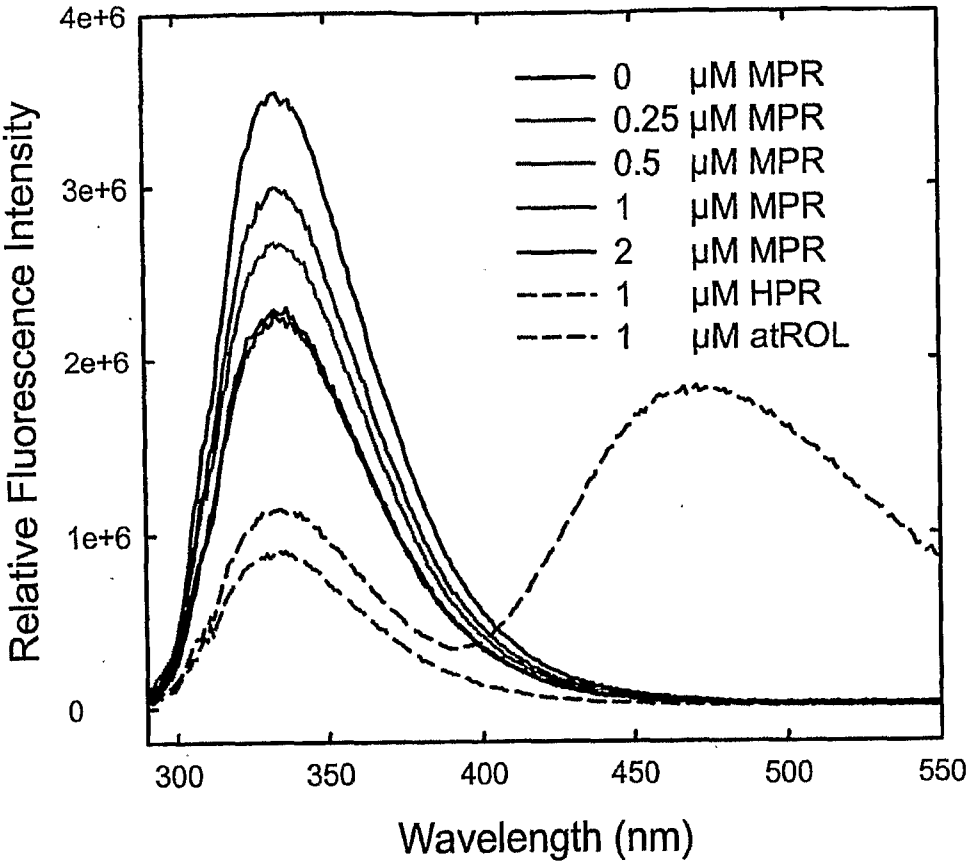

4e+6
3e+6
2e+6
1e+6
0
Relative Fluorescence Intensity
300
350
400
450
500
550
Wavelength (nm)
0 μM MPR
0.25 μM MPR
0.5 μM MPR
1 μM MPR
2 μM MPR
1 μM HPR
1 μM atROL

FIGURE 11

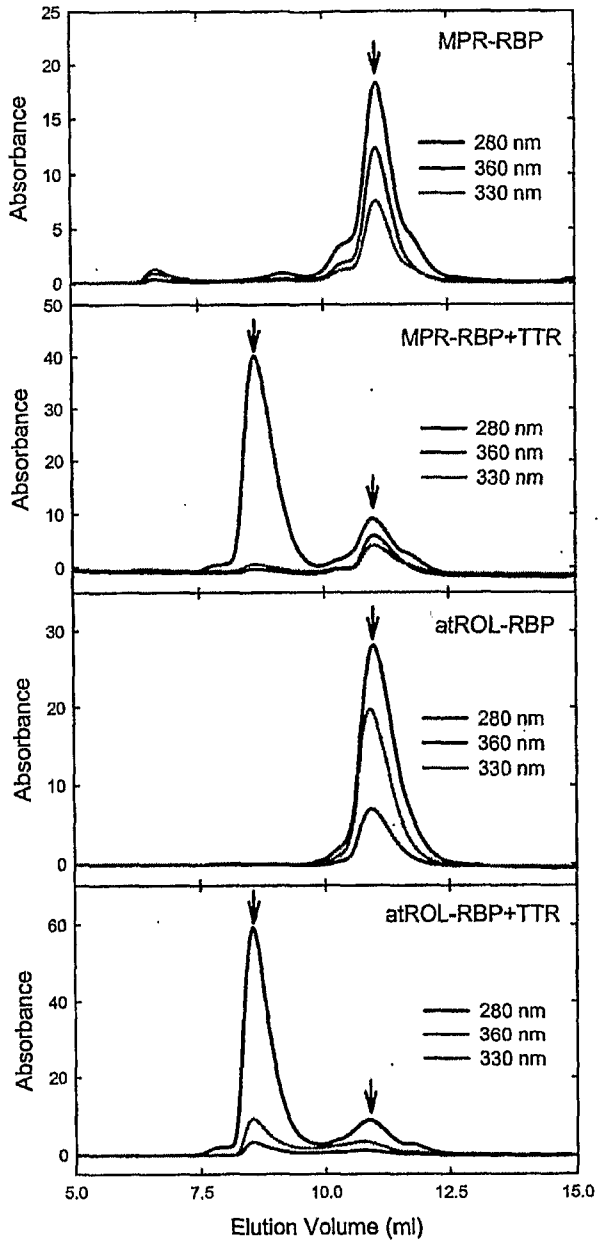
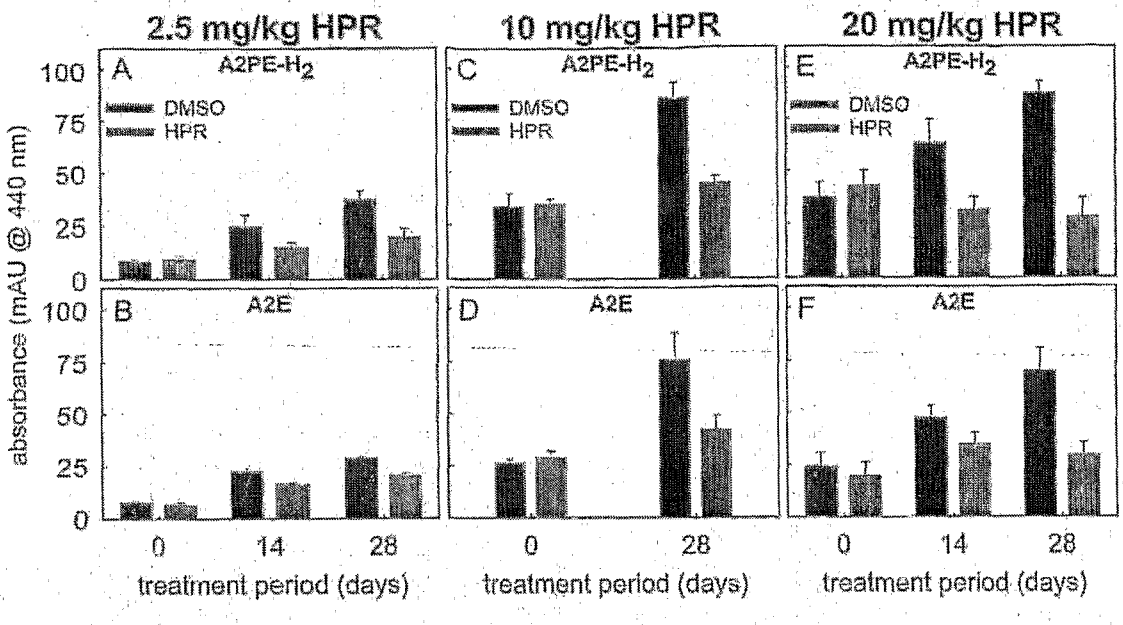

MPR-RBP
280 nm
360 nm
330 nm
MPR-RBP+TTR
280 nm
360 nm
330 nm
atROL-RBP
280 nm
360 nm
330 nm
atROL-RBP+TTR
280 nm
360 nm
330 nm
Absorbance
Elution Volume (ml)
5.0
7.5
10.0
12.5
15.0

FIGURE 12


2.5 mg/kg HPR
10 mg/kg HPR
20 mg/kg HPR
A
A2PE-H2
DMSO
HPR
B
A2E
C
D
E
F
absorbance (mAU @ 440 nm)
100
75
50
25
0
0
14
28
treatment period (days)

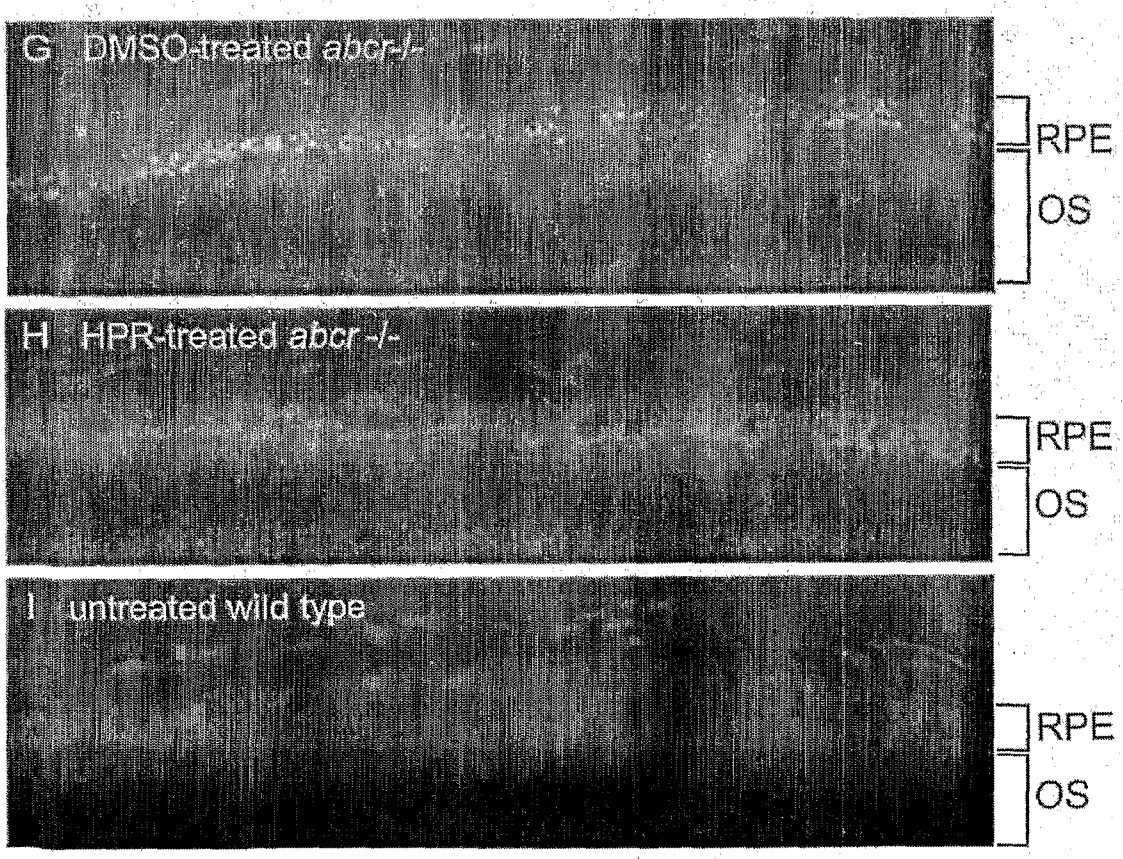

G DMSO-treated abcr-/-
H HPR-treated abcr -/-
I untreated wild type
RPE
OS

FIGURE 13

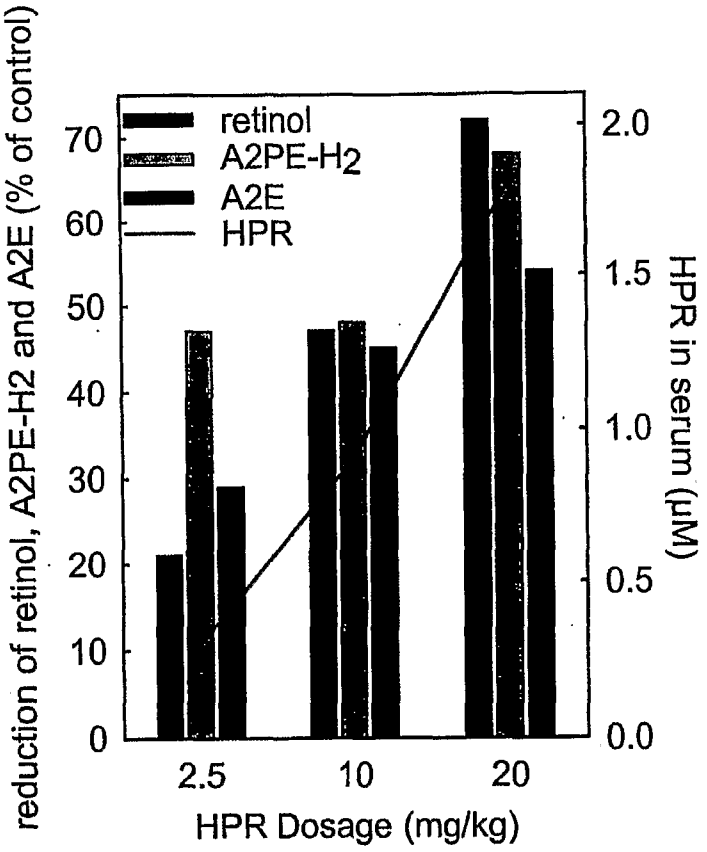

reduction of retinol, A2PE-H2 and A2E (% of control)
HPR in serum (μM)
retinol
A2PE-H2
A2E
HPR
0
10
20
30
40
50
60
70
0.0
0.5
1.0
1.5
2.0
2.5
10
20
HPR Dosage (mg/kg)

FIGURE 14

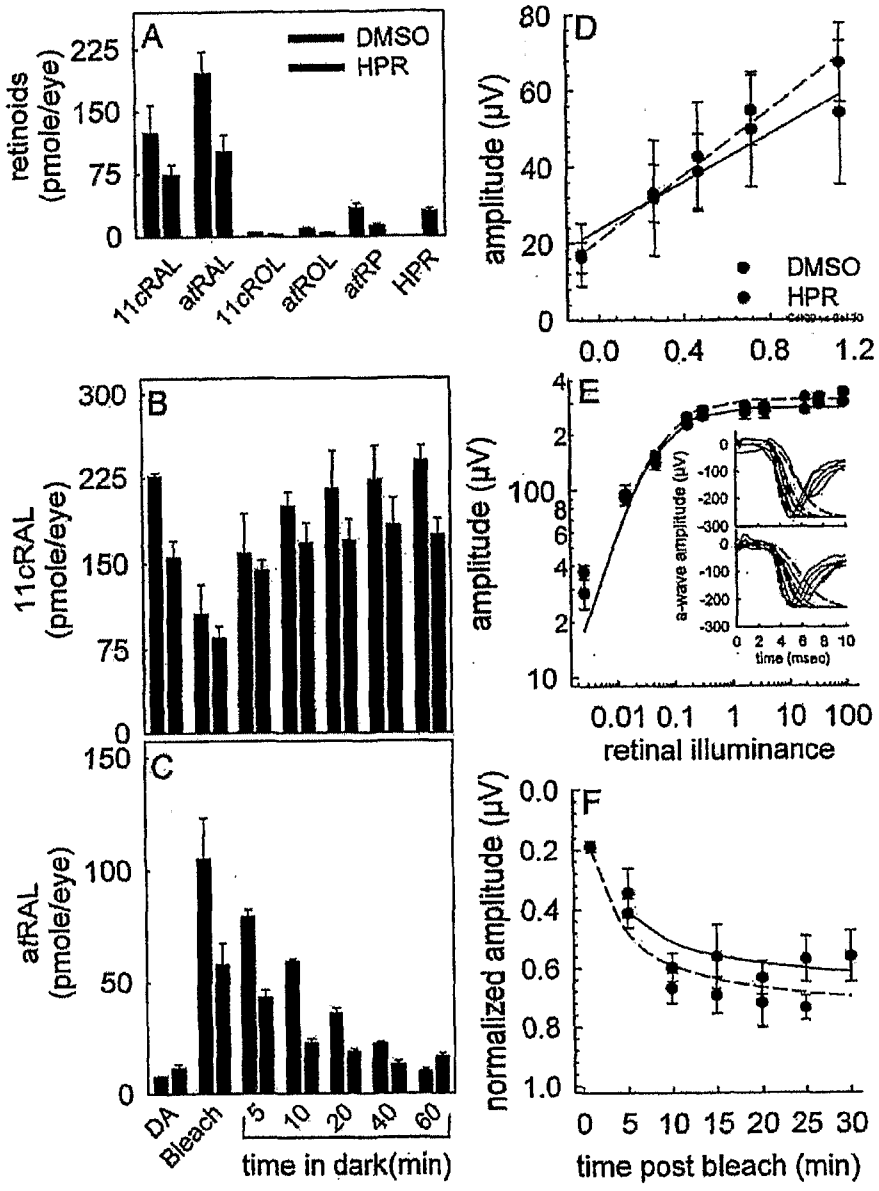

A
DMSO
HPR
retinoids (pmole/eye)
225
150
75
0
11cRAL
atRAL
11cROL
atROL
atRP
HPR
B
11cRAL (pmole/eye)
300
225
150
75
0
C
atRAL (pmole/eye)
150
100
50
0
DA
Bleach
5
10
20
40
60
time in dark(min)
D
amplitude (μV)
80
60
40
20
0
DMSO
HPR
0.0
0.4
0.8
1.2
E
amplitude (μV)
100
10
a-wave amplitude (μV)
time (msec)
0.01 0.1 1 10 100
retinal illuminance
F
normalized amplitude (μV)
0.0
0.2
0.4
0.6
0.8
1.0
0 5 10 15 20 25 30
time post bleach (min)

FIGURE 15

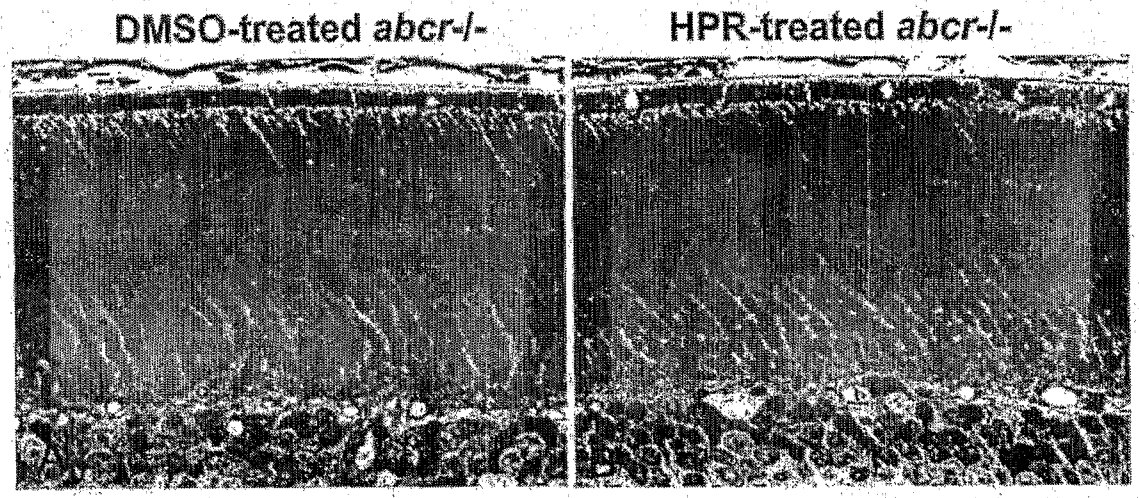


FIGURE 16

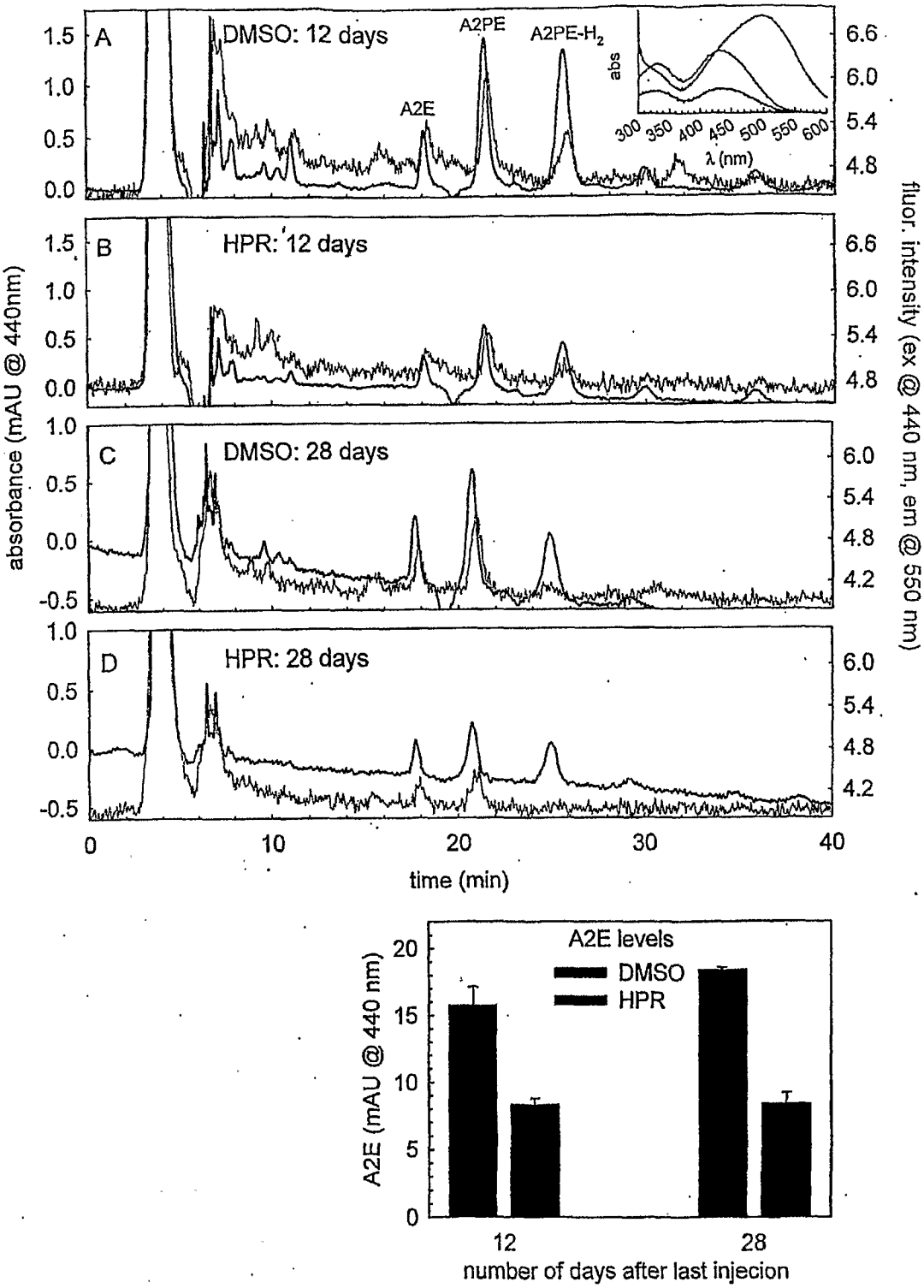

A
DMSO: 12 days
A2E
A2PE
A2PE-H2
abs
λ (nm)
B
HPR: 12 days
C
DMSO: 28 days
D
HPR: 28 days
absorbance (mAU @ 440nm)
fluor. intensity (ex @ 440 nm, em @ 550 nm)
time (min)
A2E levels
DMSO
HPR
A2E (mAU @ 440 nm)
number of days after last injecion

FIGURE 17

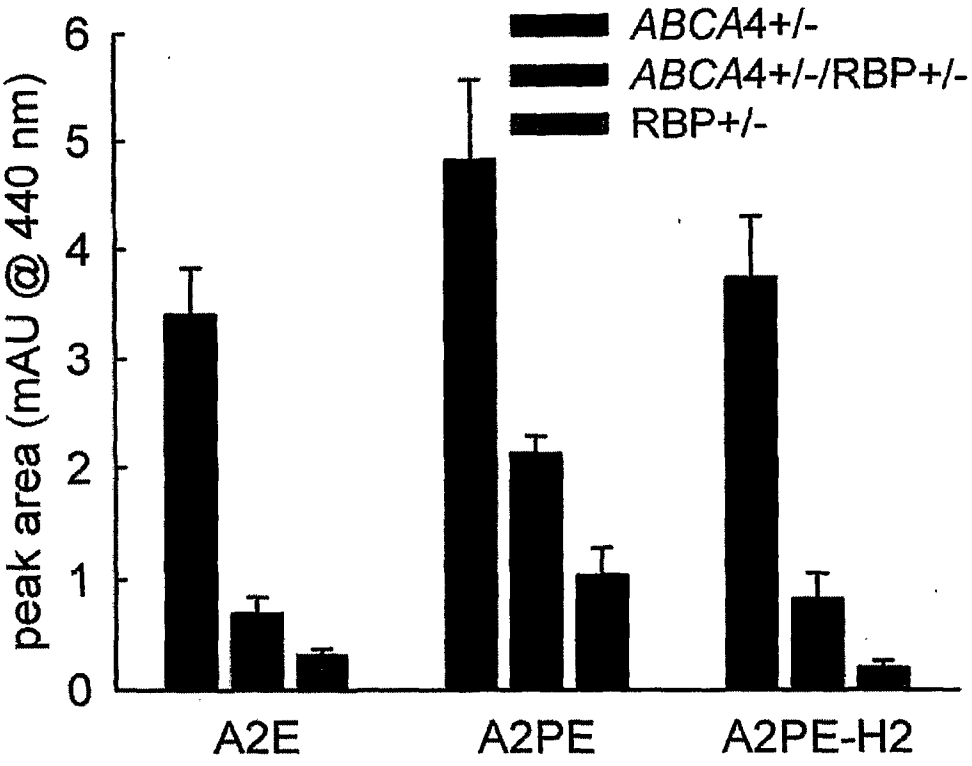

ABCA4+/-
ABCA4+/-/RBP+/-
RBP+/-
peak area (mAU @ 440 nm)
0
1
2
3
4
5
6
A2E
A2PE
A2PE-H2

FIGURE 18