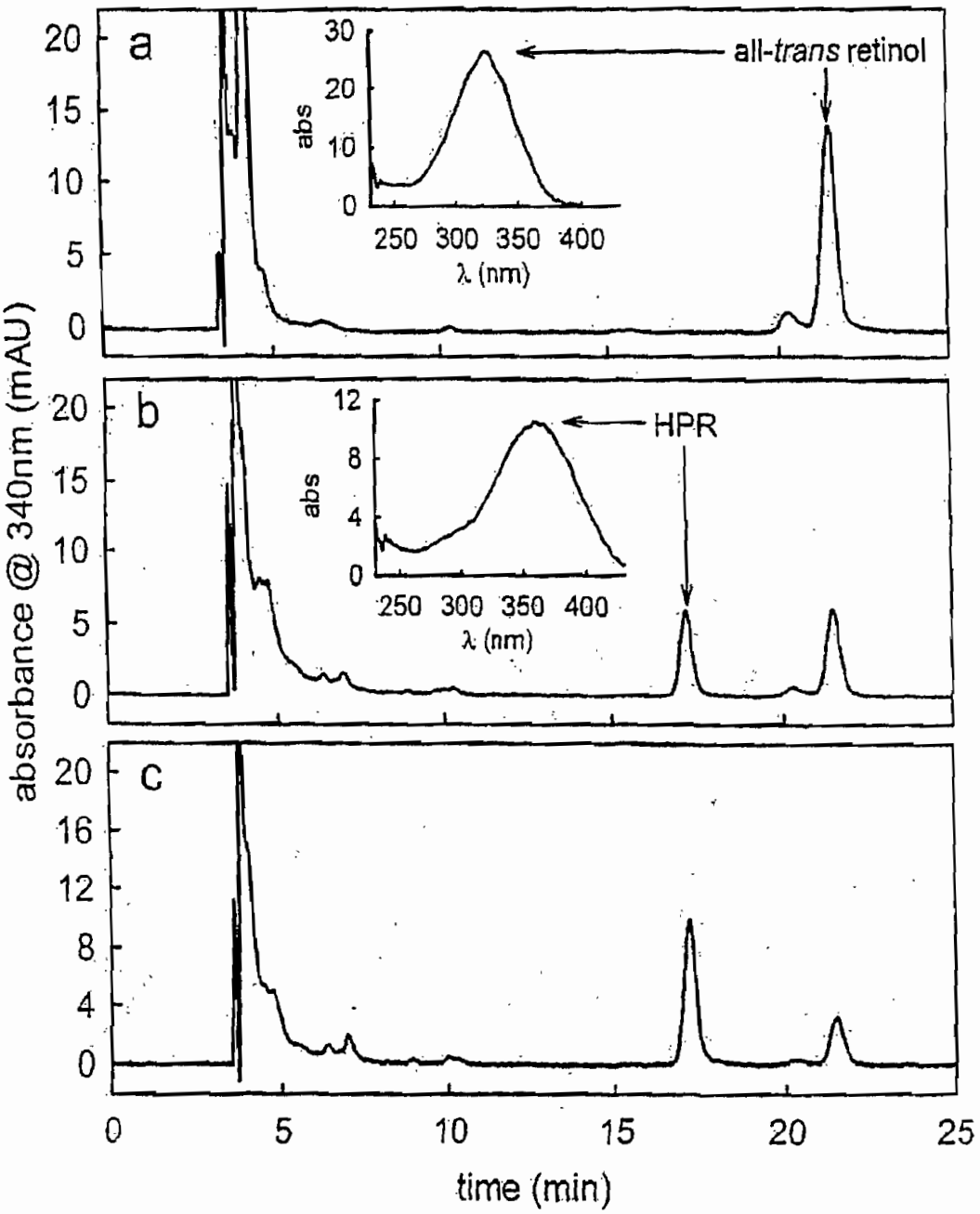

a
b
c
all-trans retinol
HPR
abs
λ (nm)
absorbance @ 340nm (mAU)
time (min)

Figure 1 a - c

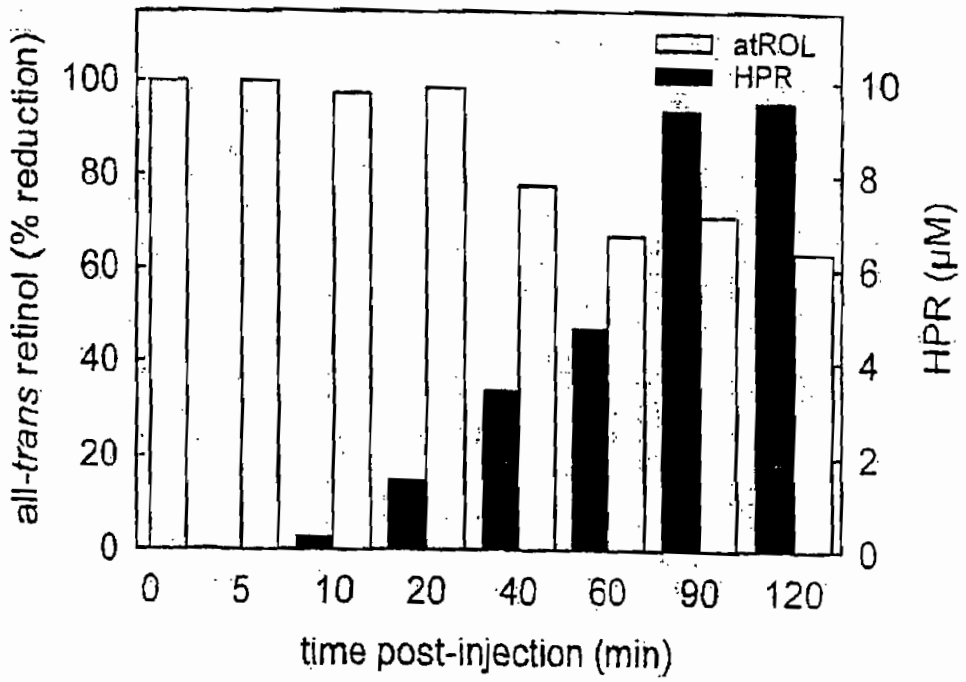

atROL
HPR
all-trans retinol (% reduction)
HPR (μM)
time post-injection (min)
0
20
40
60
80
100
0
2
4
6
8
10
0
5
10
20
40
60
90
120

Figure 2a

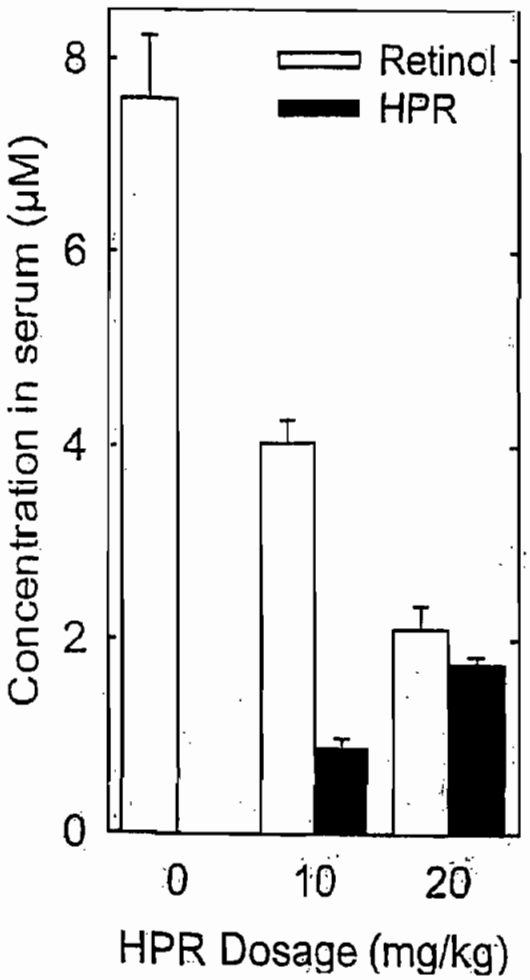

Retinol
HPR
Concentration in serum (μM)
0
2
4
6
8
0
10
20
HPR Dosage (mg/kg)

Figure 2b

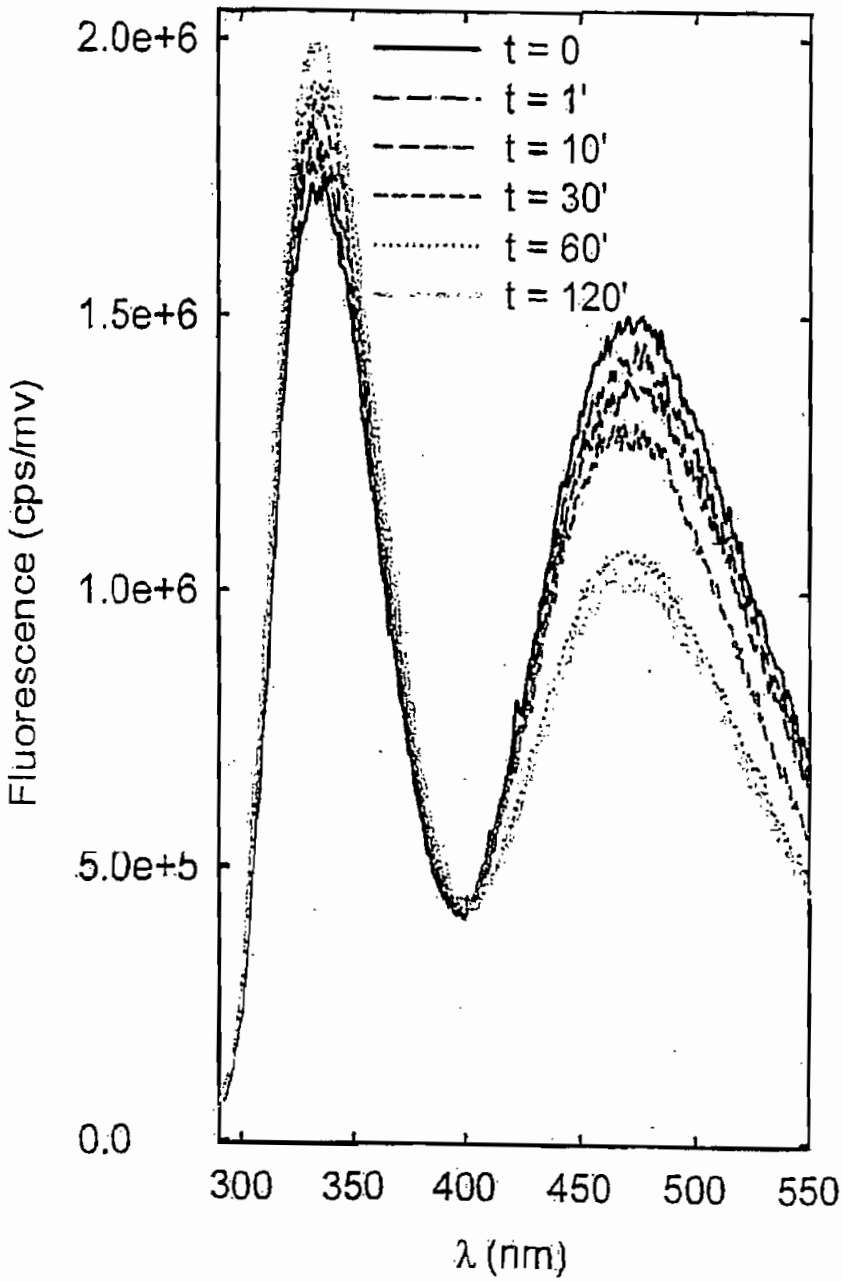

2.0e+6
1.5e+6
1.0e+6
5.0e+5
0.0
Fluorescence (cps/mv)
t = 0
t = 1'
t = 10'
t = 30'
t = 60'
t = 120'
300
350
400
450
500
550
λ (nm)

Figure 3a

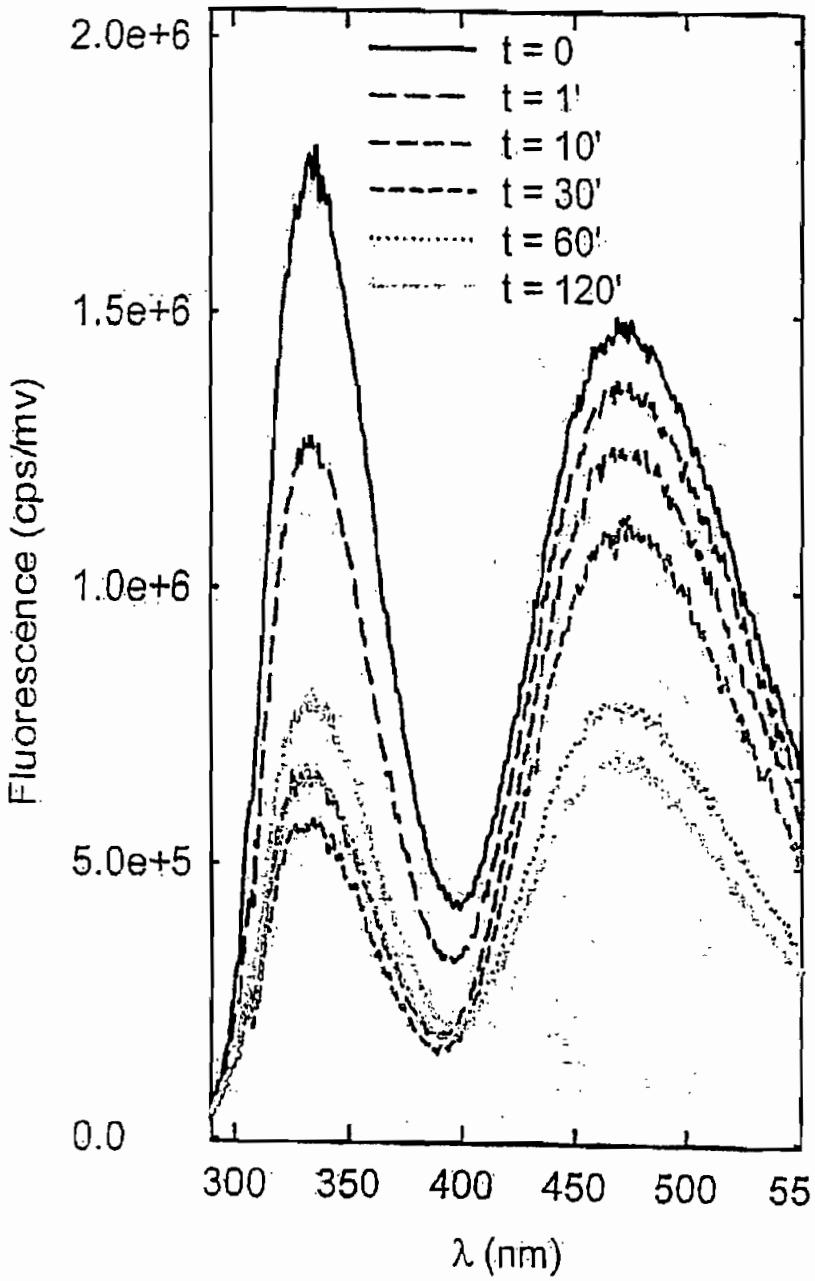

2.0e+6
1.5e+6
1.0e+6
5.0e+5
0.0
Fluorescence (cps/mv)
t = 0
t = 1'
t = 10'
t = 30'
t = 60'
t = 120'
300
350
400
450
500
55
λ (nm)

Figure 3b

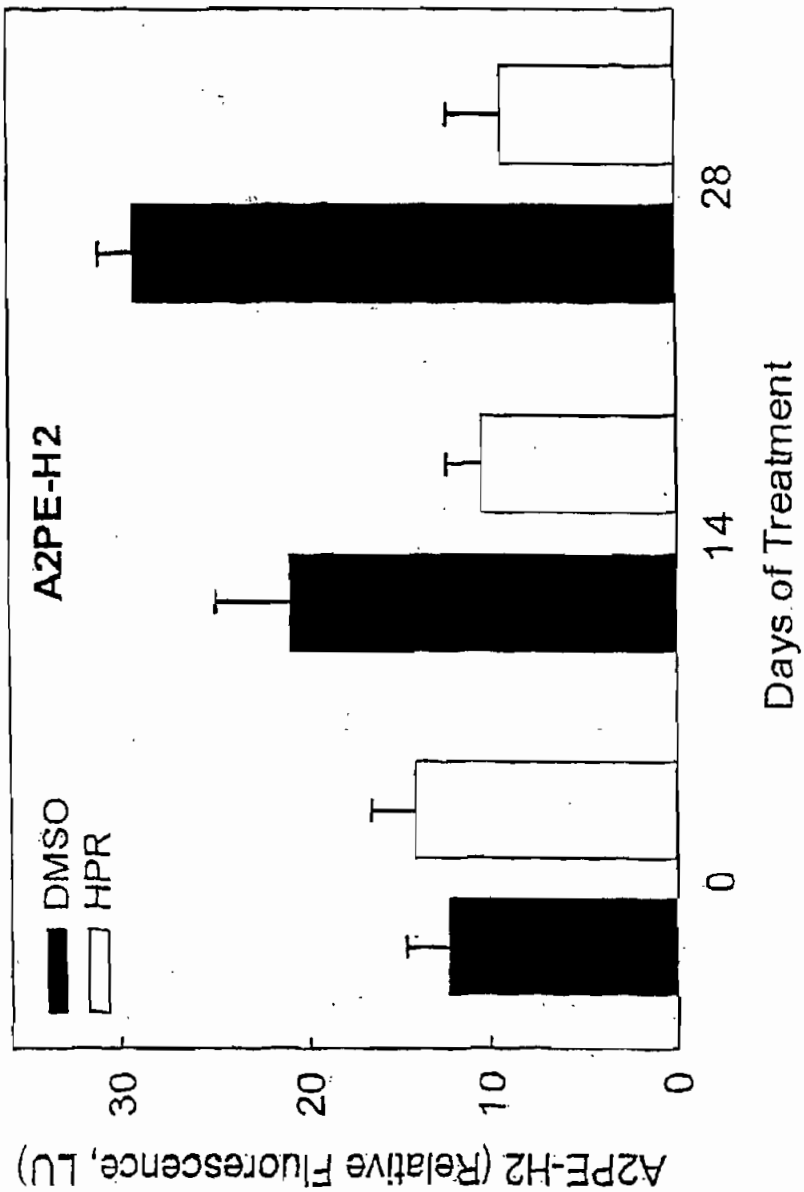

A2PE-H2
DMSO
HPR
A2PE-H2 (Relative Fluorescence, LU)
0
10
20
30
0
14
28
Days of Treatment

Figure 4a

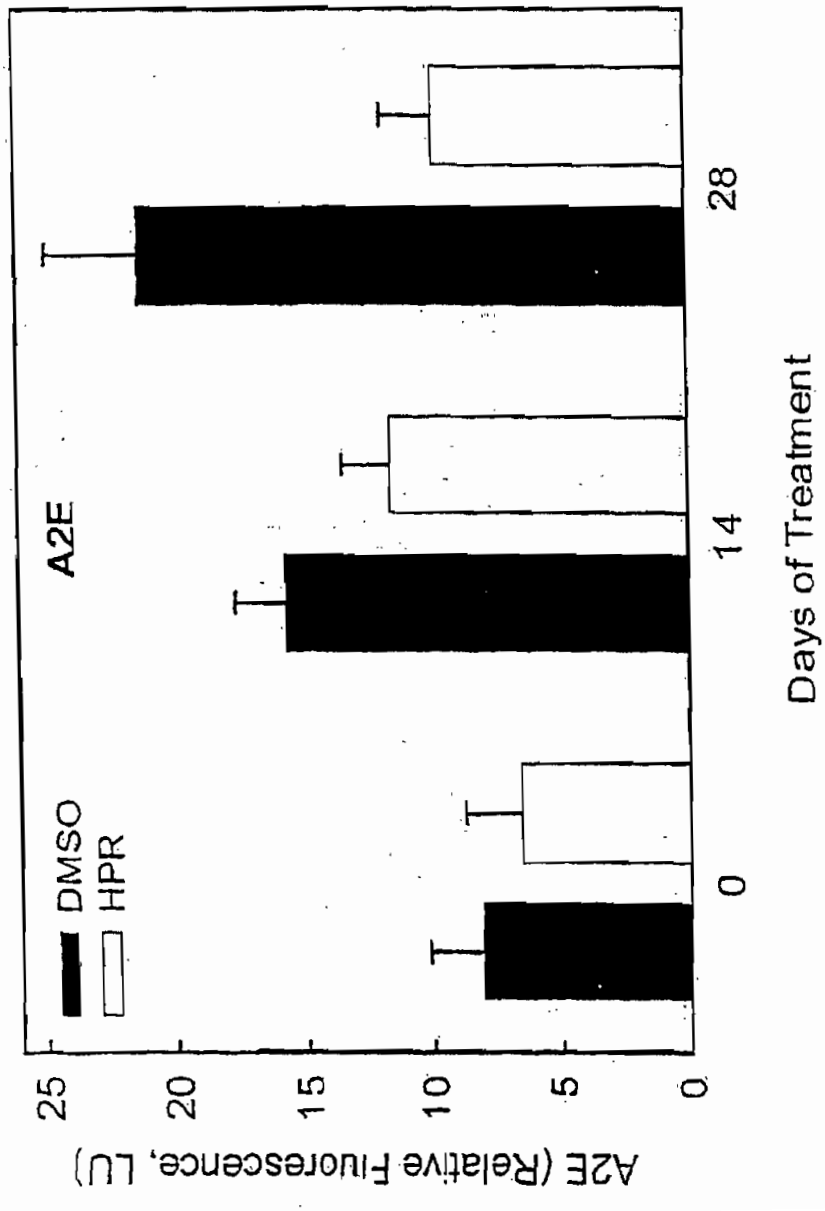

A2E (Relative Fluorescence, LU)
25
20
15
10
5
0
DMSO
HPR
A2E
0
14
28
Days of Treatment

Figure 4b

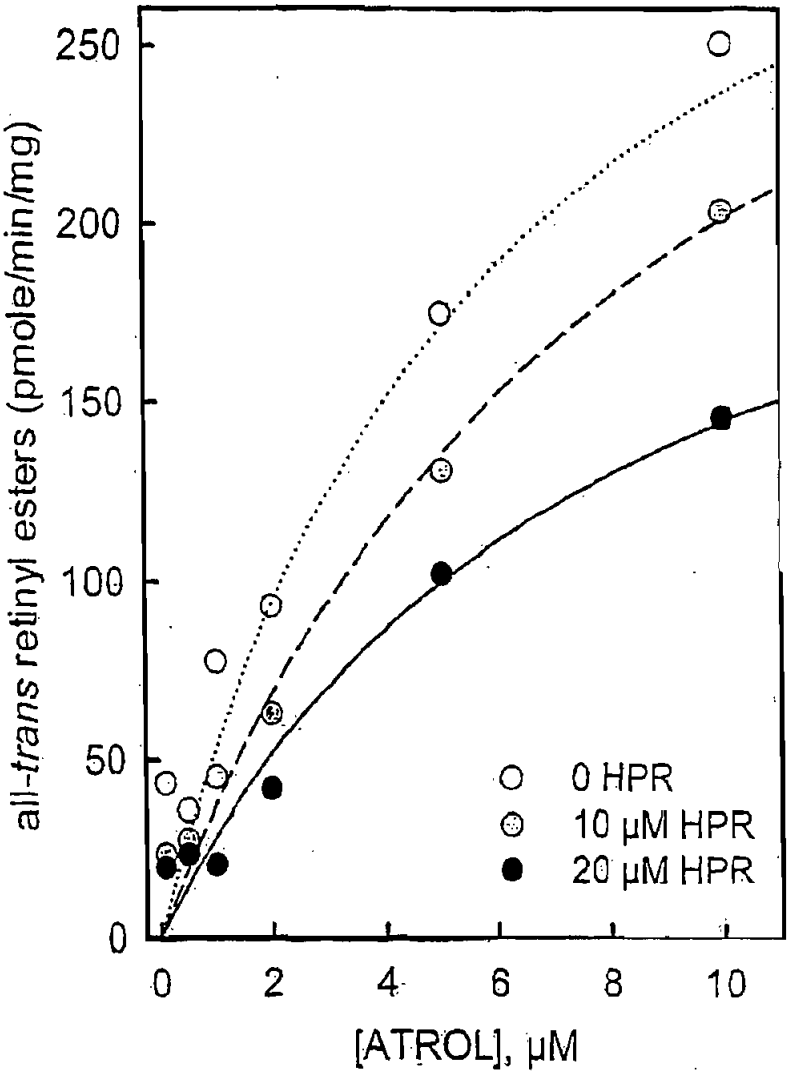

250
200
150
100
50
0
all-trans retinyl esters (pmole/min/mg)
0
2
4
6
8
10
[ATROL], µM
0 HPR
10 µM HPR
20 µM HPR

Figure 5

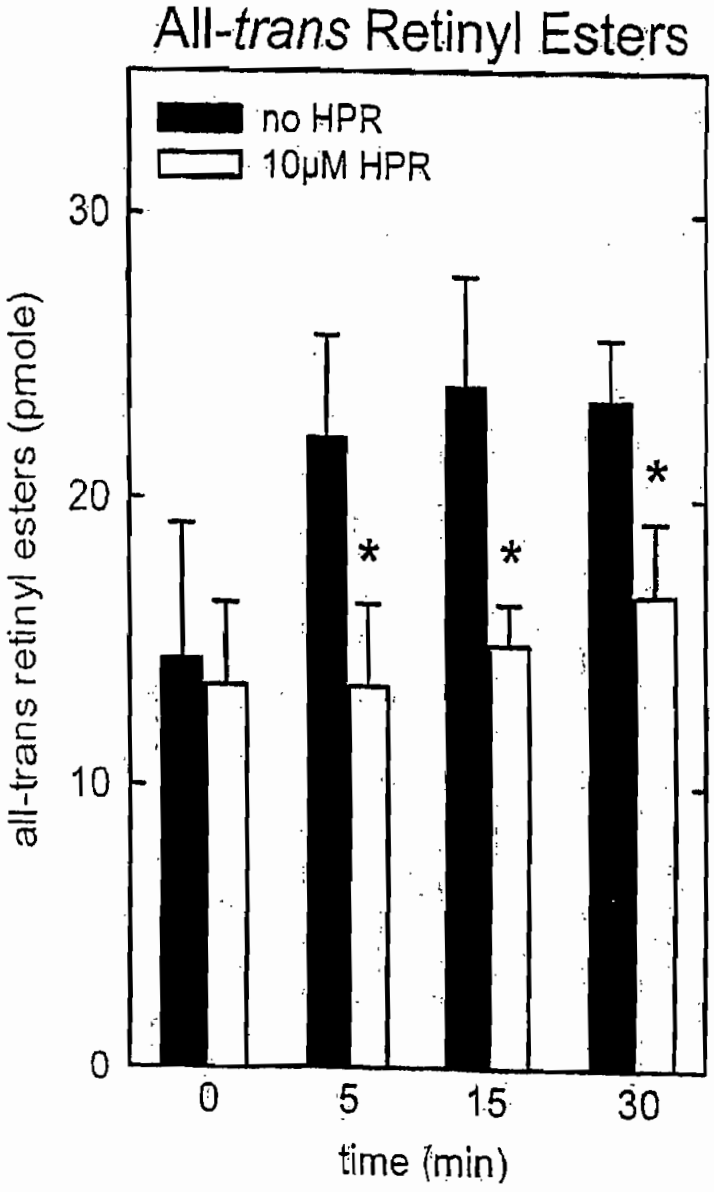

All-trans Retinyl Esters
no HPR
10μM HPR
all-trans retinyl esters (pmole)
0
10
20
30
*
*
*
0
5
15
30
time (min)

Figure 6a

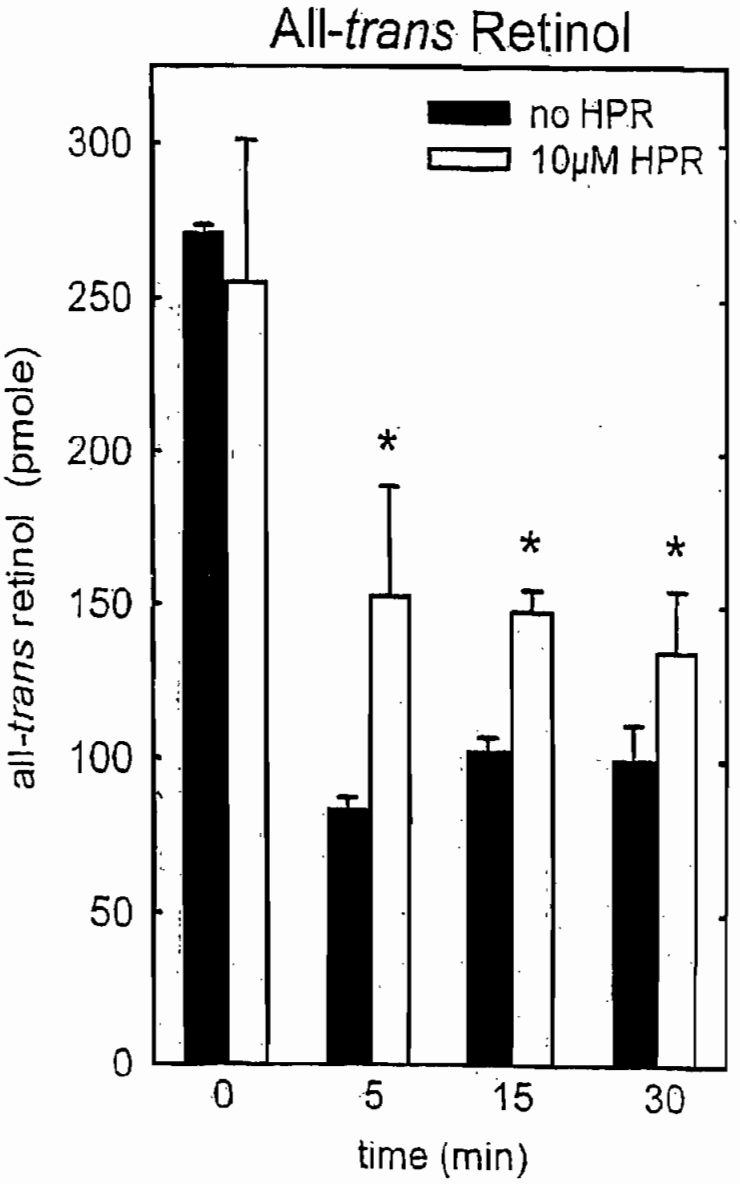

All-trans Retinol
no HPR
10μM HPR
all-trans retinol (pmole)
300
250
200
150
100
50
0
*
*
*
0
5
15
30
time (min)

Figure 6c

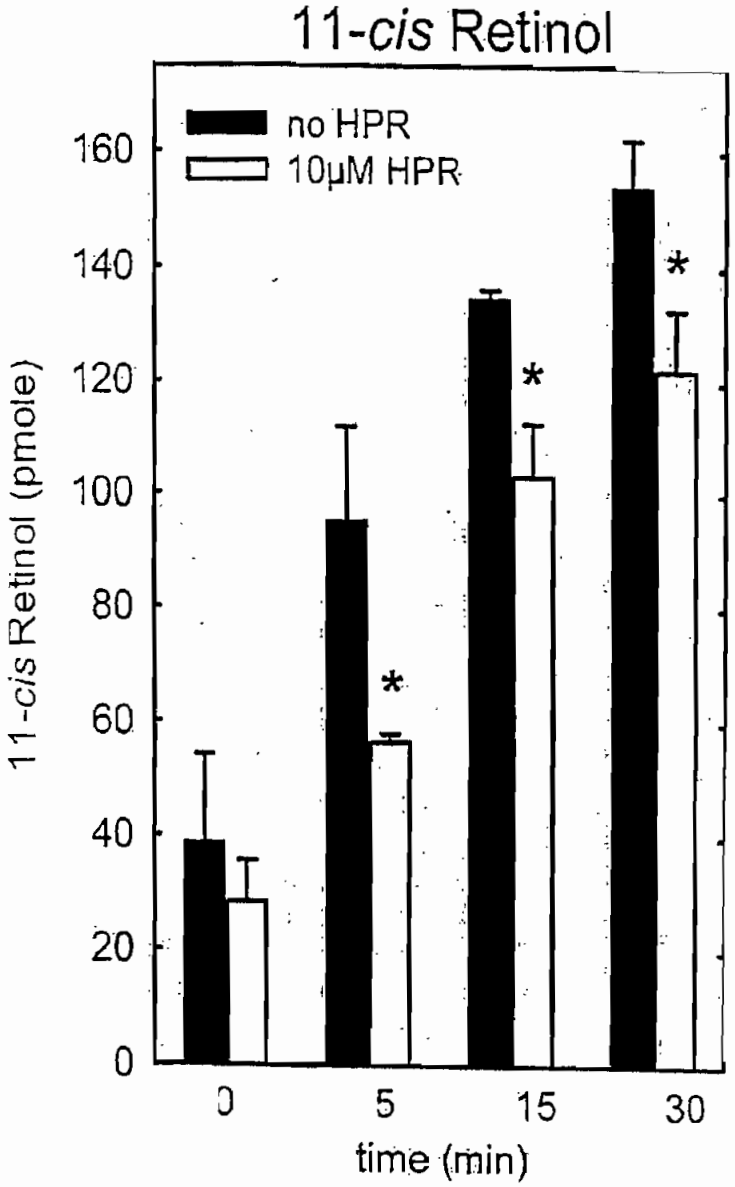

11-cis Retinol
no HPR
10μM HPR
11-cis Retinol (pmole)
160
140
120
100
80
60
40
20
0
0
5
15
30
time (min)
*
*
*

Figure 6b

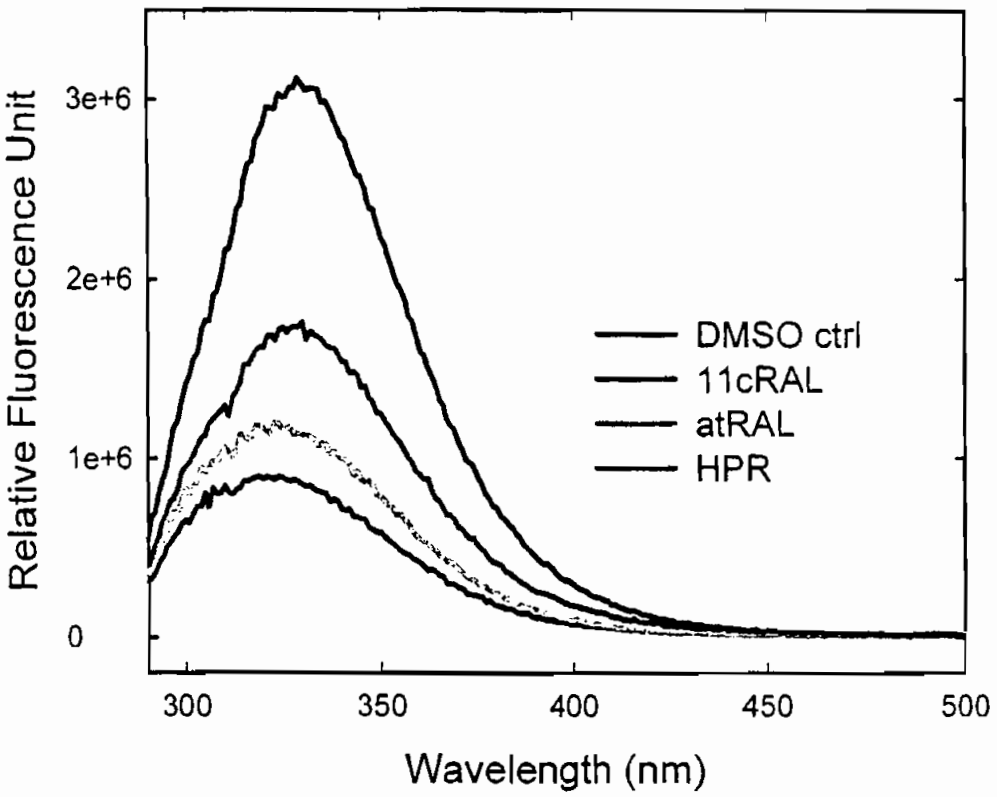

Relative Fluorescence Unit
3e+6
2e+6
1e+6
0
300
350
400
450
500
Wavelength (nm)
DMSO ctrl
11cRAL
atRAL
HPR

FIGURE 7

8a

8b

8c

8d

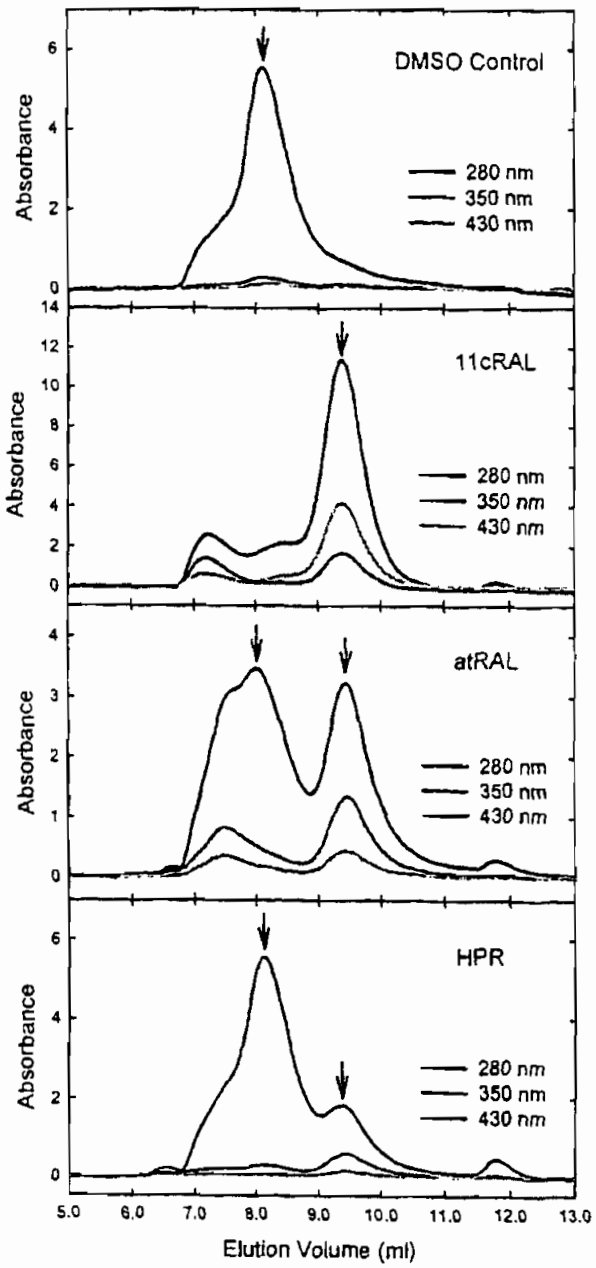


FIGURE 8

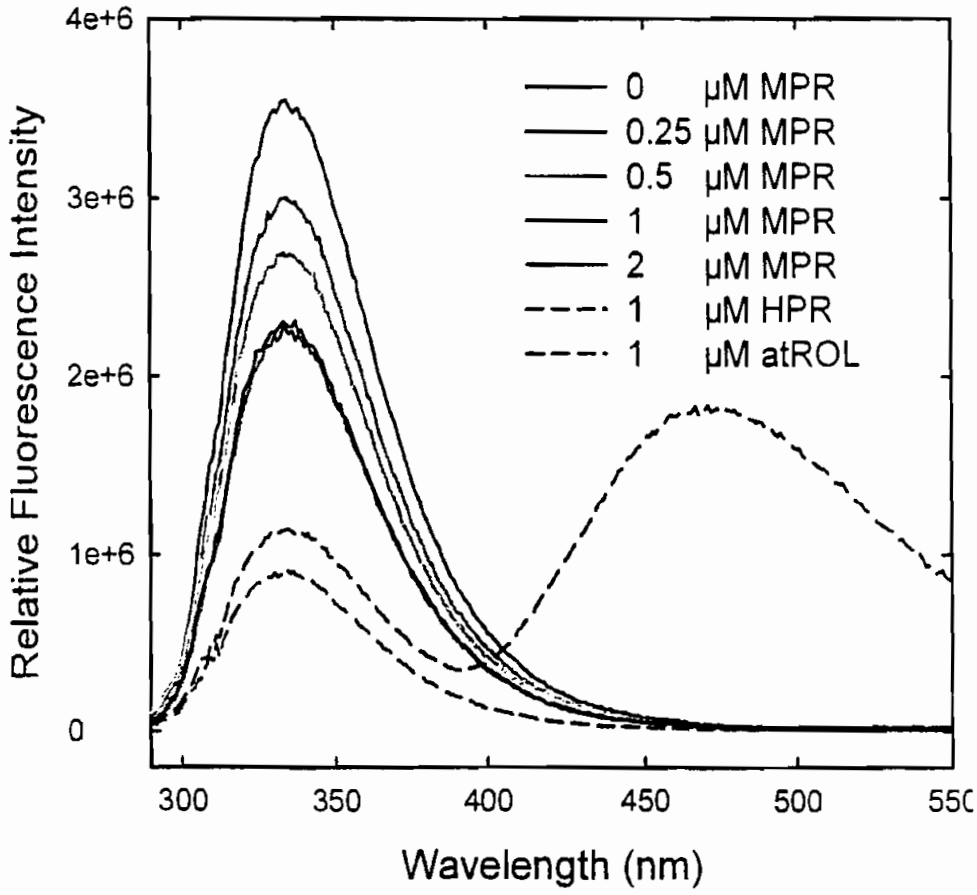

4e+6
3e+6
2e+6
1e+6
0
Relative Fluorescence Intensity
300
350
400
450
500
550
Wavelength (nm)
0 μM MPR
0.25 μM MPR
0.5 μM MPR
1 μM MPR
2 μM MPR
1 μM HPR
1 μM atROL

FIGURE 9

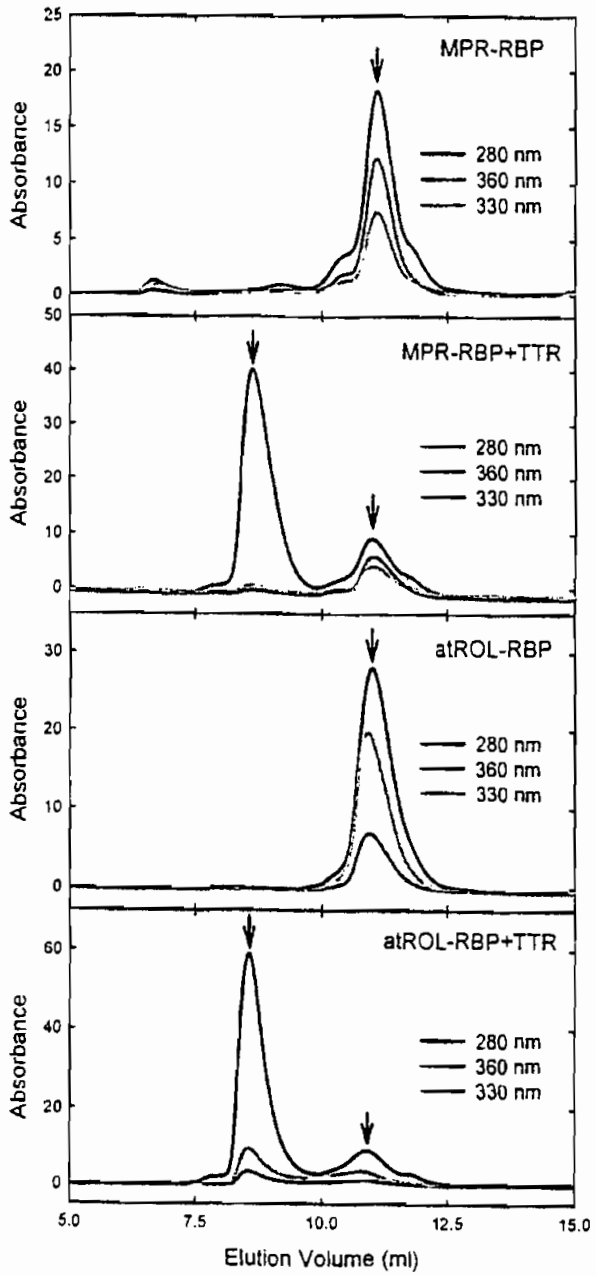

MPR-RBP
MPR-RBP+TTR
atROL-RBP
atROL-RBP+TTR
280 nm
360 nm
330 nm
Absorbance
Elution Volume (ml)
5.0
7.5
10.0
12.5
15.0

FIGURE 10

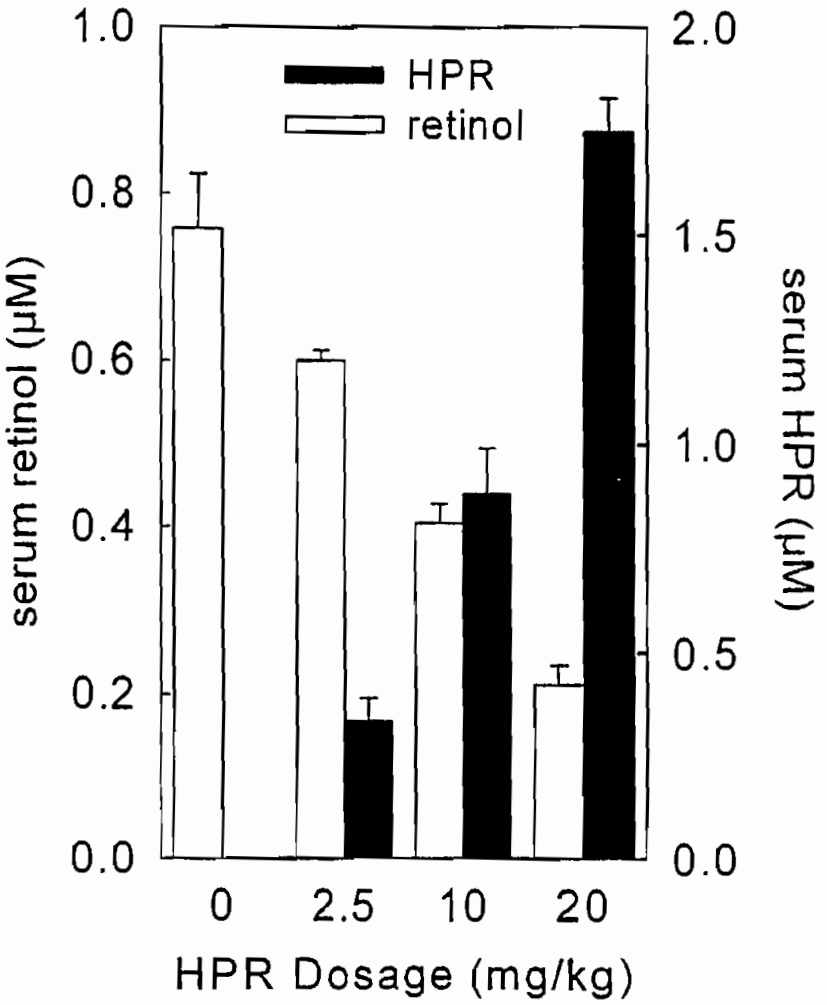

1.0
0.8
0.6
0.4
0.2
0.0
serum retinol (μM)
2.0
1.5
1.0
0.5
0.0
serum HPR (μM)
HPR
retinol
0
2.5
10
20
HPR Dosage (mg/kg)

FIGURE 11

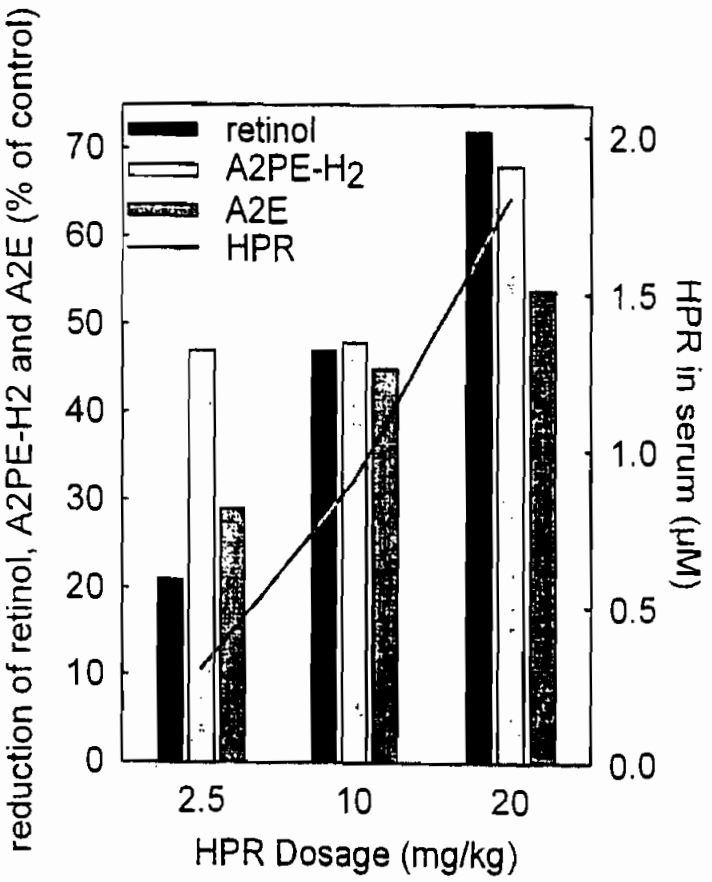

reduction of retinol, A2PE-H2 and A2E (% of control)
HPR in serum (μM)
HPR Dosage (mg/kg)
retinol
A2PE-H2
A2E
HPR
0
10
20
30
40
50
60
70
0.0
0.5
1.0
1.5
2.0
2.5
10
20

FIGURE 12

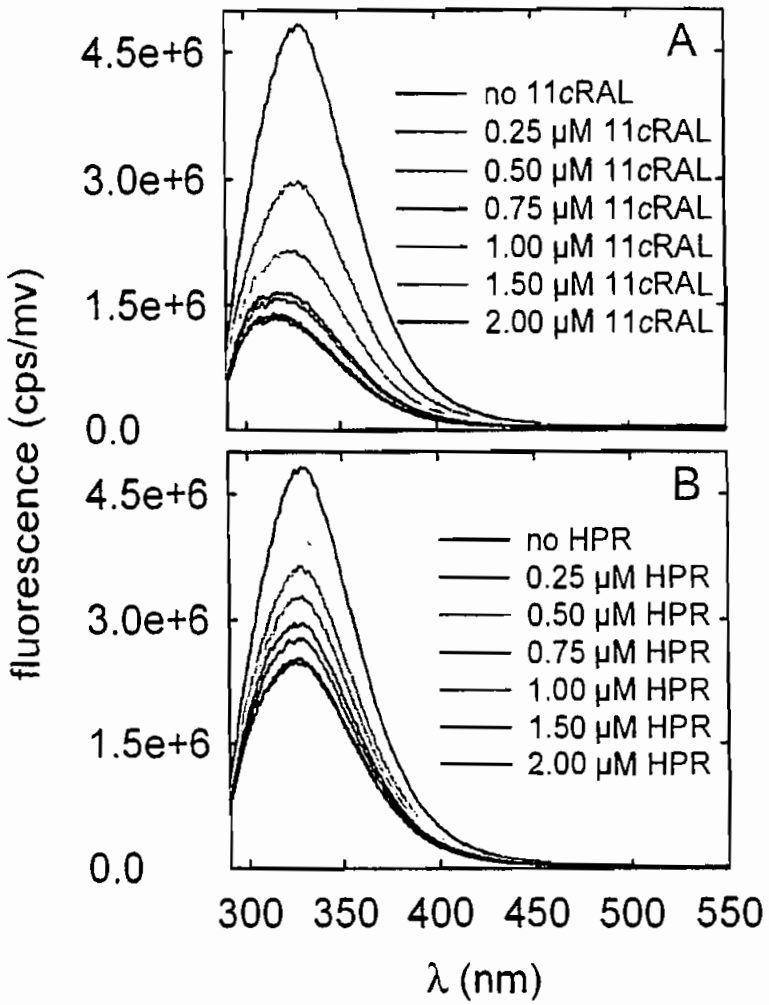

A
no 11cRAL
0.25 µM 11cRAL
0.50 µM 11cRAL
0.75 µM 11cRAL
1.00 µM 11cRAL
1.50 µM 11cRAL
2.00 µM 11cRAL
B
no HPR
0.25 µM HPR
0.50 µM HPR
0.75 µM HPR
1.00 µM HPR
1.50 µM HPR
2.00 µM HPR
4.5e+6
3.0e+6
1.5e+6
0.0
fluorescence (cps/mv)
300 350 400 450 500 550
λ (nm)

FIGURE 13

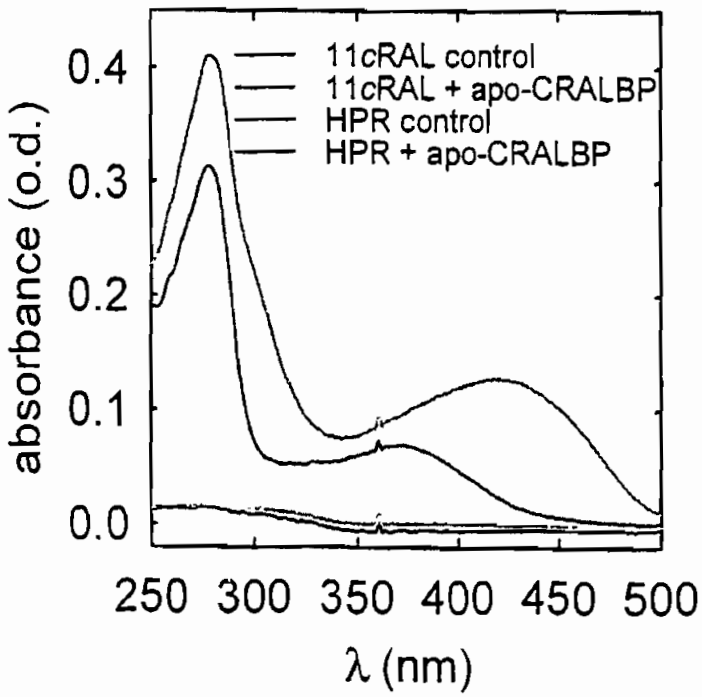

11cRAL control
11cRAL + apo-CRALBP
HPR control
HPR + apo-CRALBP
absorbance (o.d.)
0.4
0.3
0.2
0.1
0.0
250 300 350 400 450 500
λ (nm)

FIGURE 14

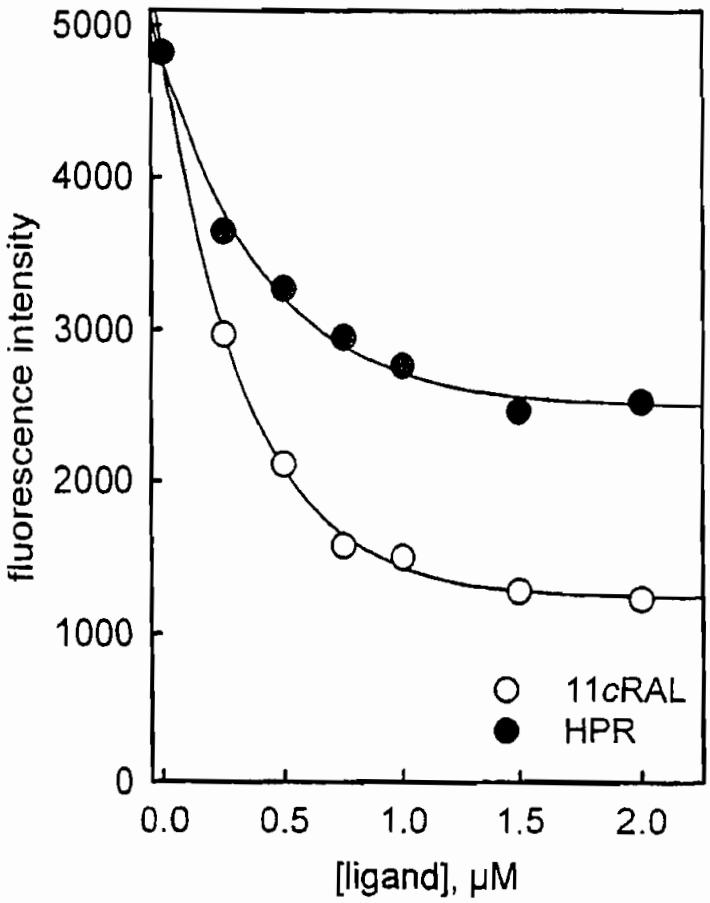
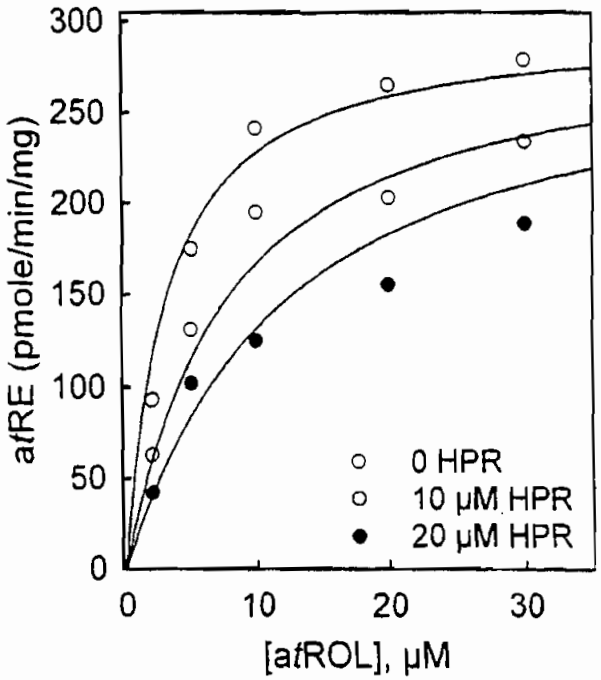

5000
4000
3000
2000
1000
0
fluorescence intensity
0.0
0.5
1.0
1.5
2.0
[ligand], μM
11cRAL
HPR

FIGURE 15


300
250
200
150
100
50
0
afRE (pmole/min/mg)
0 HPR
10 μM HPR
20 μM HPR
0
10
20
30
[atROL], μM

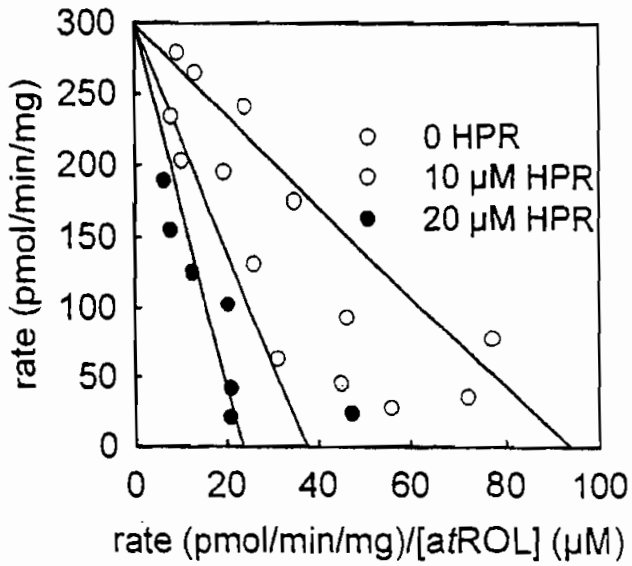

300
250
200
150
100
50
0
rate (pmol/min/mg)
0 HPR
10 μM HPR
20 μM HPR
0
20
40
60
80
100
rate (pmol/min/mg)/[atROL] (μM)

FIGURE 16

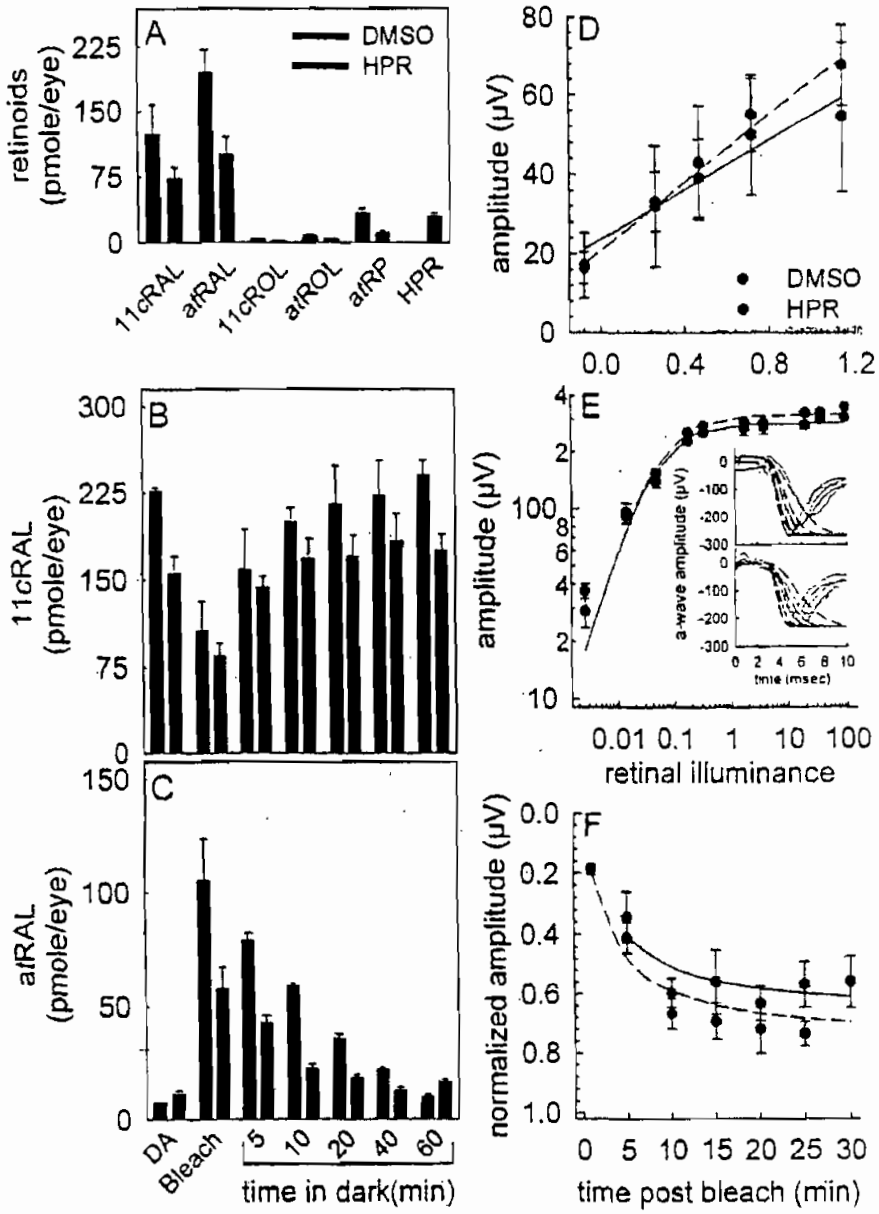
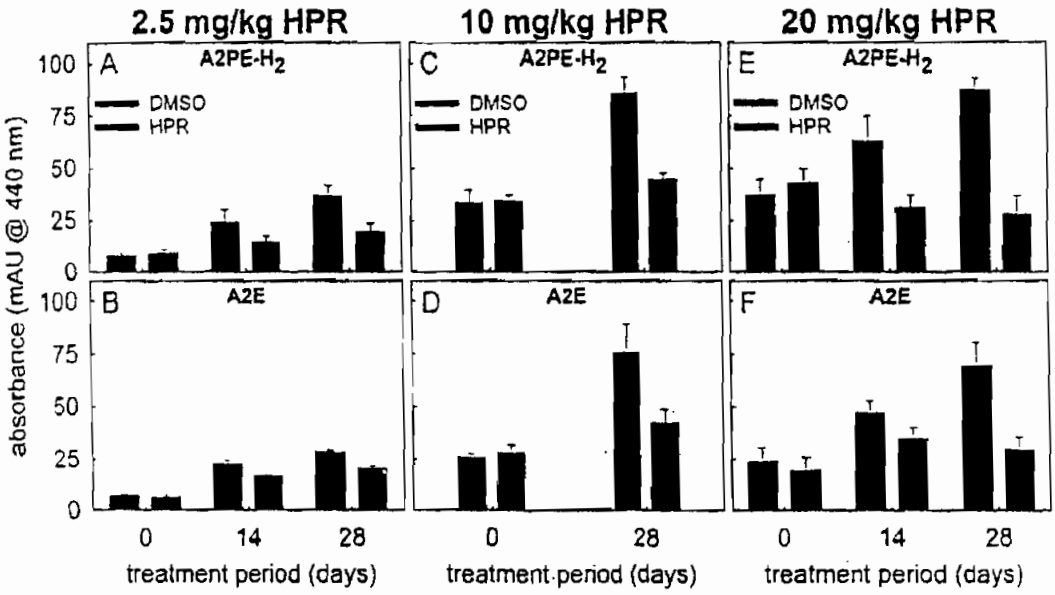

A
DMSO
HPR
retinoids (pmole/eye)
225
150
75
0
11cRAL
atRAL
11cROL
atROL
atRP
HPR
B
11cRAL (pmole/eye)
300
225
150
75
0
C
atRAL (pmole/eye)
150
100
50
0
DA
Bleach
5
10
20
40
60
time in dark(min)
D
amplitude (μV)
80
60
40
20
0
DMSO
HPR
0.0
0.4
0.8
1.2
E
amplitude (μV)
100
a-wave amplitude (μV)
time (msec)
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 17


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

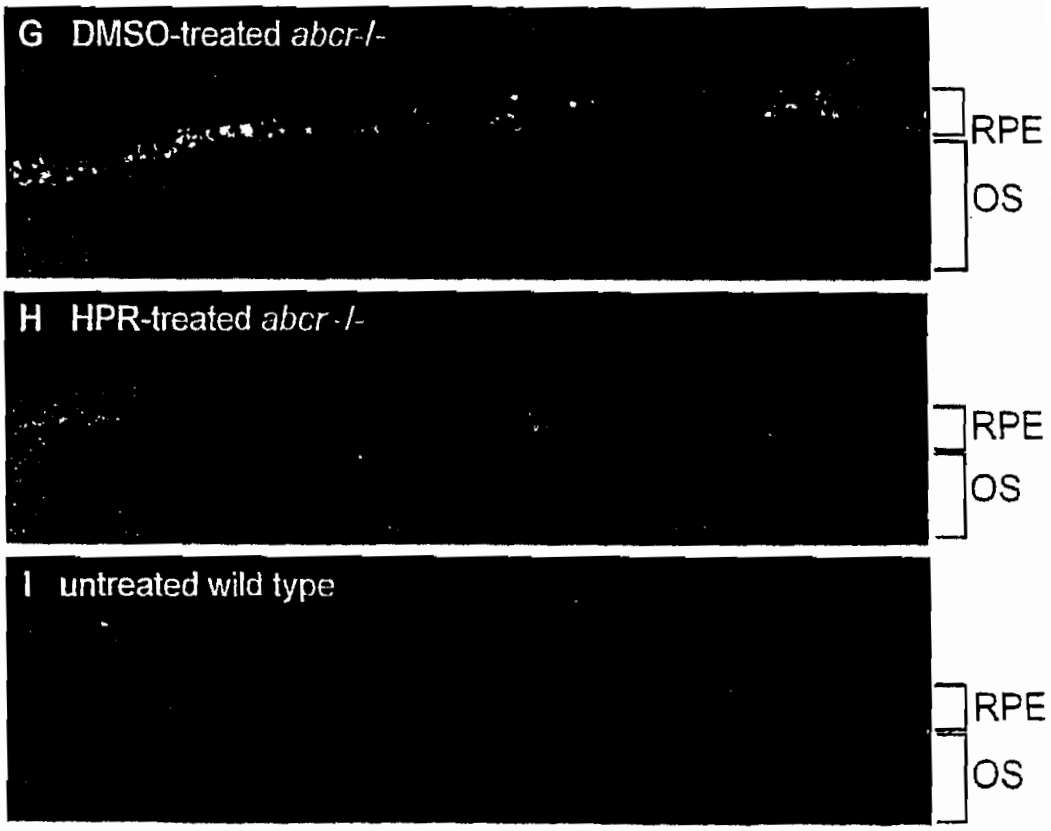

G DMSO-treated abcr-/-
H HPR-treated abcr-/-
I untreated wild type
RPE
OS
RPE
OS
RPE
OS

FIGURE 18

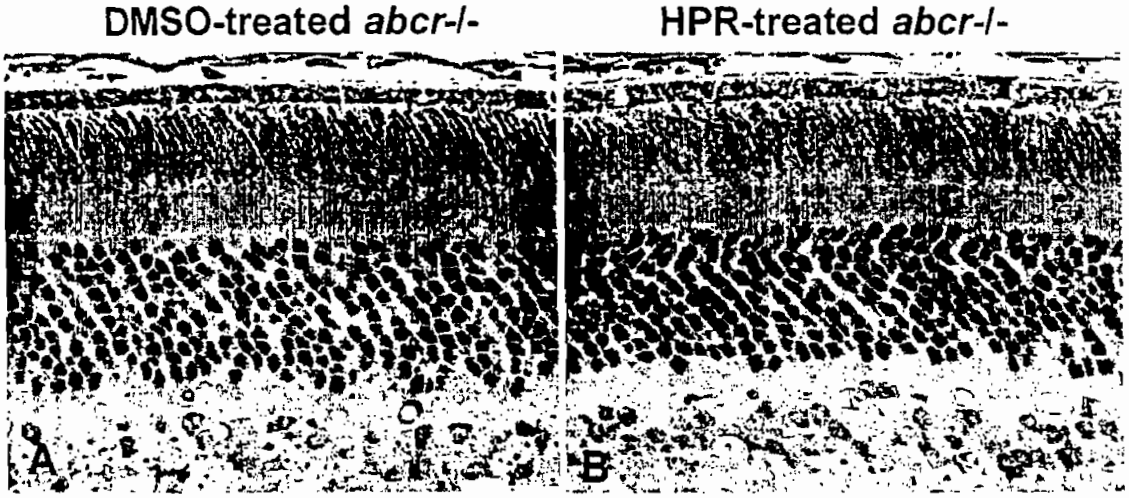


FIGURE 19

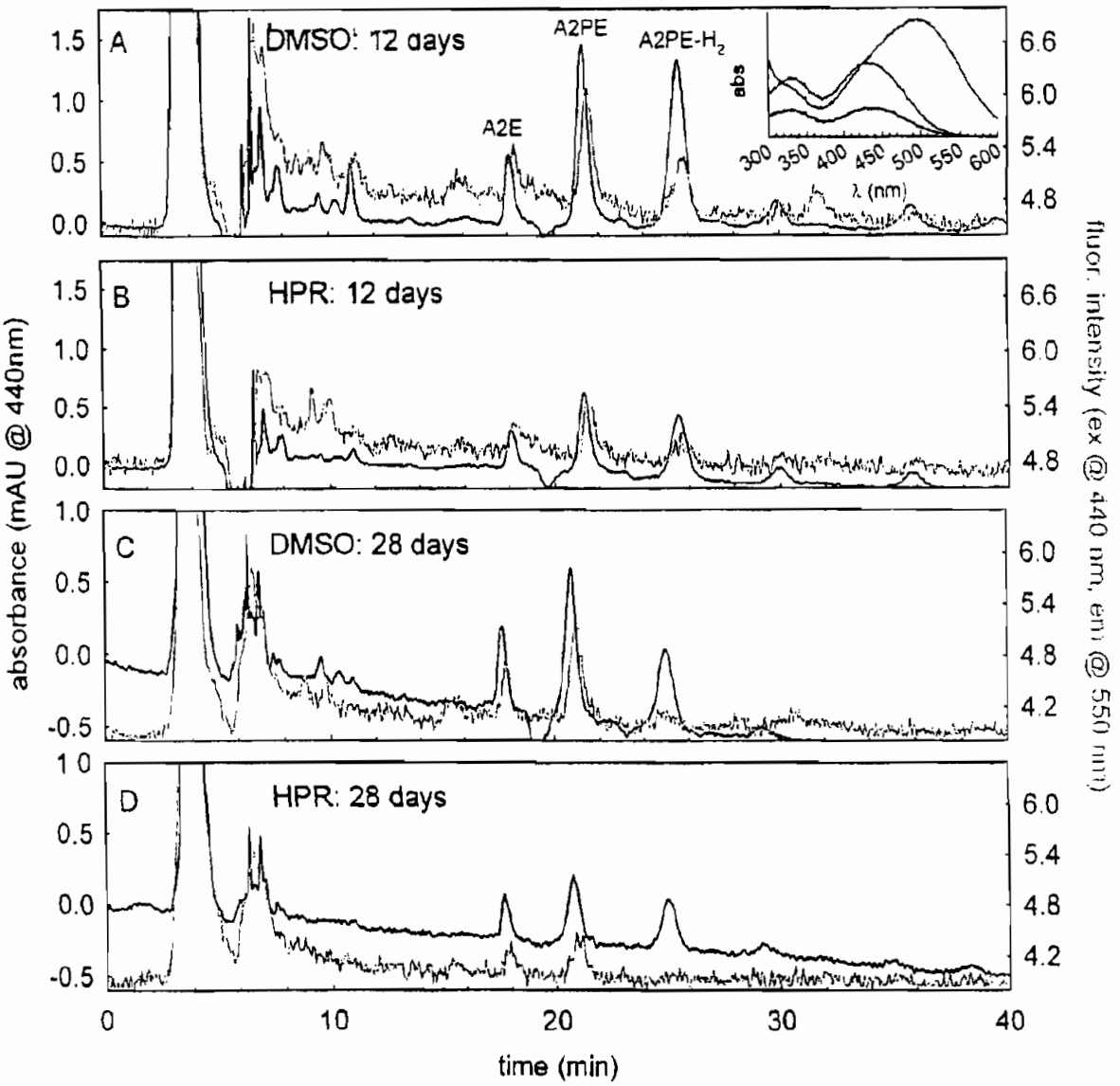
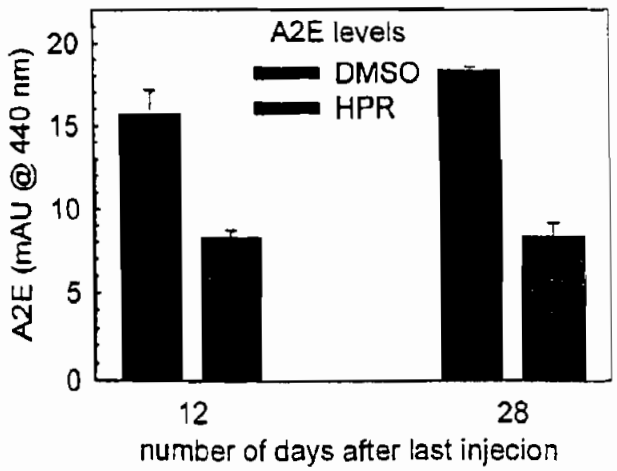

A
DMSO: 12 days
A2PE
A2PE-H2
A2E
abs
300 350 400 450 500 550 600
λ (nm)
B
HPR: 12 days
C
DMSO: 28 days
D
HPR: 28 days
absorbance (mAU @ 440nm)
fluor. intensity (ex @ 440 nm, em @ 550 nm)
time (min)

FIGURE 20


A2E levels
DMSO
HPR
A2E (mAU @ 440 nm)
number of days after last injecion