

FIG. 1



FIG.2



FIG.4

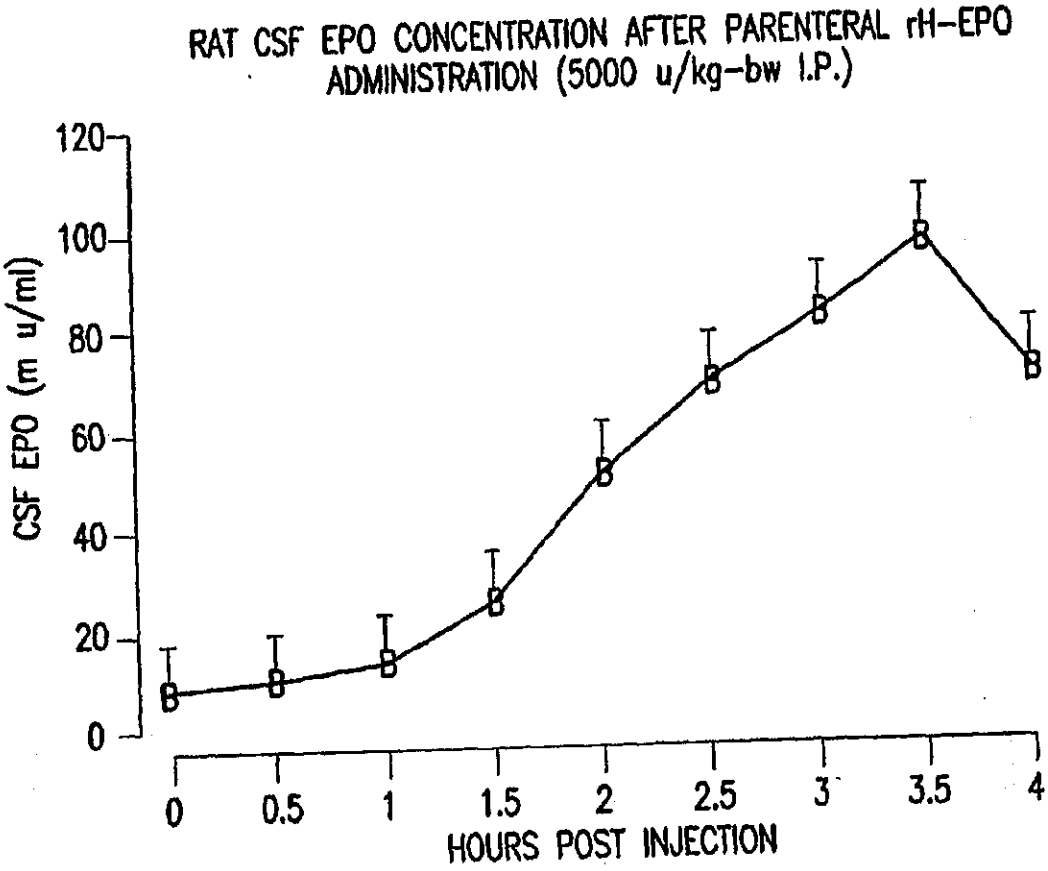

RAT CSF EPO CONCENTRATION AFTER PARENTERAL rH-EPO ADMINISTRATION (5000 u/kg-bw I.P.)
CSF EPO (m u/ml)
120
100
80
60
40
20
0
0
0.5
1
1.5
2
2.5
3
3.5
4
HOURS POST INJECTION

FIG.5

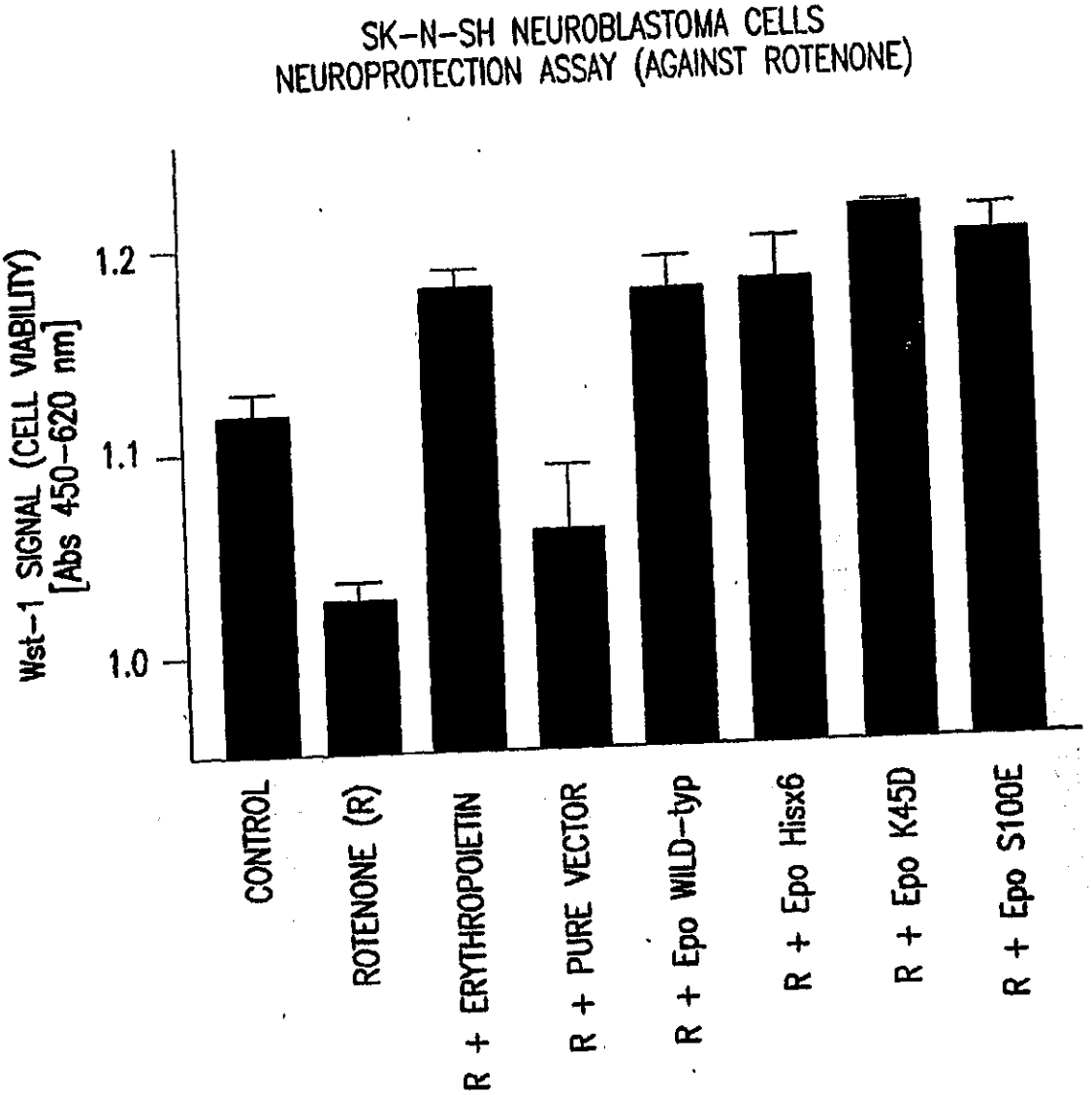

SK-N-SH NEUROBLASTOMA CELLS
NEUROPROTECTION ASSAY (AGAINST ROTENONE)
Wst-1 SIGNAL (CELL VIABILITY)
[Abs 450-620 nm]
1.2
1.1
1.0
CONTROL
ROTENONE (R)
R + ERYTHROPOIETIN
R + PURE VECTOR
R + Epo WILD-typ
R + Epo Hisx6
R + Epo K45D
R + Epo S100E

FIG.6A

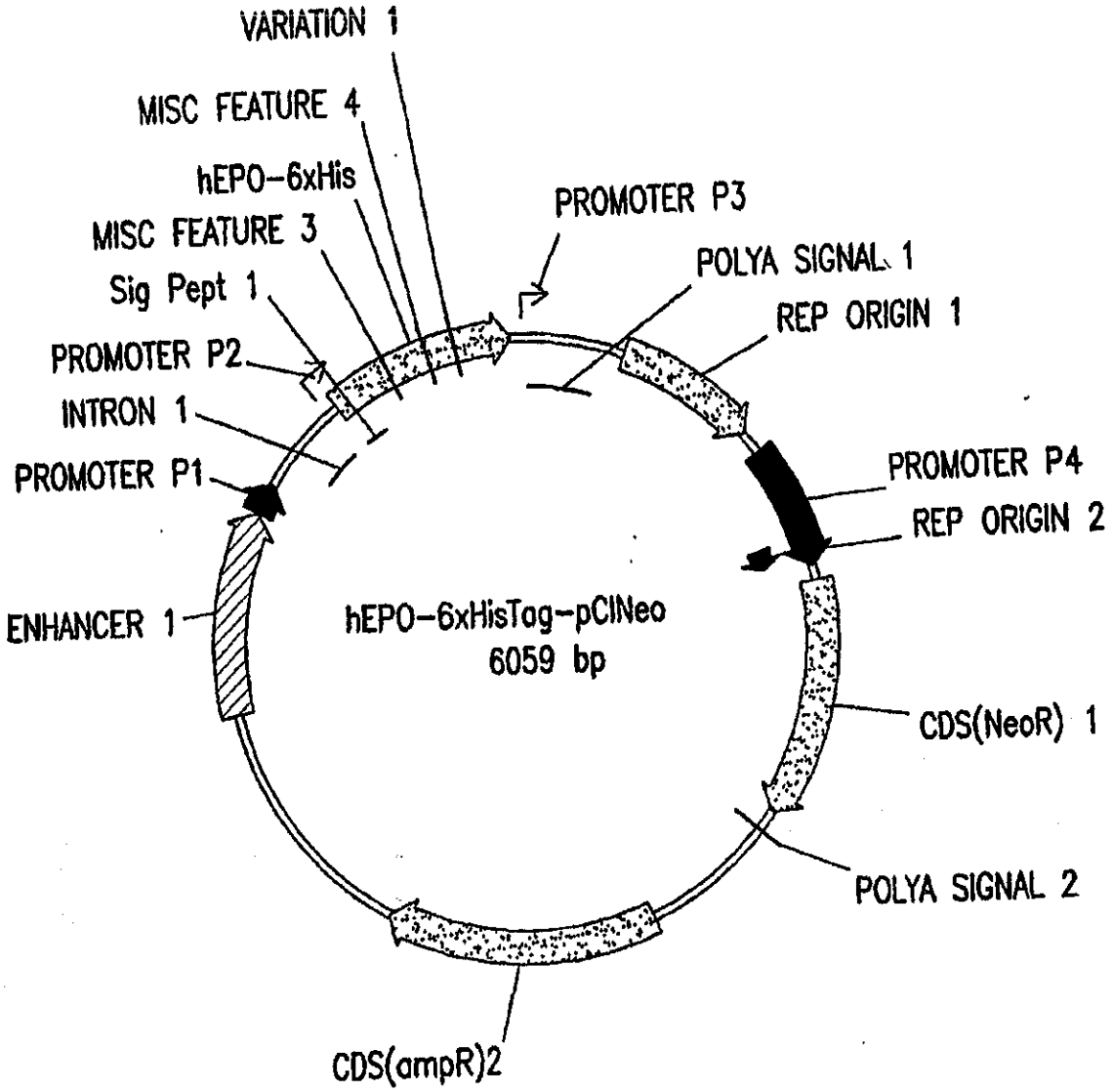

VARIATION 1
MISC FEATURE 4
hEPO-6xHis
MISC FEATURE 3
Sig Pept 1
PROMOTER P2
INTRON 1
PROMOTER P1
ENHANCER 1
PROMOTER P3
POLYA SIGNAL 1
REP ORIGIN 1
PROMOTER P4
REP ORIGIN 2
CDS(NeoR) 1
POLYA SIGNAL 2
CDS(ampR)2
hEPO-6xHisTag-pCINeo
6059 bp

FIG.6B

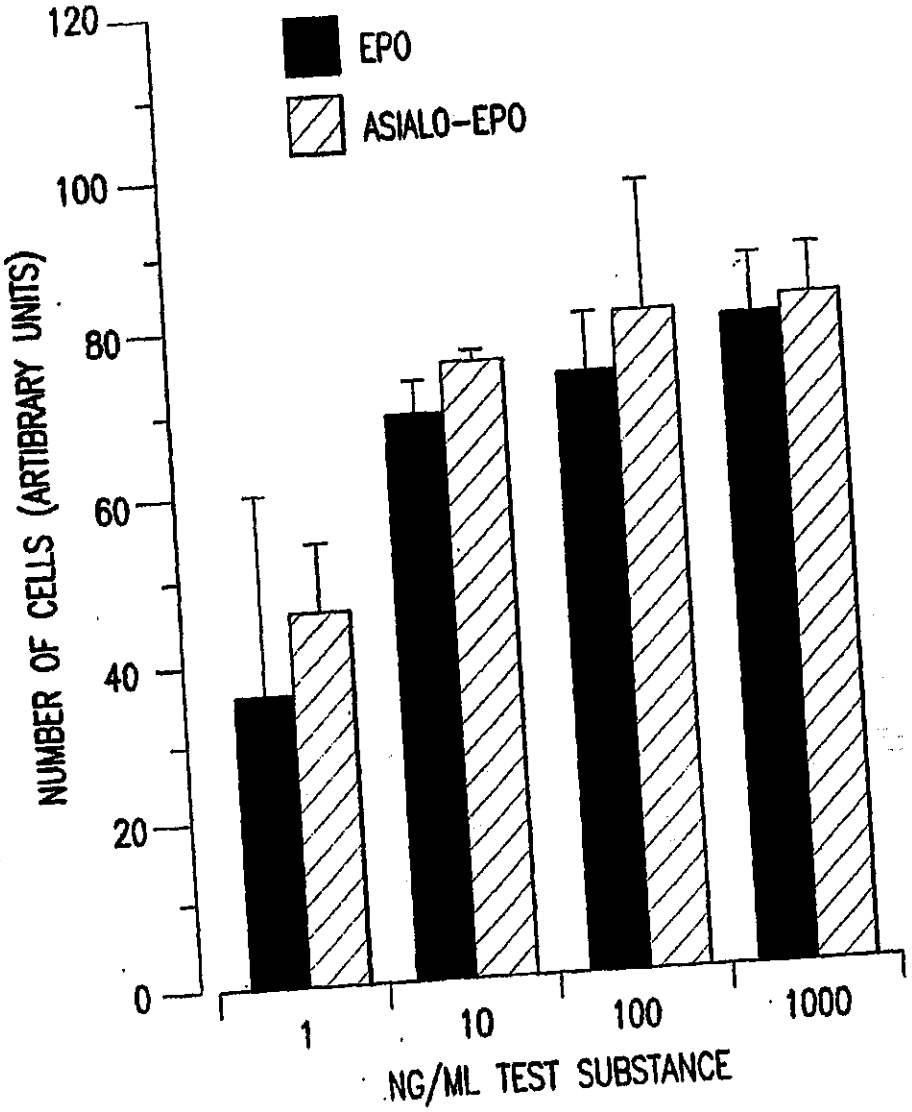

120
100
80
60
40
20
0
EPO
ASIALO-EPO
NUMBER OF CELLS (ARTIBRARY UNITS)
1
10
100
1000
NG/ML TEST SUBSTANCE

FIG.7

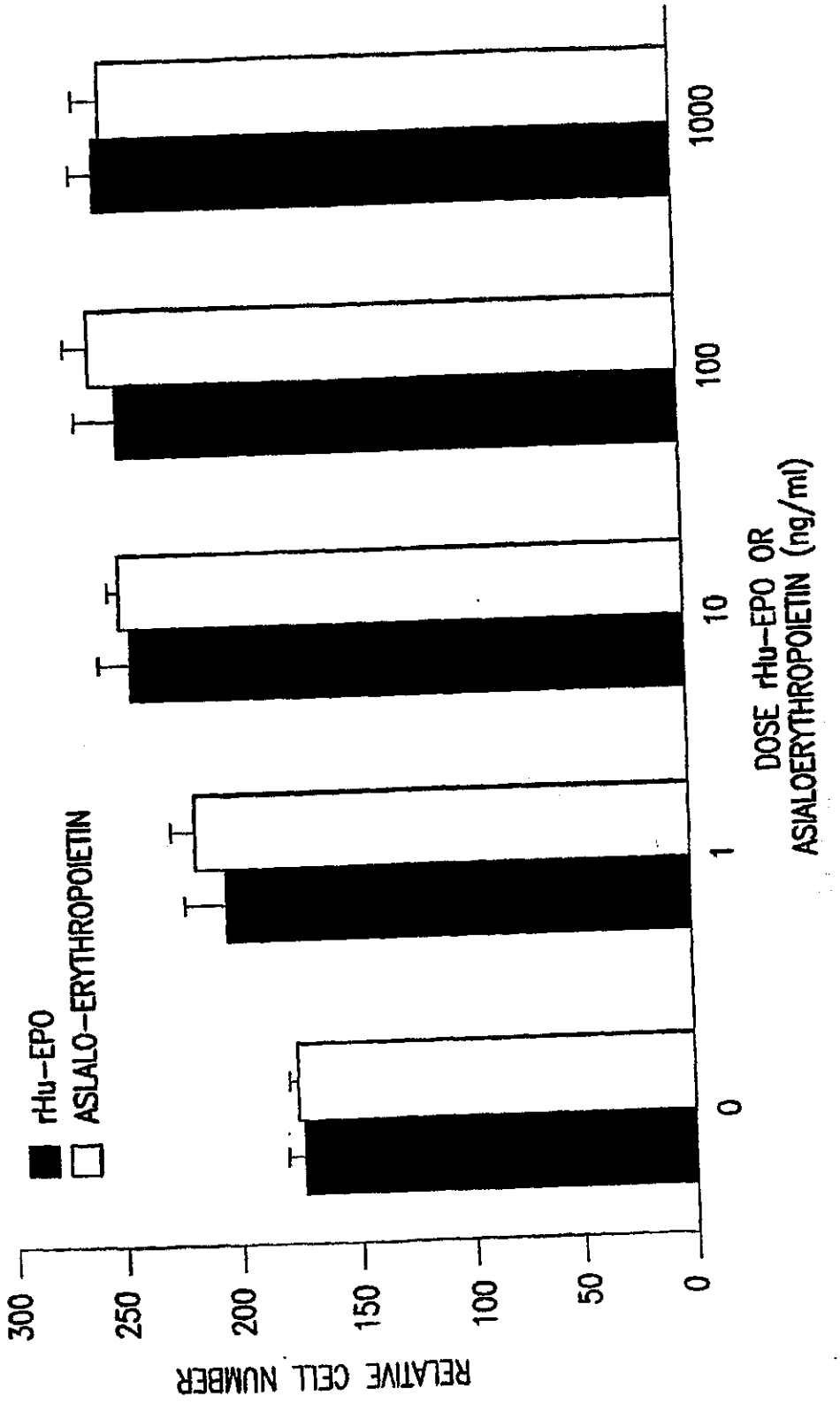

RELATIVE CELL NUMBER
300
250
200
150
100
50
0
rHu-EPO
ASIALO-ERYTHROPOIETIN
0
1
10
100
1000
DOSE rHu-EPO OR
ASIALOERYTHROPOIETIN (ng/ml)

FIG.8

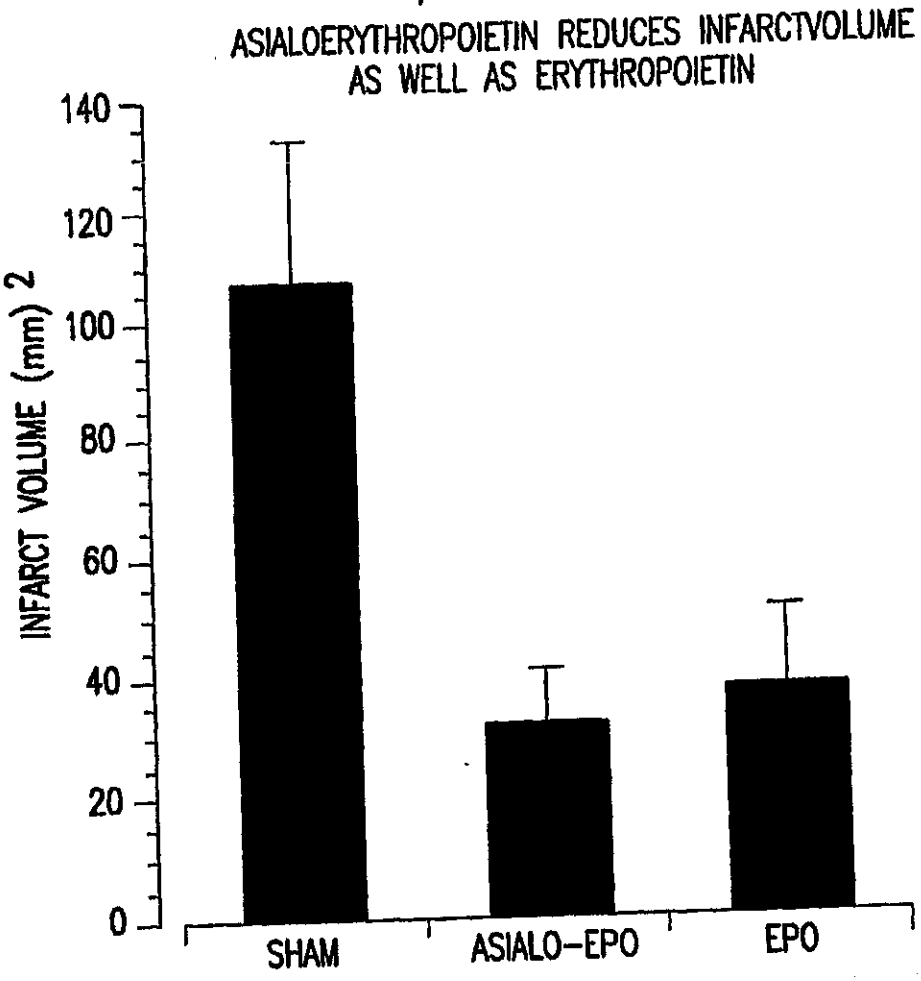
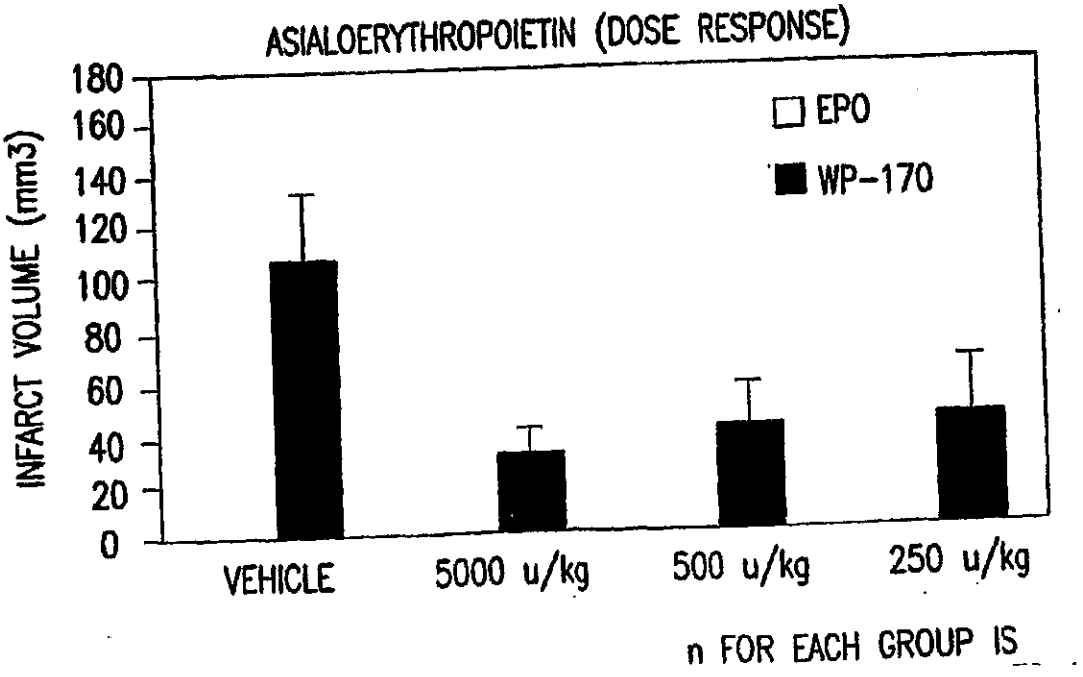

ASIALOERYTHROPOIETIN REDUCES INFARCTVOLUME
AS WELL AS ERYTHROPOIETIN
INFARCT VOLUME (mm) 2
140
120
100
80
60
40
20
0
SHAM
ASIALO-EPO
EPO

FIG.9


ASIALOERYTHROPOIETIN (DOSE RESPONSE)
INFARCT VOLUME (mm3)
180
160
140
120
100
80
60
40
20
0
EPO
WP-170
VEHICLE
5000 u/kg
500 u/kg
250 u/kg
n FOR EACH GROUP IS

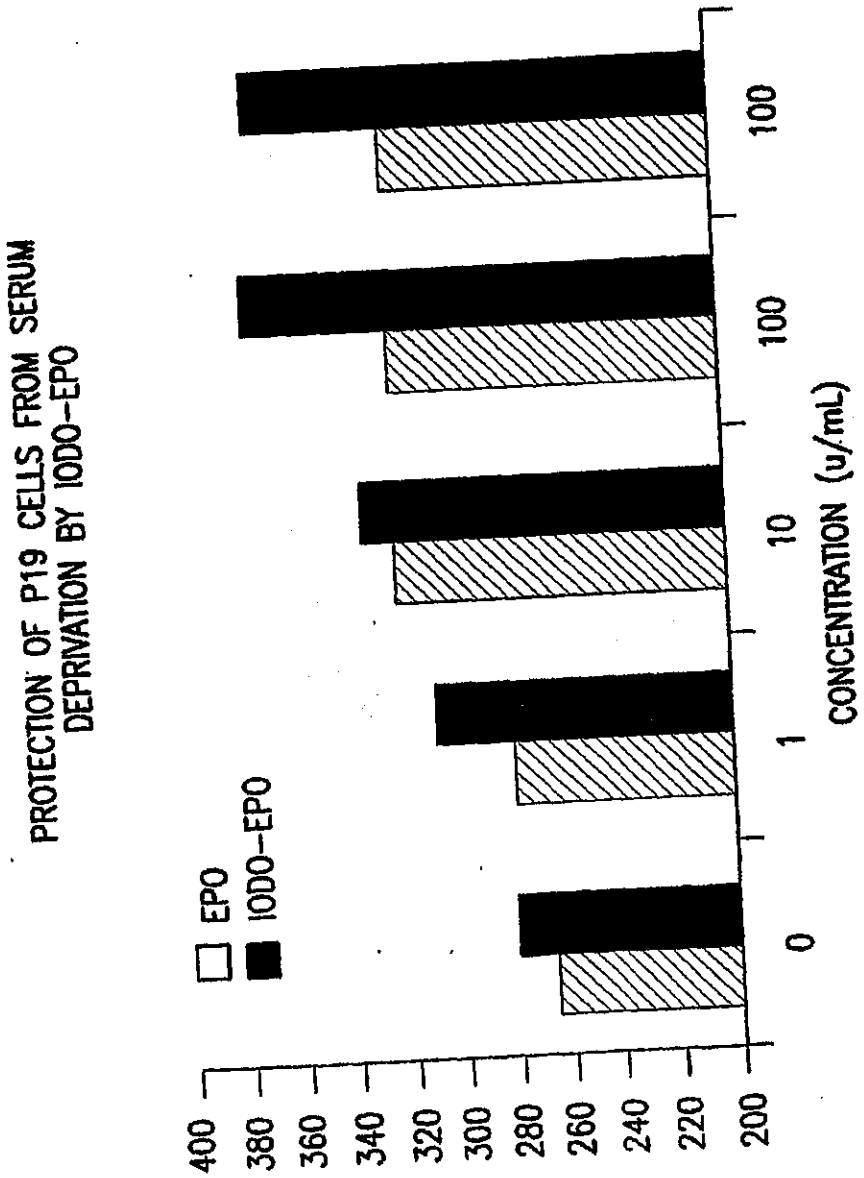

PROTECTION OF P19 CELLS FROM SERUM DEPRIVATION BY IODO-EPO
EPO
IODO-EPO
400
380
360
340
320
300
280
260
240
220
200
0
1
10
100
100
CONCENTRATION (u/mL)

FIG. 11

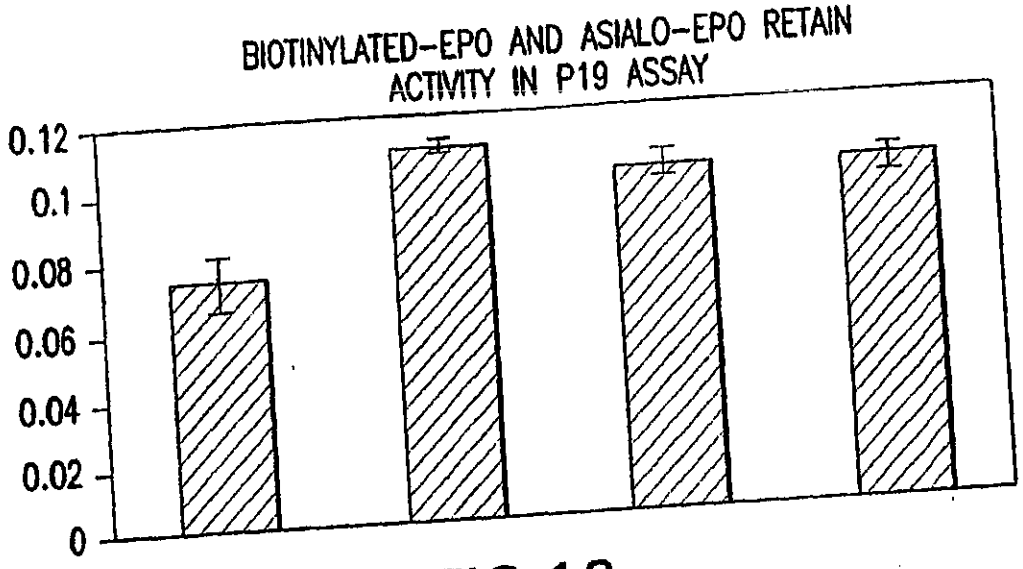
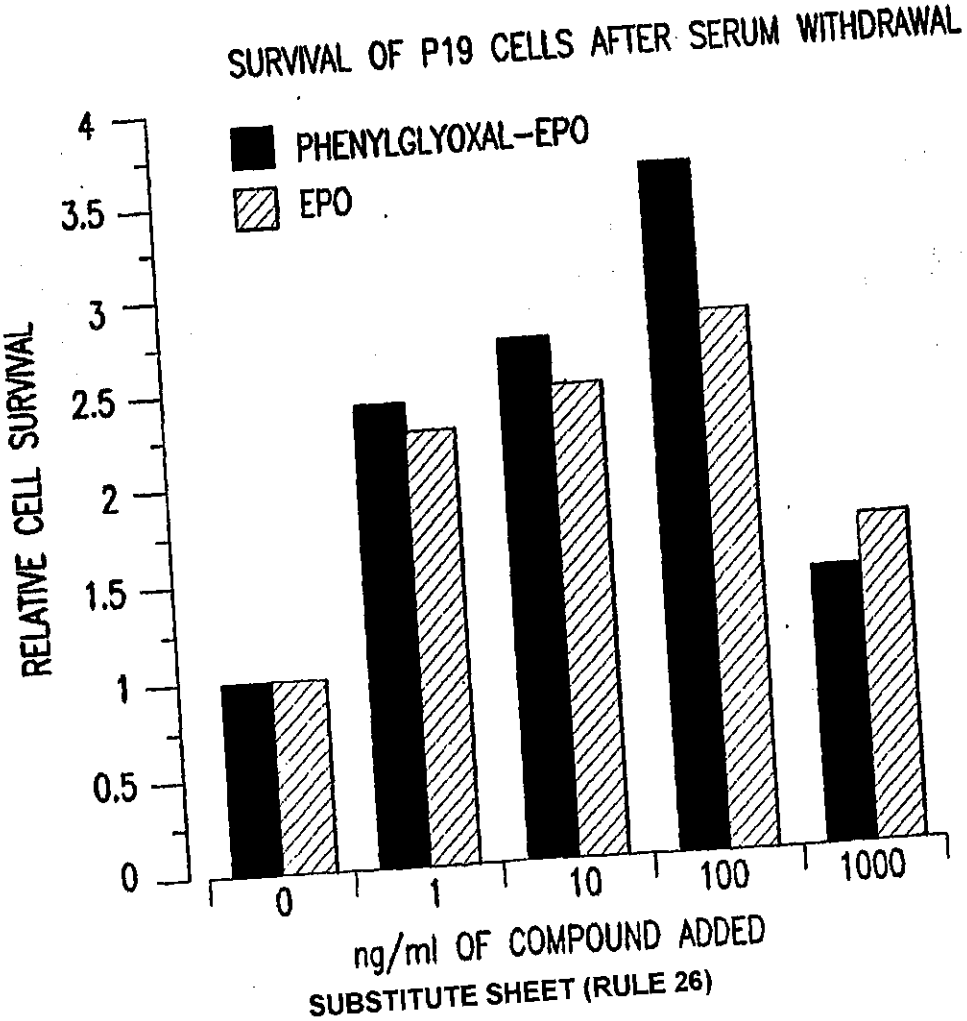

BIOTINYLATED-EPO AND ASIALO-EPO RETAIN ACTIVITY IN P19 ASSAY
0.12
0.1
0.08
0.06
0.04
0.02
0

FIG.12


SURVIVAL OF P19 CELLS AFTER SERUM WITHDRAWAL
PHENYLGLYOXAL-EPO
EPO
RELATIVE CELL SURVIVAL
4
3.5
3
2.5
2
1.5
1
0.5
0
0
1
10
100
1000
ng/ml OF COMPOUND ADDED

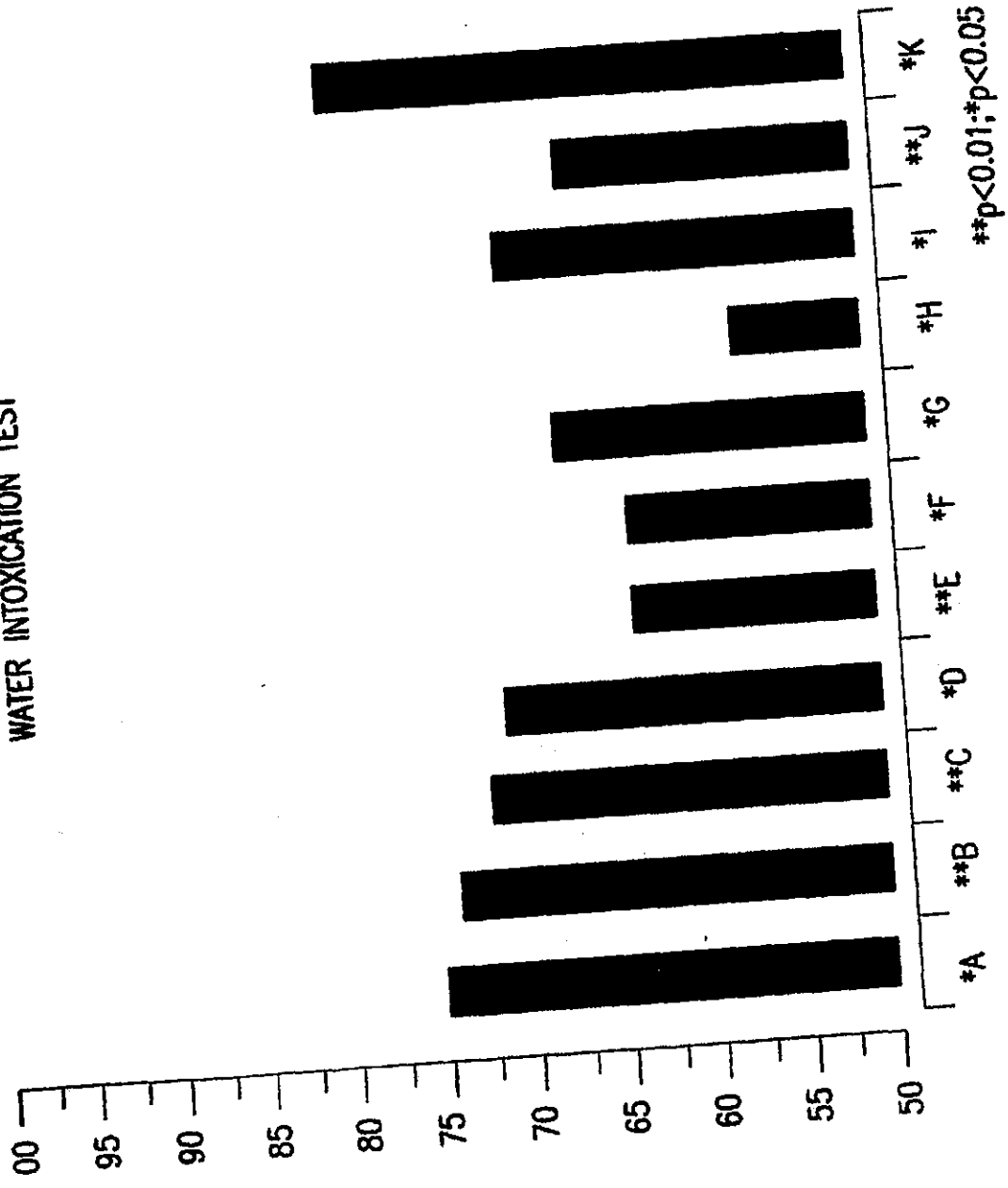

WATER INTOXICATION TEST
100
95
90
85
80
75
70
65
60
55
50
*A
**B
**C
*D
**E
*F
*G
*H
*I
**J
*K
**p<0.01;*p<0.05

FIG.14

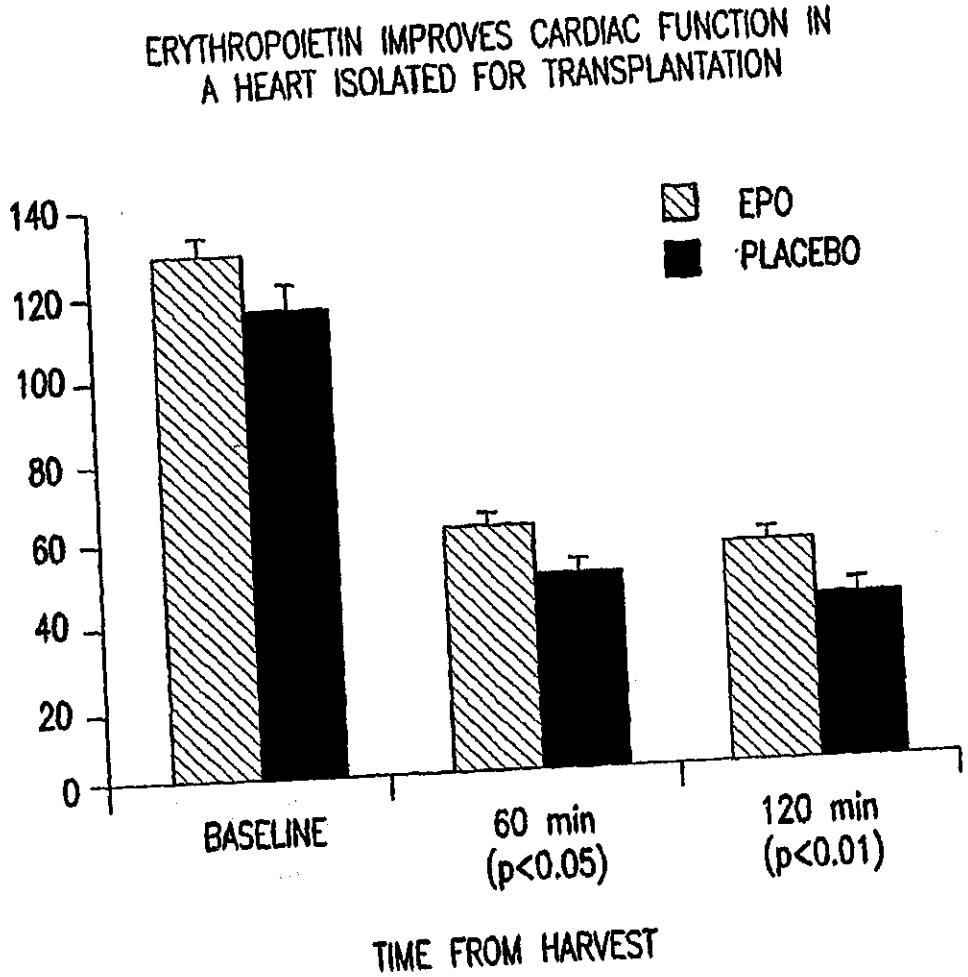

ERYTHROPOIETIN IMPROVES CARDIAC FUNCTION IN A HEART ISOLATED FOR TRANSPLANTATION
EPO
PLACEBO
140
120
100
80
60
40
20
0
BASELINE
60 min (p<0.05)
120 min (p<0.01)
TIME FROM HARVEST

FIG.15

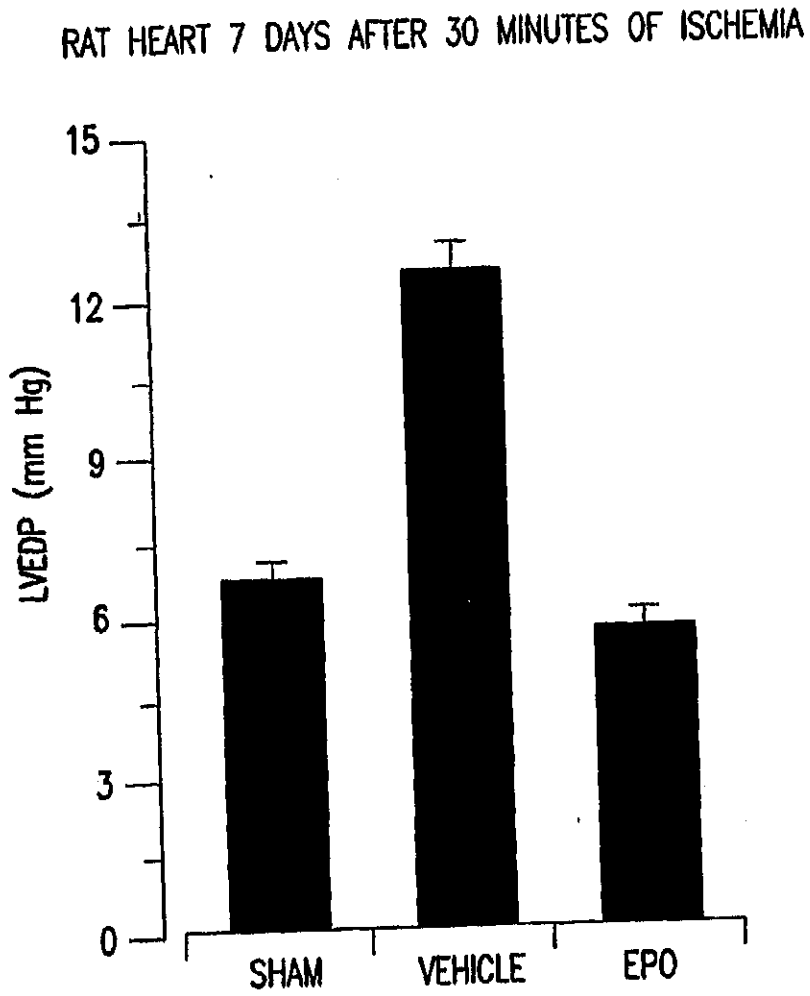

RAT HEART 7 DAYS AFTER 30 MINUTES OF ISCHEMIA
LVEDP (mm Hg)
15
12
9
6
3
0
SHAM
VEHICLE
EPO

FIG.16

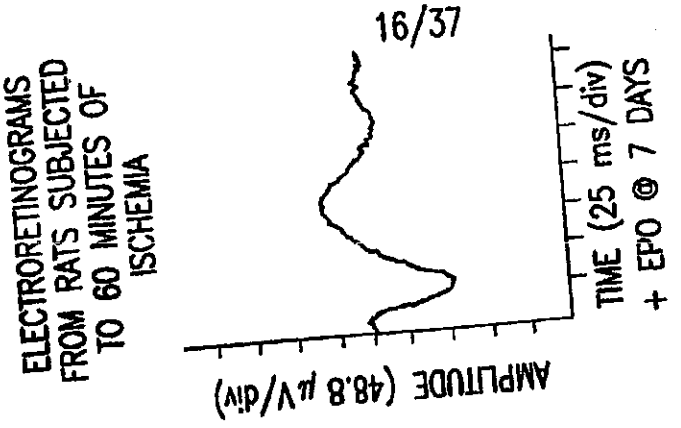


FIG.17D

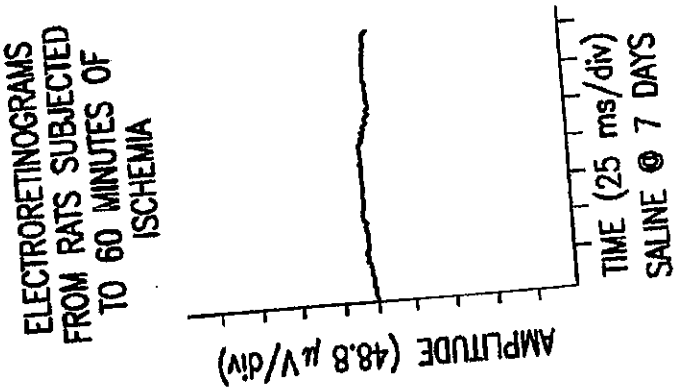


FIG.17C

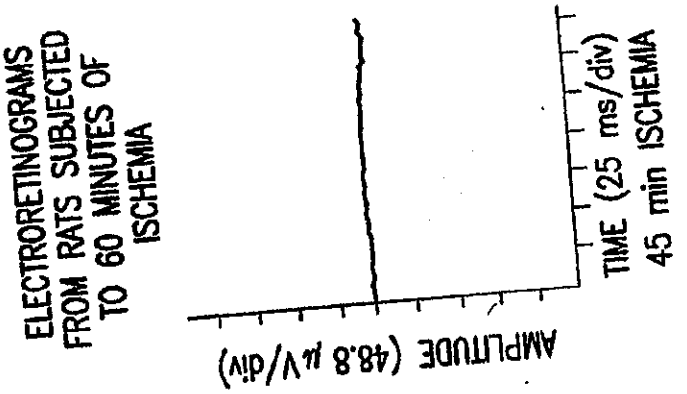


FIG.17B

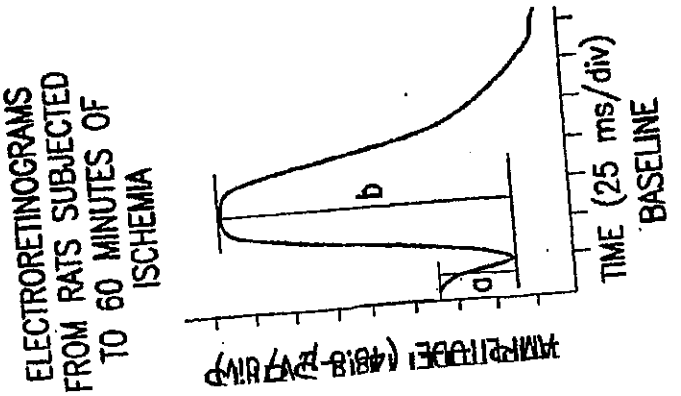


FIG.17A

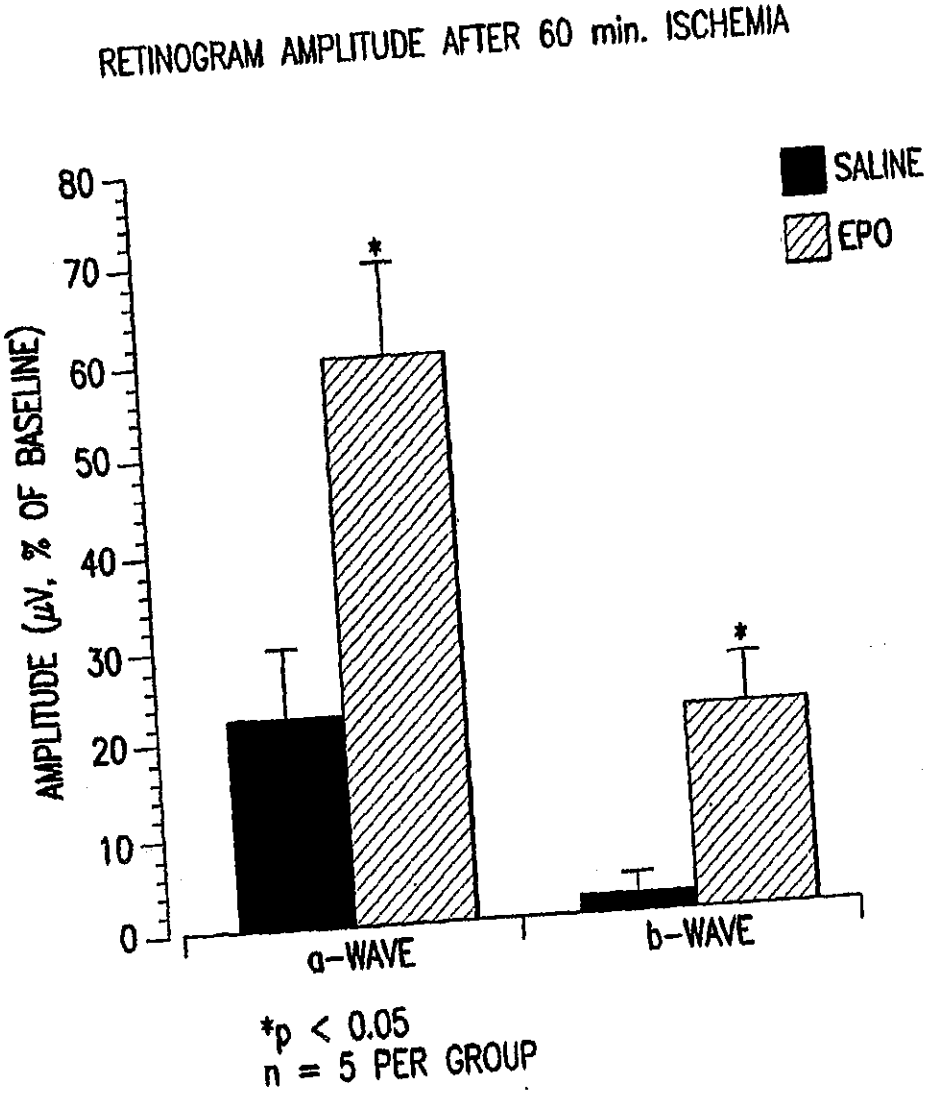

RETINOGRAM AMPLITUDE AFTER 60 min. ISCHEMIA
SALINE
EPO
AMPLITUDE (μV, % OF BASELINE)
80
70
60
50
40
30
20
10
0
*
*
a-WAVE
b-WAVE
*p < 0.05
n = 5 PER GROUP

FIG.18

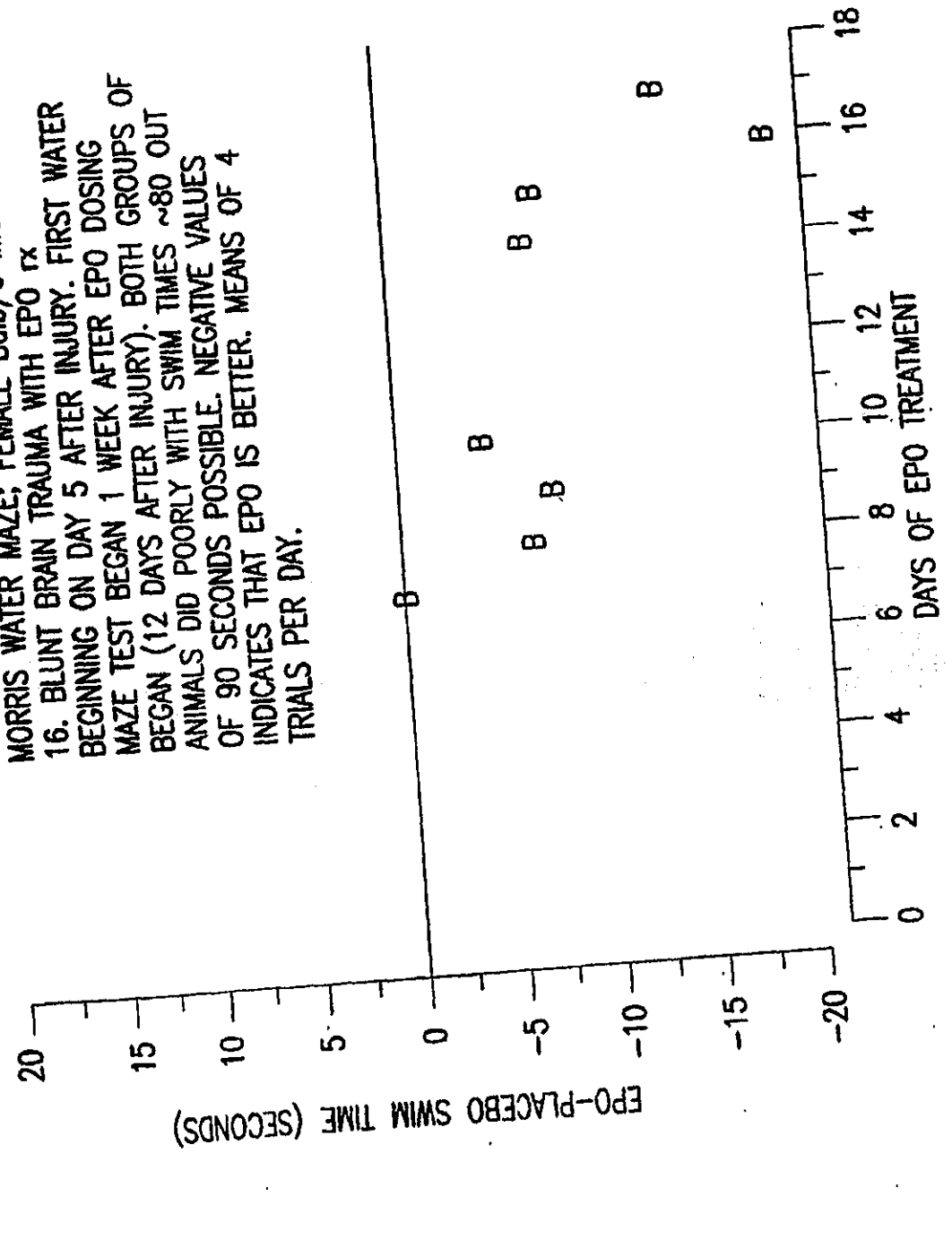

MORRIS WATER MAZE; FEMALE Balb/c MICE n=
16. BLUNT BRAIN TRAUMA WITH EPO rx
BEGINNING ON DAY 5 AFTER INJURY. FIRST WATER
MAZE TEST BEGAN 1 WEEK AFTER EPO DOSING
BEGAN (12 DAYS AFTER INJURY). BOTH GROUPS OF
ANIMALS DID POORLY WITH SWIM TIMES ~80 OUT
OF 90 SECONDS POSSIBLE. NEGATIVE VALUES
INDICATES THAT EPO IS BETTER. MEANS OF 4
TRIALS PER DAY.
EPO-PLACEBO SWIM TIME (SECONDS)
20
15
10
5
0
-5
-10
-15
-20
0
2
4
6
8
10
12
14
16
18
DAYS OF EPO TREATMENT
B

FIG.19

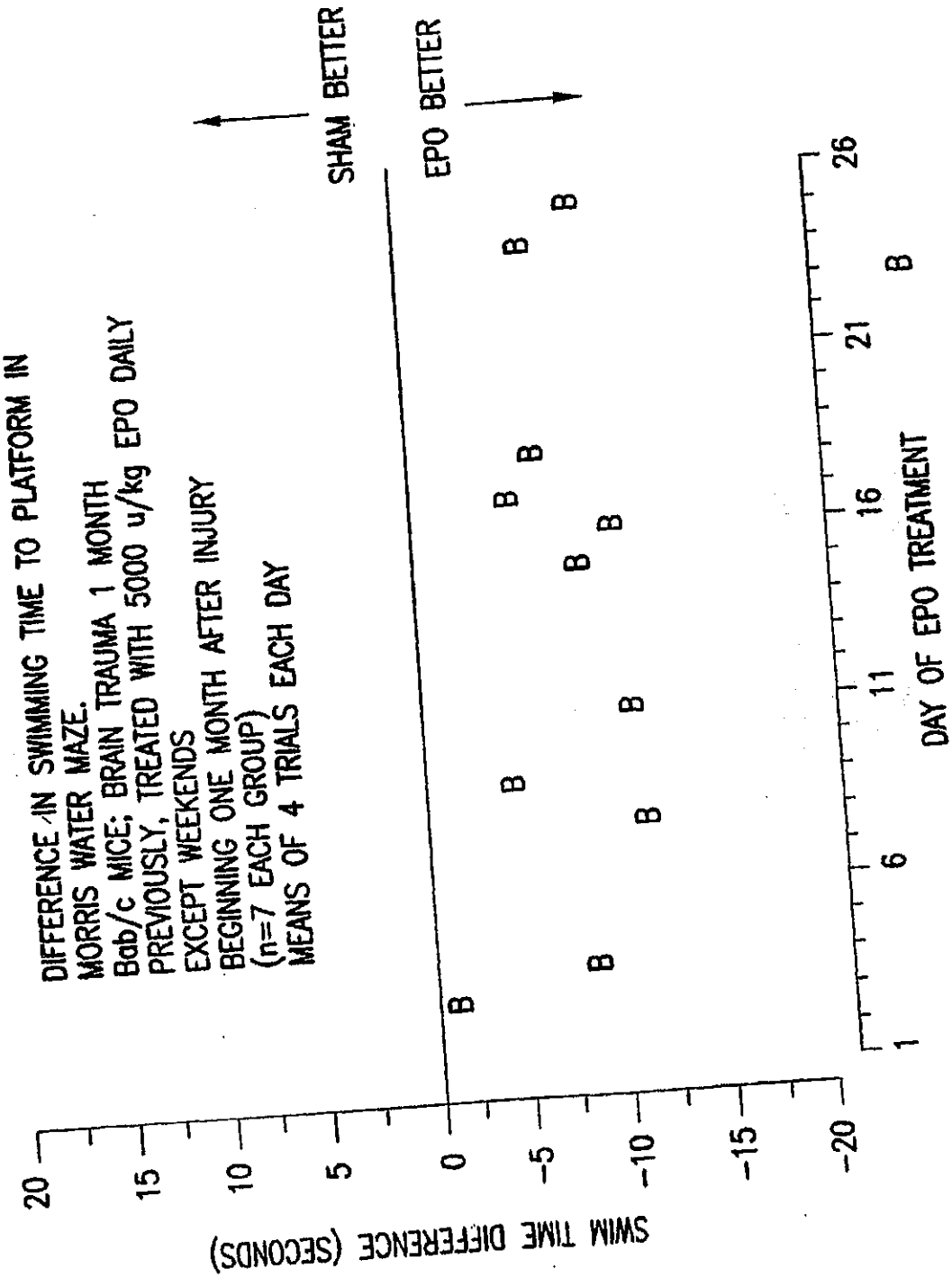

DIFFERENCE IN SWIMMING TIME TO PLATFORM IN MORRIS WATER MAZE.
Bab/c MICE; BRAIN TRAUMA 1 MONTH PREVIOUSLY, TREATED WITH 5000 u/kg EPO DAILY EXCEPT WEEKENDS
BEGINNING ONE MONTH AFTER INJURY
(n=7 EACH GROUP)
MEANS OF 4 TRIALS EACH DAY
SHAM BETTER
EPO BETTER
SWIM TIME DIFFERENCE (SECONDS)
20
15
10
5
0
-5
-10
-15
-20
1
6
11
16
21
26
DAY OF EPO TREATMENT

FIG.20

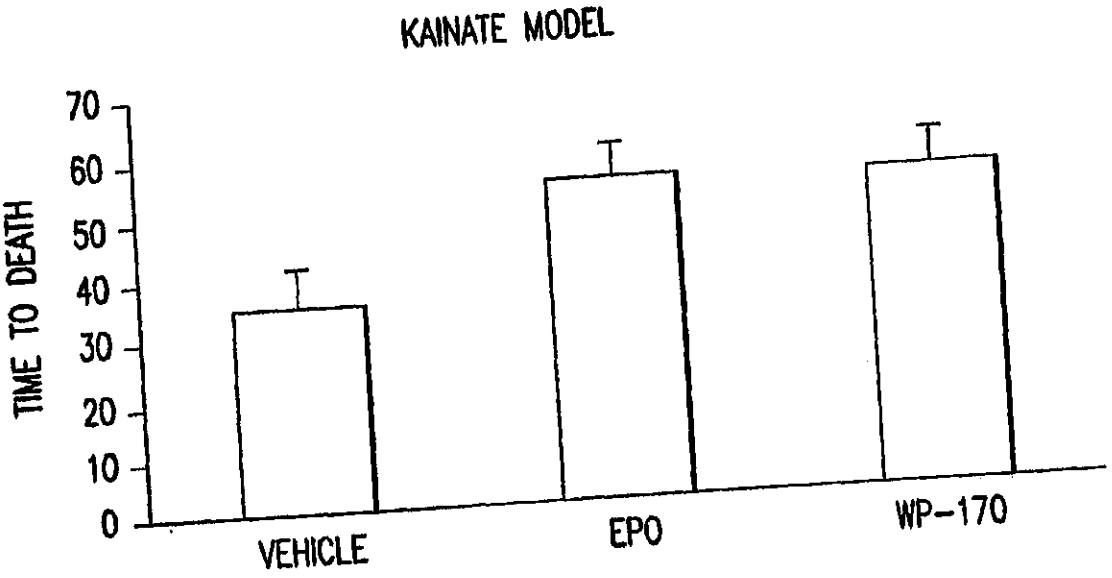

KAINATE MODEL
TIME TO DEATH
70
60
50
40
30
20
10
0
VEHICLE
EPO
WP-170

FIG.21

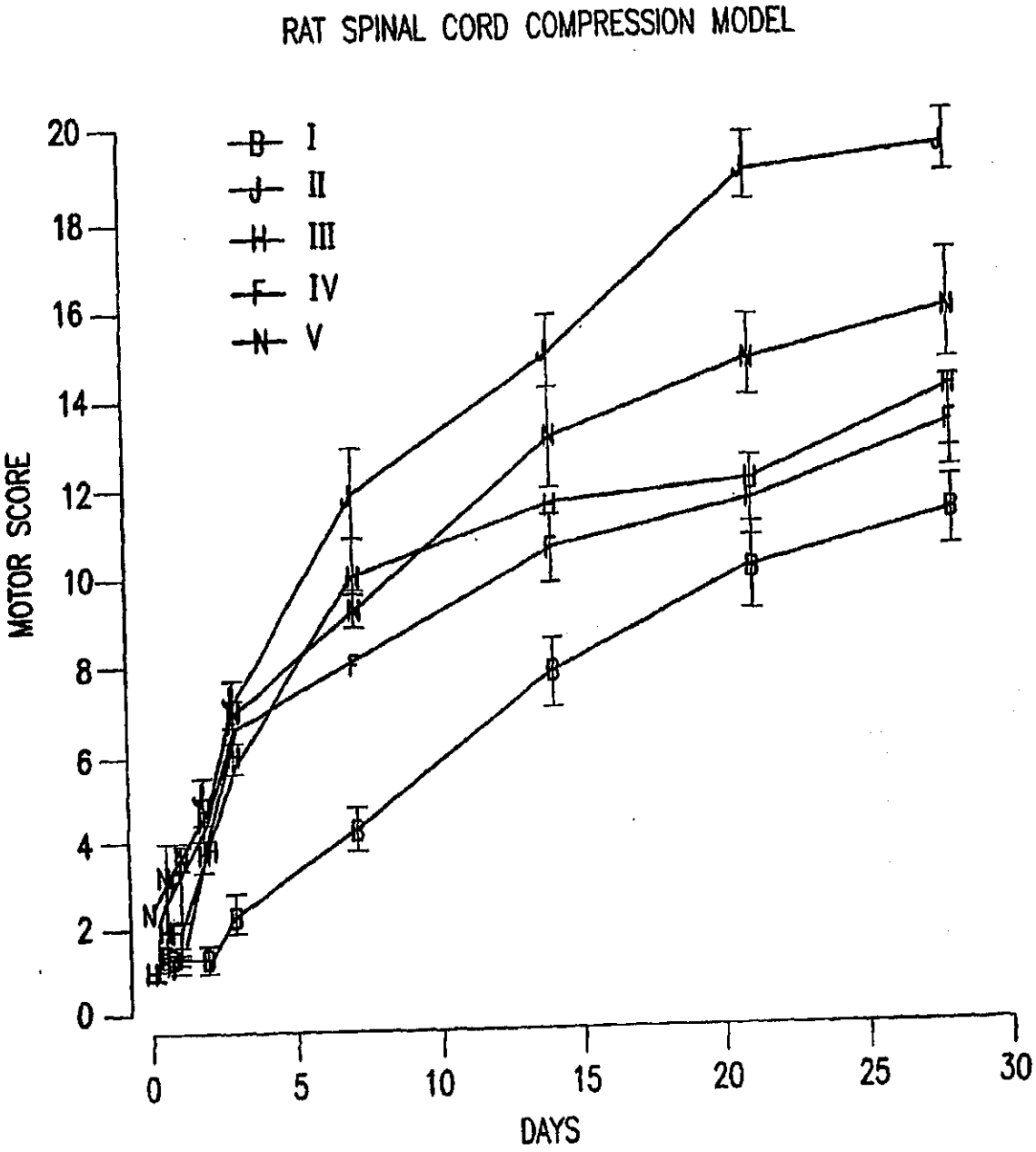

RAT SPINAL CORD COMPRESSION MODEL
MOTOR SCORE
DAYS
I
II
III
IV
V
0
2
4
6
8
10
12
14
16
18
20
0
5
10
15
20
25
30

FIG.22

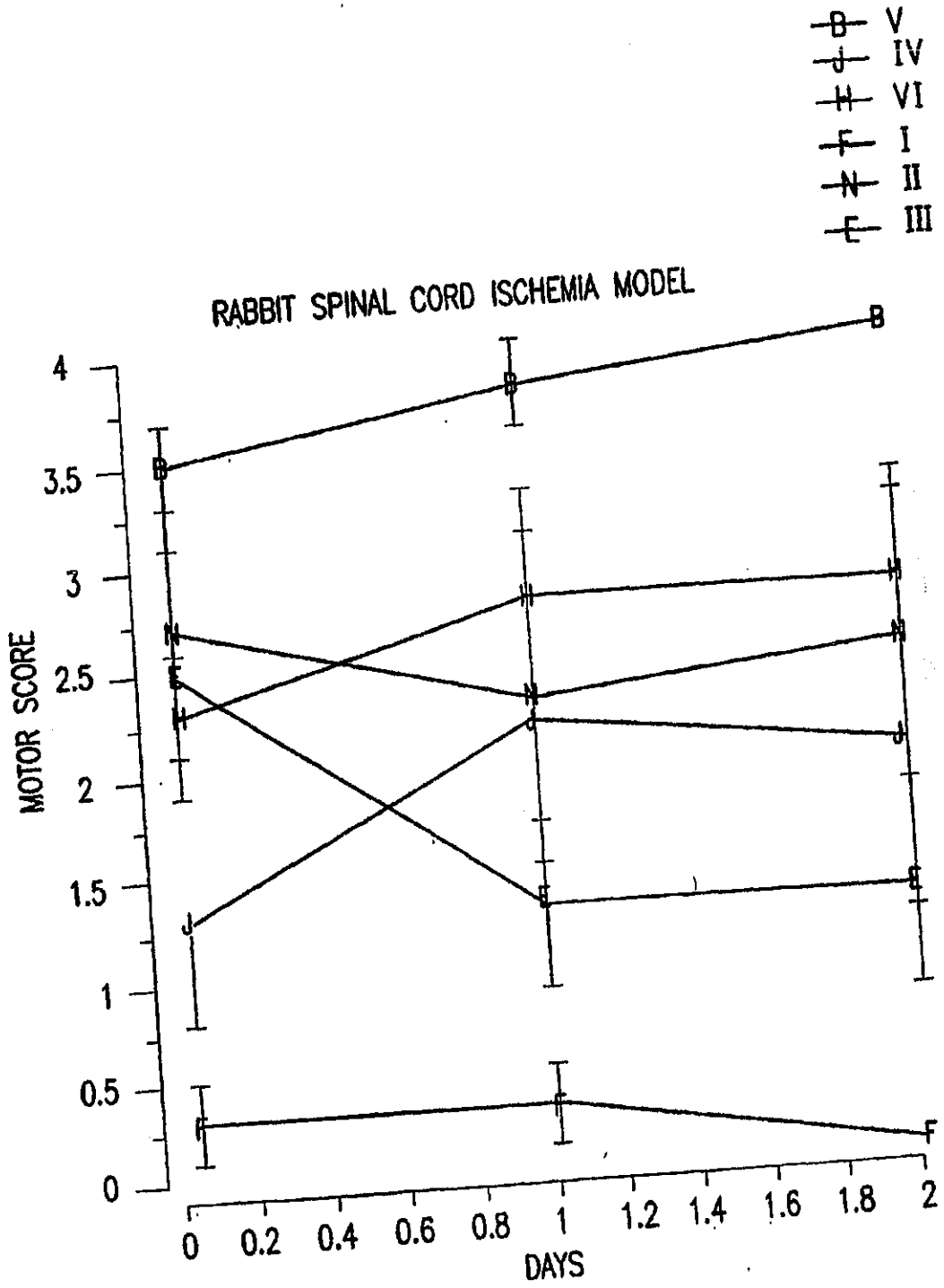

V
IV
VI
I
II
III
RABBIT SPINAL CORD ISCHEMIA MODEL
MOTOR SCORE
4
3.5
3
2.5
2
1.5
1
0.5
0
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
DAYS

FIG.23

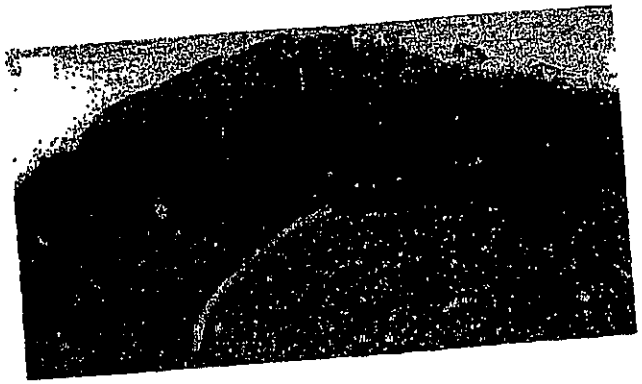


FIG.24A

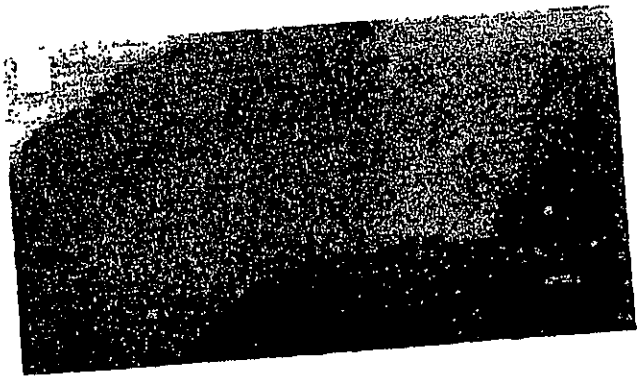


FIG.24B

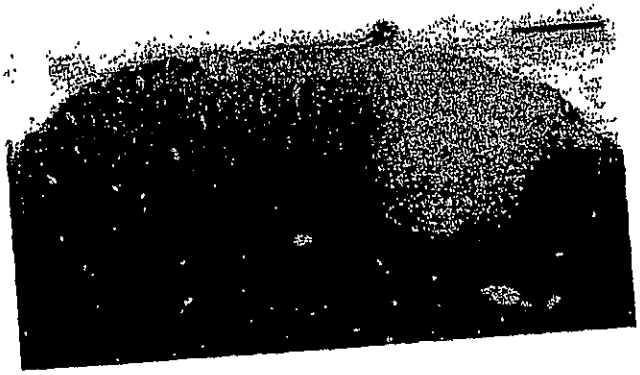


FIG.24C

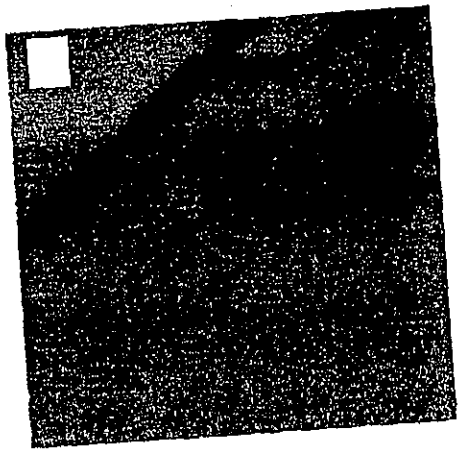


FIG.25A

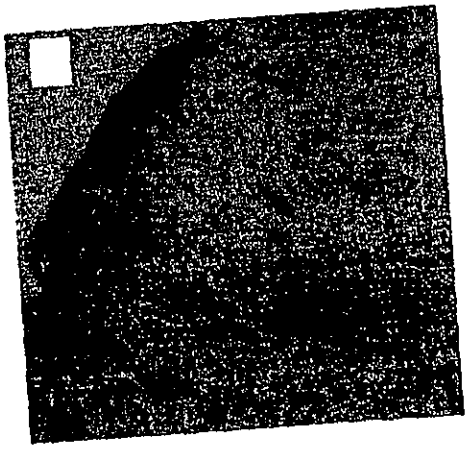
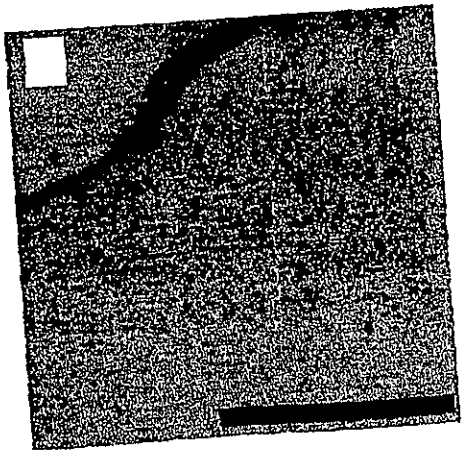


FIG.25B



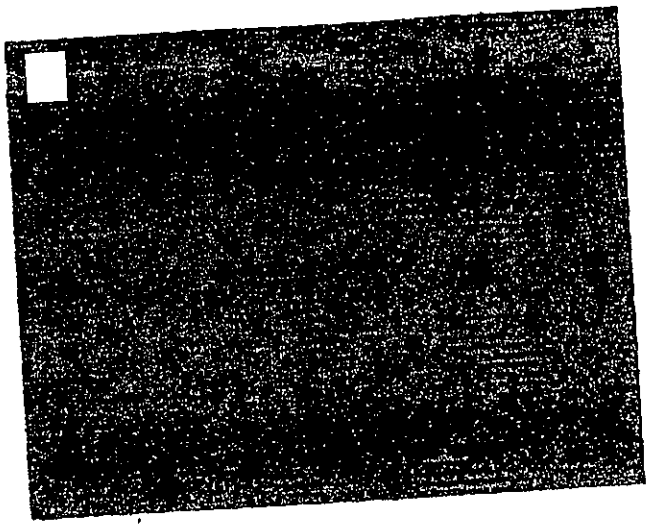


FIG.26A

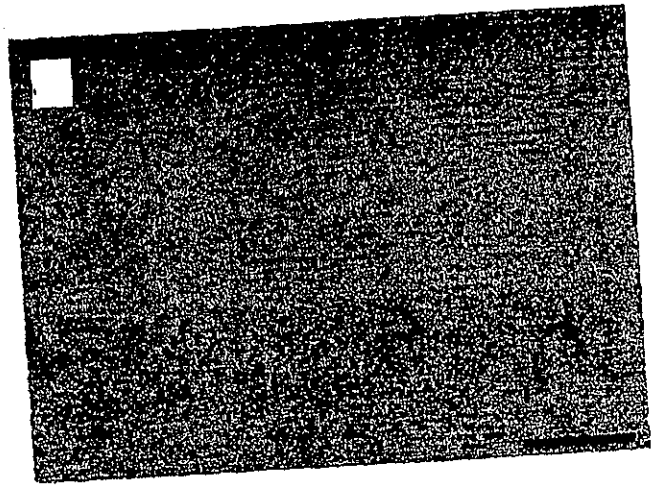


FIG.26B

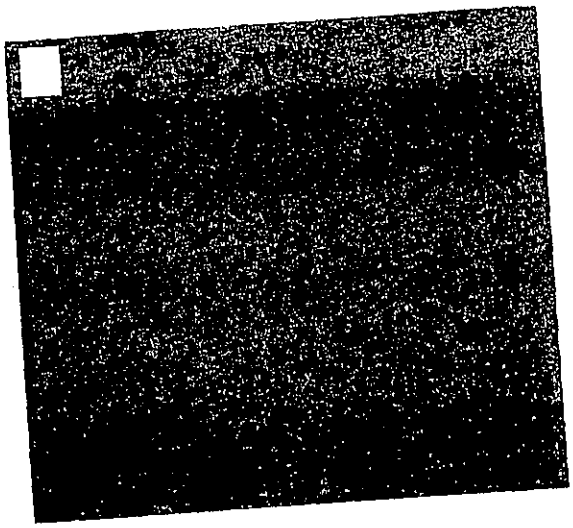


FIG.27A



FIG.27B

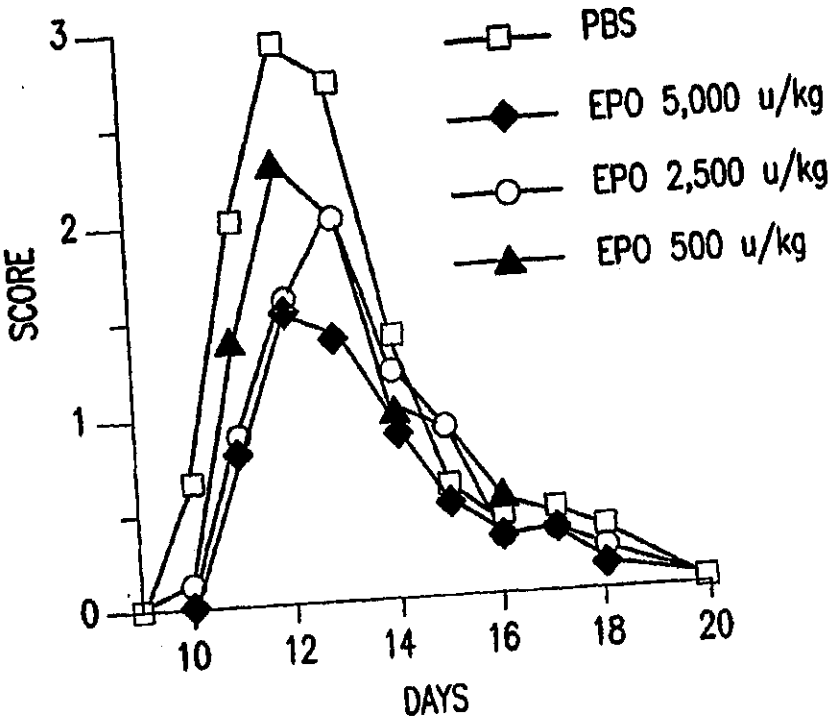

PBS
EPO 5,000 u/kg
EPO 2,500 u/kg
EPO 500 u/kg
SCORE
0
1
2
3
10
12
14
16
18
20
DAYS

FIG.28

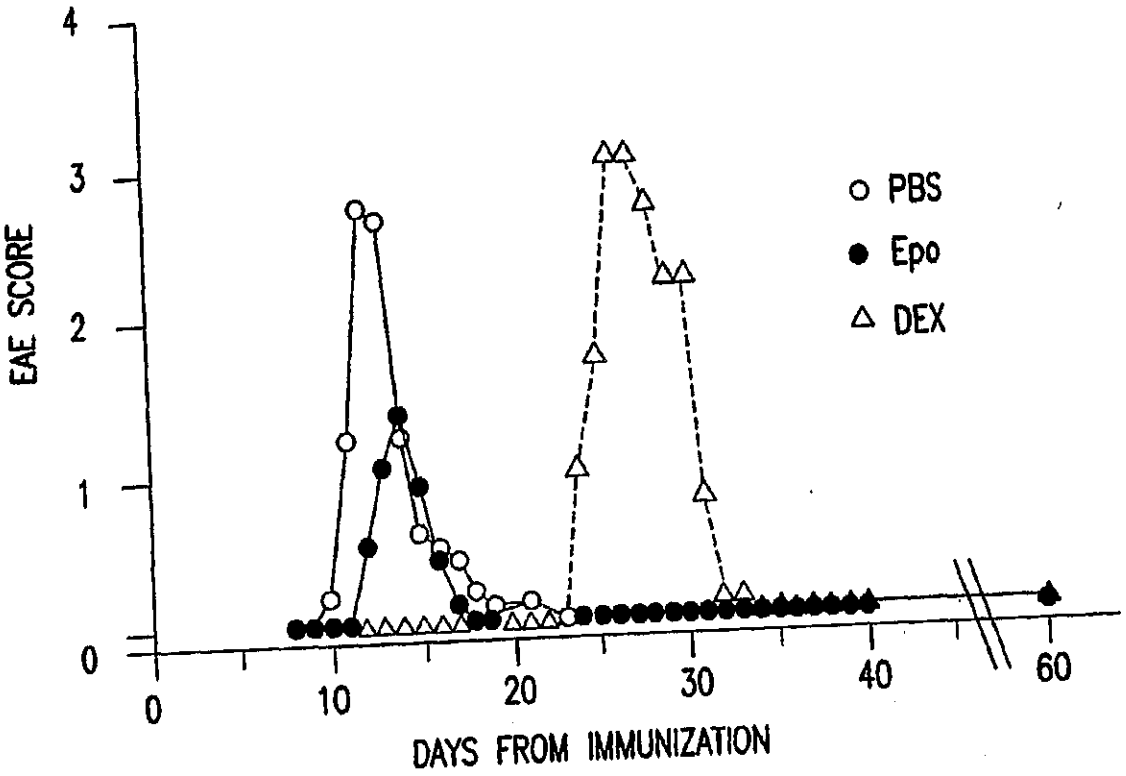

EAE SCORE
4
3
2
1
0
0
10
20
30
40
60
DAYS FROM IMMUNIZATION
PBS
Epo
DEX

FIG.29

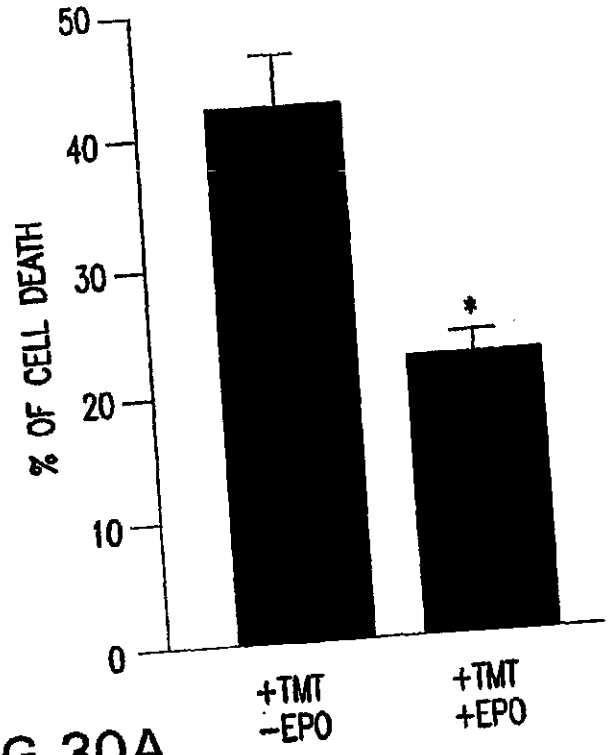


FIG.30A

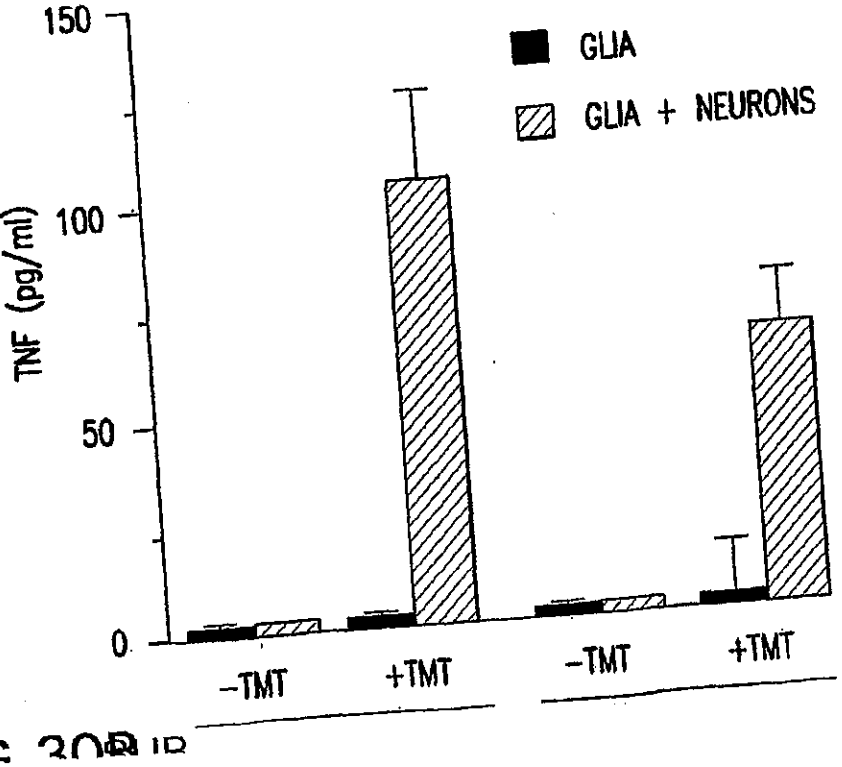


FIG. 30B

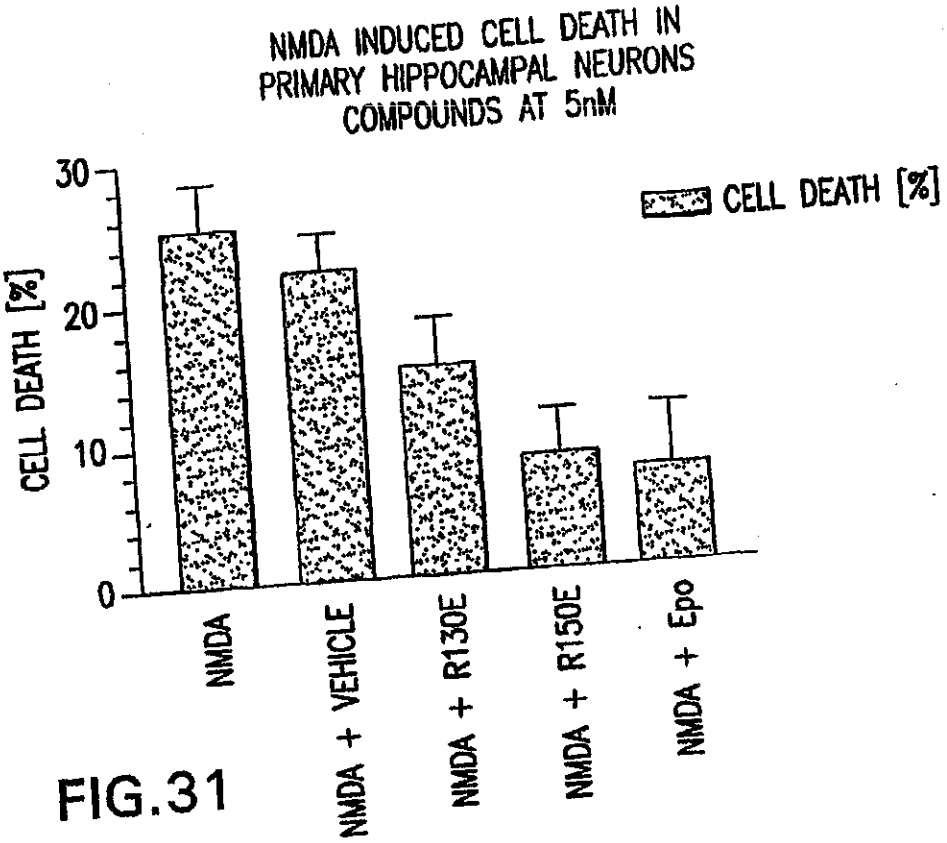
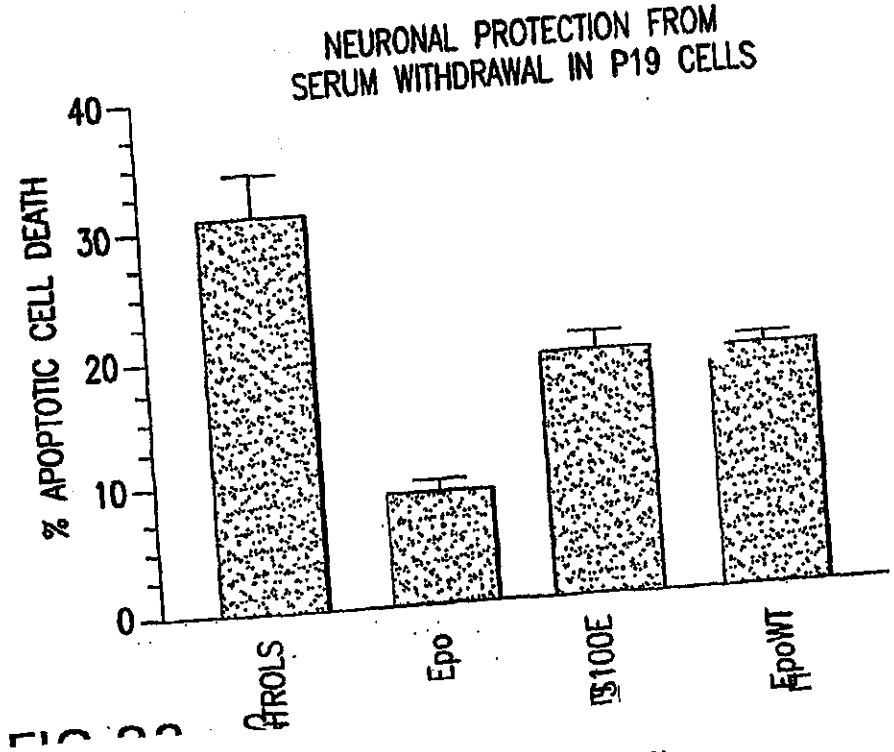

NMDA INDUCED CELL DEATH IN
PRIMARY HIPPOCAMPAL NEURONS
COMPOUNDS AT 5nM
CELL DEATH [%]
CELL DEATH [%]
30
20
10
0
NMDA
NMDA + VEHICLE
NMDA + R130E
NMDA + R150E
NMDA + Epo

FIG.31


NEURONAL PROTECTION FROM
SERUM WITHDRAWAL IN P19 CELLS
% APOPTOTIC CELL DEATH
40
30
20
10
0
CTROLS
Epo
S100E
EpoWT

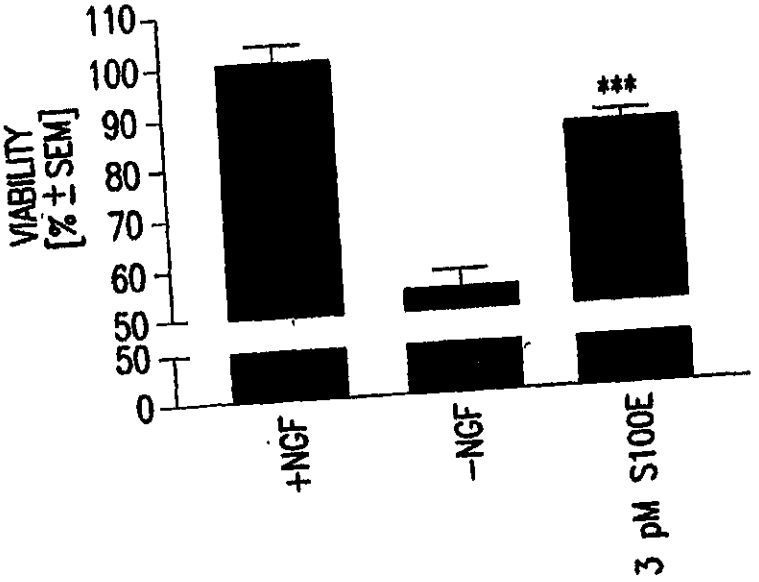


FIG.33A

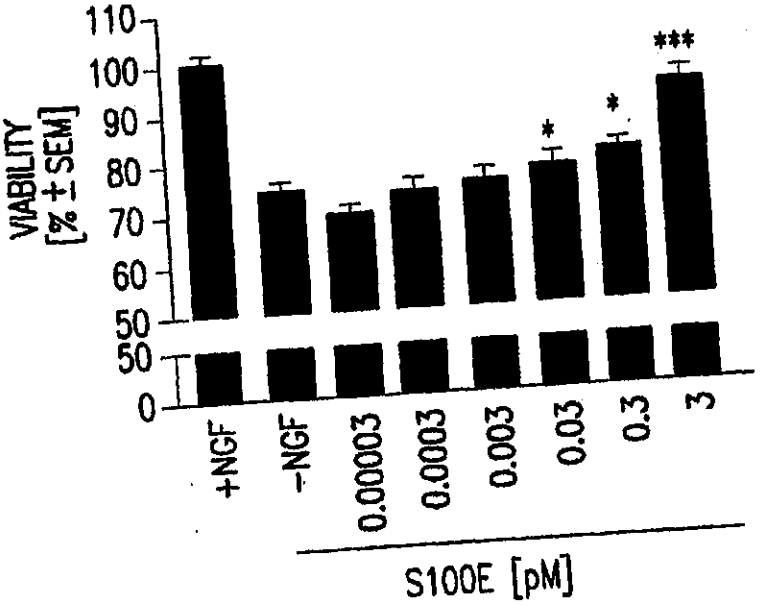


FIG.33B

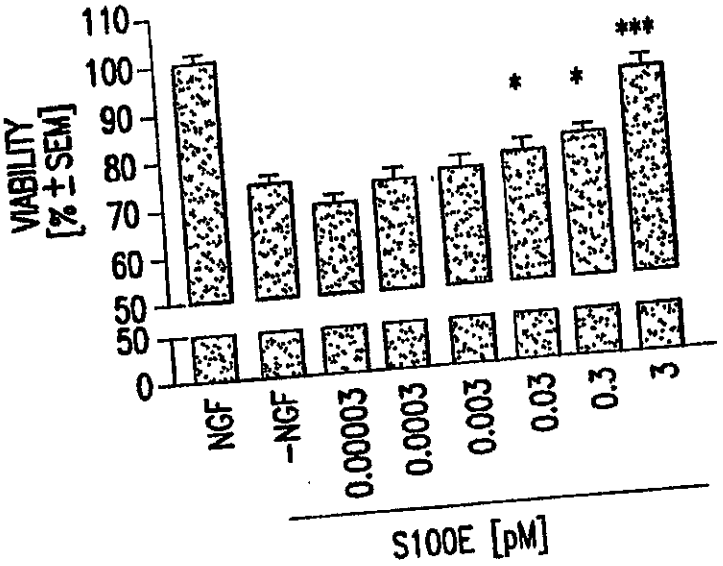


FIG.34A

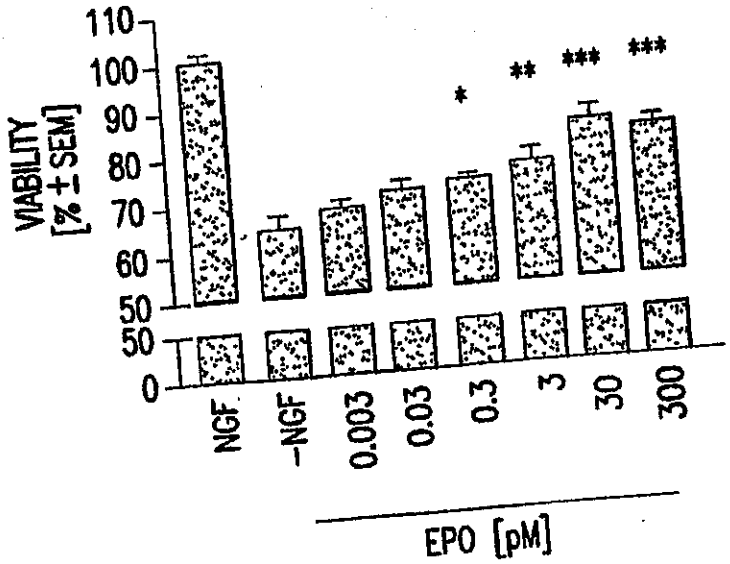


FIG.34B

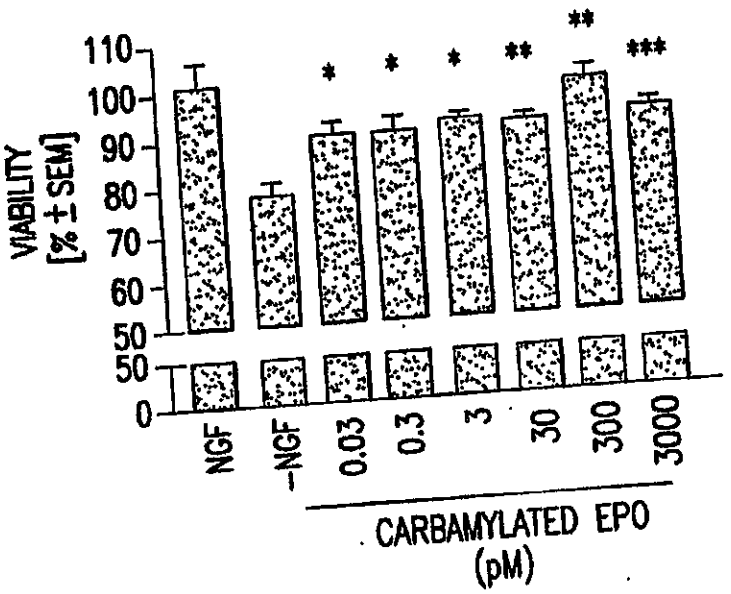

VIABILITY
[% ± SEM]
110
100
90
80
70
60
50
50
0
NGF
-NGF
0.03
0.3
3
30
300
3000
CARBAMYLATED EPO
(pM)
*
*
*
**
**
***

FIG.34C

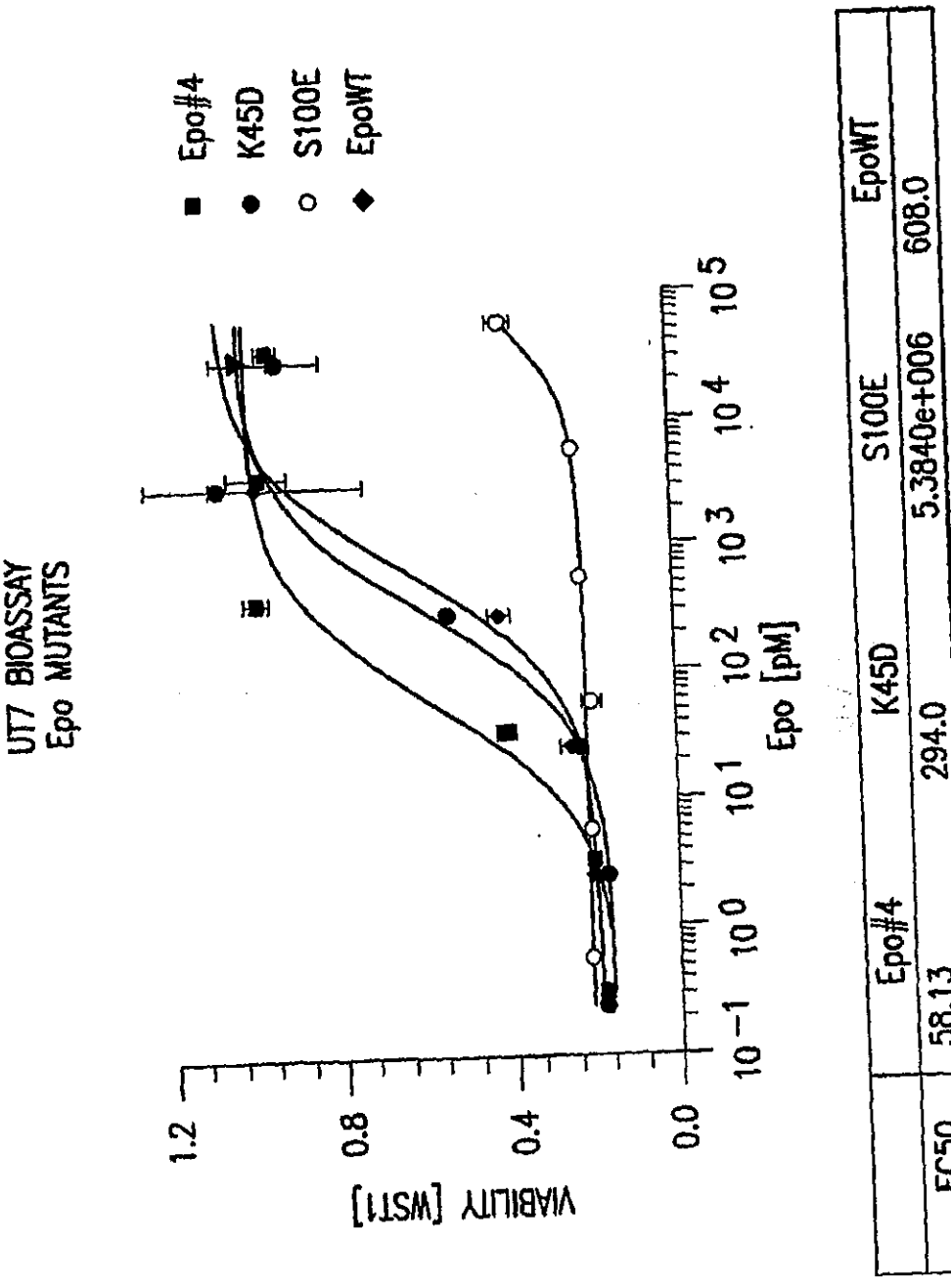
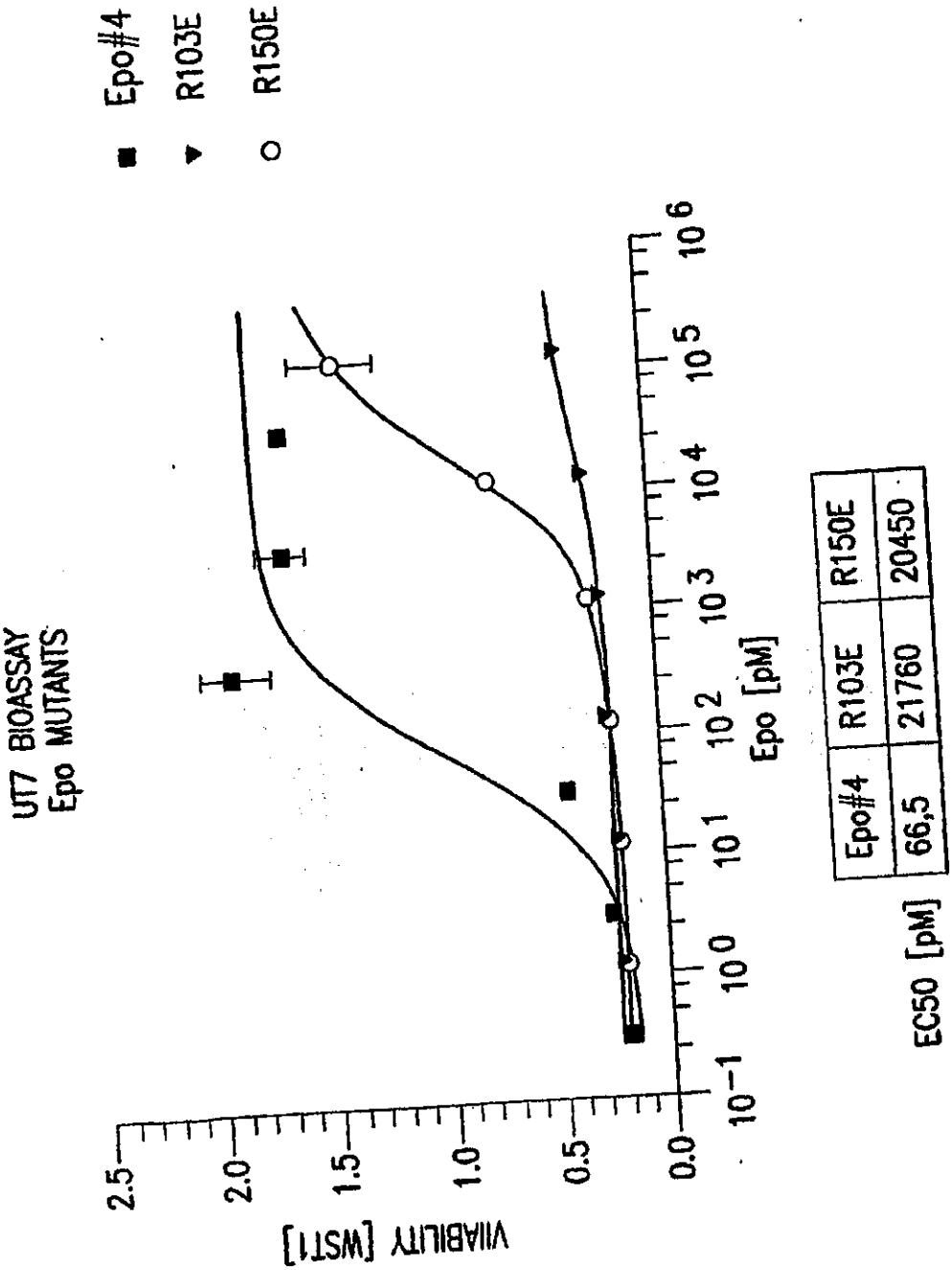

UT7 BIOASSAY
Epo MUTANTS
Epo#4
K45D
S100E
EpoWT
VIABILITY [WST1]
1.2
0.8
0.4
0.0
10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5}
Epo [pM]
EC50
58.13
294.0
5.3840e+006
608.0

FIG.35



EC50 [pM]	Epo#4	R103E	R150E
	66,5	21760	20450

FIG.36

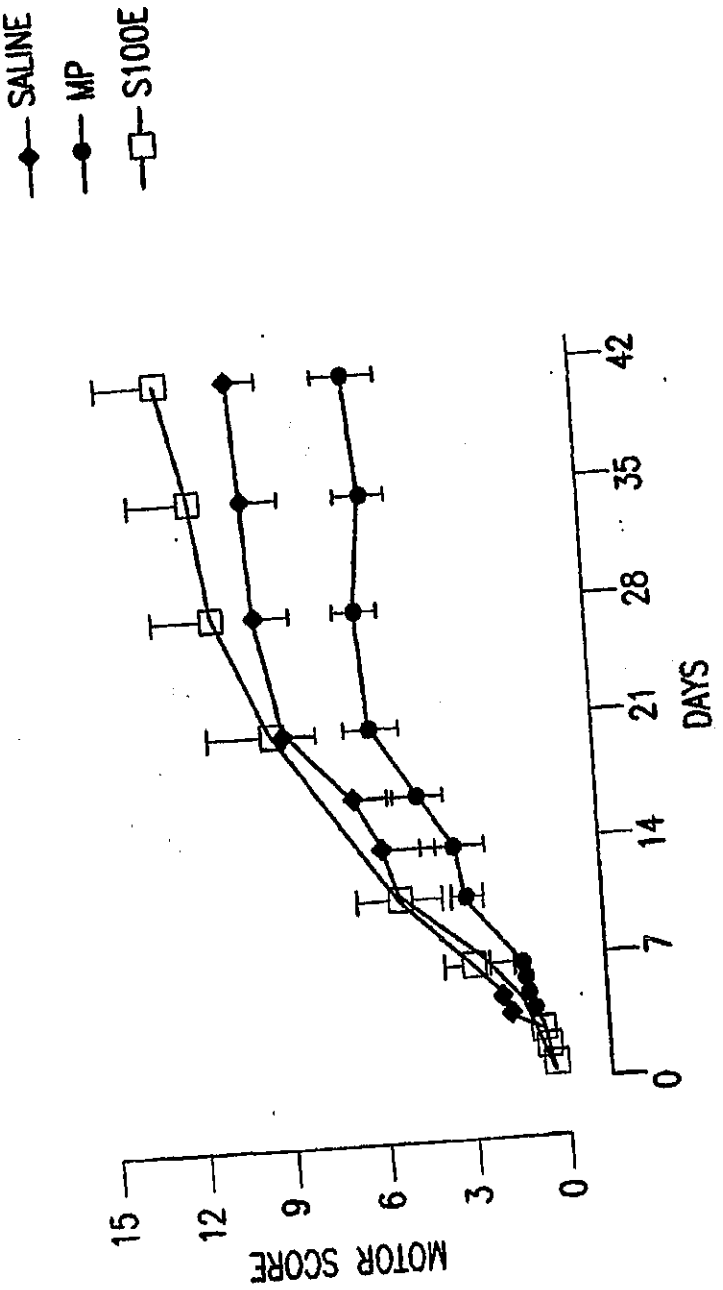


FIG.37

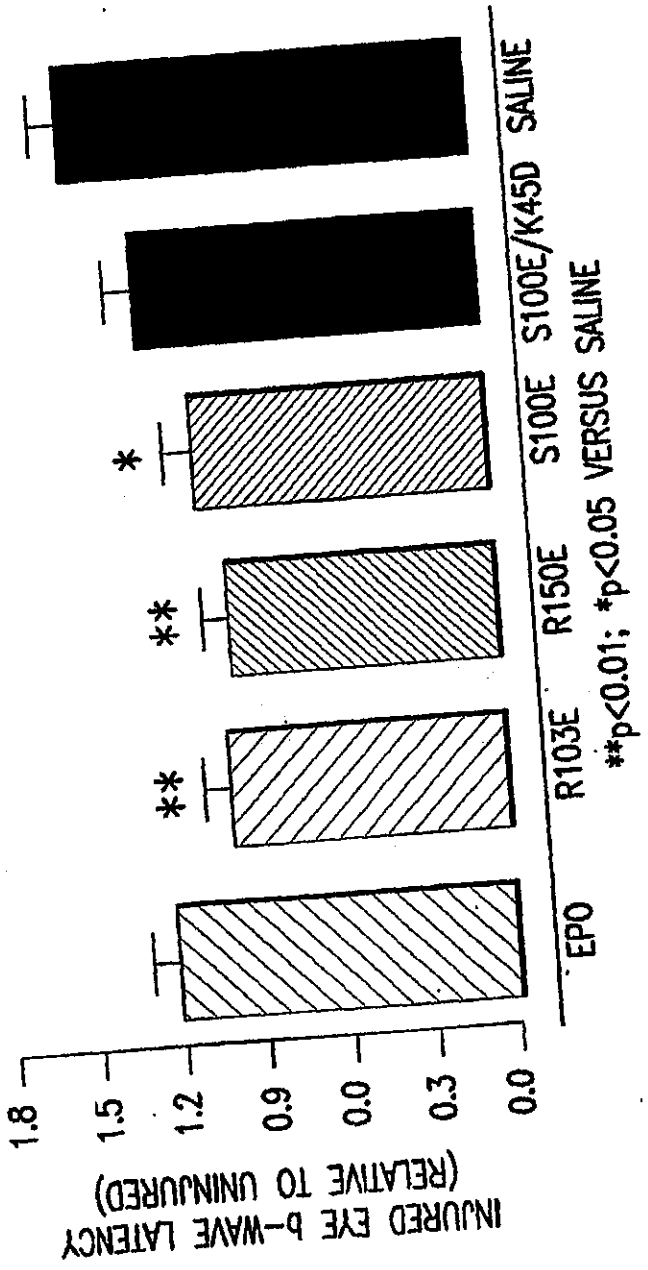

INJURED EYE b-WAVE LATENCY
(RELATIVE TO UNINJURED)
1.8
1.5
1.2
0.9
0.0
0.3
0.0
EPO
R103E
R150E
S100E
S100E/K45D
SALINE
*
**
**
**p<0.01; *p<0.05 VERSUS SALINE

FIG.38