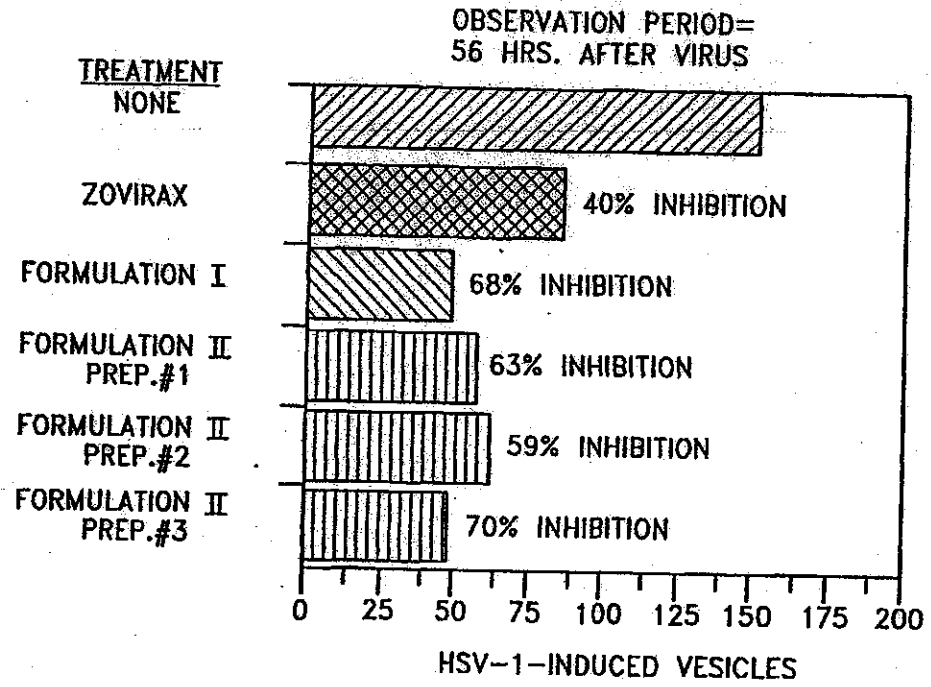

OBSERVATION PERIOD=
56 HRS. AFTER VIRUS
TREATMENT
NONE
ZOVIRAX
40% INHIBITION
FORMULATION I
68% INHIBITION
FORMULATION II
PREP.#1
63% INHIBITION
FORMULATION II
PREP.#2
59% INHIBITION
FORMULATION II
PREP.#3
70% INHIBITION
0 25 50 75 100 125 150 175 200
HSV-1-INDUCED VESICLES

FIG. 1

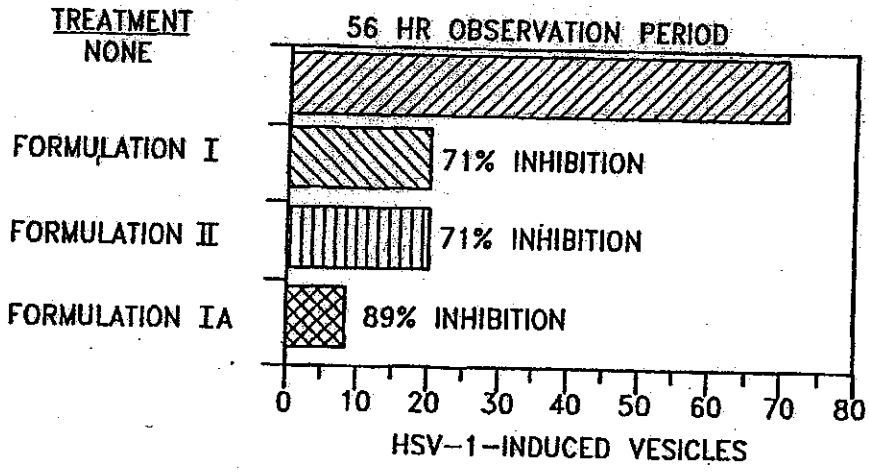

TREATMENT
NONE
56 HR OBSERVATION PERIOD
FORMULATION I
71% INHIBITION
FORMULATION II
71% INHIBITION
FORMULATION IA
89% INHIBITION
0 10 20 30 40 50 60 70 80
HSV-1-INDUCED VESICLES

FIG.2

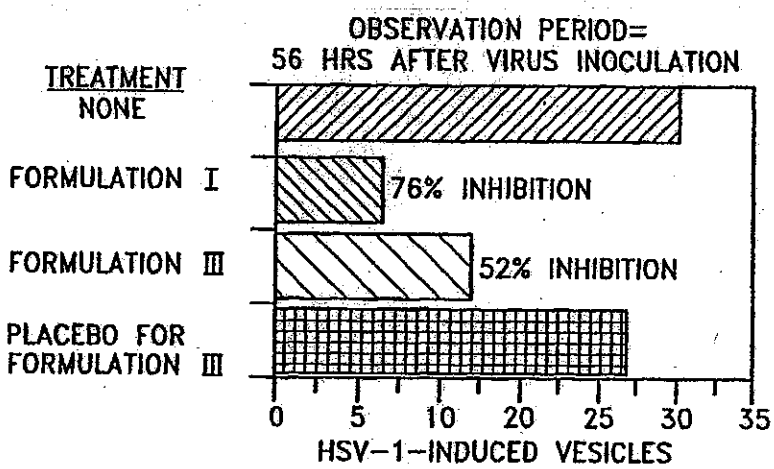

OBSERVATION PERIOD=
56 HRS AFTER VIRUS INOCULATION
TREATMENT
NONE
FORMULATION I
76% INHIBITION
FORMULATION III
52% INHIBITION
PLACEBO FOR
FORMULATION III
0
5
10
20
25
30
35
HSV-1-INDUCED VESICLES

FIG. 3A

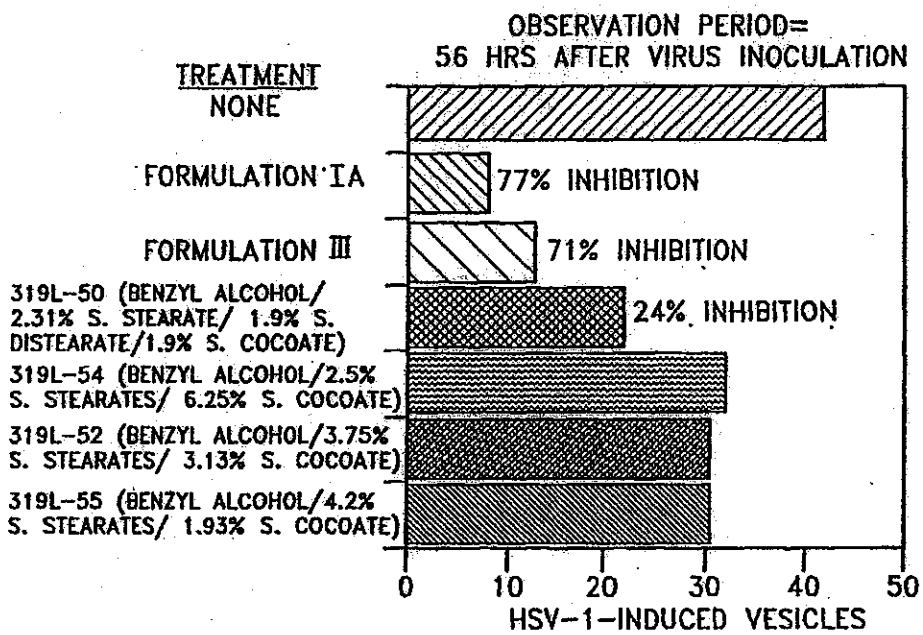

OBSERVATION PERIOD=
56 HRS AFTER VIRUS INOCULATION
TREATMENT
NONE
FORMULATION IA
77% INHIBITION
FORMULATION III
71% INHIBITION
319L-50 (BENZYL ALCOHOL/ 2.31% S. STEARATE/ 1.9% S. DISTEARATE/1.9% S. COCOATE)
24% INHIBITION
319L-54 (BENZYL ALCOHOL/2.5% S. STEARATES/ 6.25% S. COCOATE)
319L-52 (BENZYL ALCOHOL/3.75% S. STEARATES/ 3.13% S. COCOATE)
319L-55 (BENZYL ALCOHOL/4.2% S. STEARATES/ 1.93% S. COCOATE)
0
10
20
30
40
50
HSV-1-INDUCED VESICLES

FIG.3B

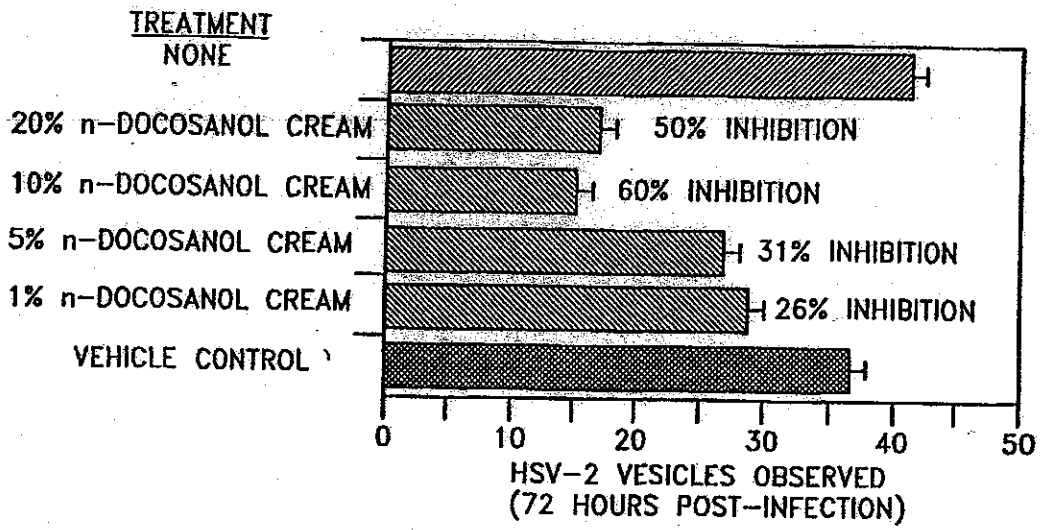

TREATMENT
NONE
20% n-DOCOSANOL CREAM
10% n-DOCOSANOL CREAM
5% n-DOCOSANOL CREAM
1% n-DOCOSANOL CREAM
VEHICLE CONTROL
50% INHIBITION
60% INHIBITION
31% INHIBITION
26% INHIBITION
0
10
20
30
40
50
HSV-2 VESICLES OBSERVED
(72 HOURS POST-INFECTION)

FIG. 4

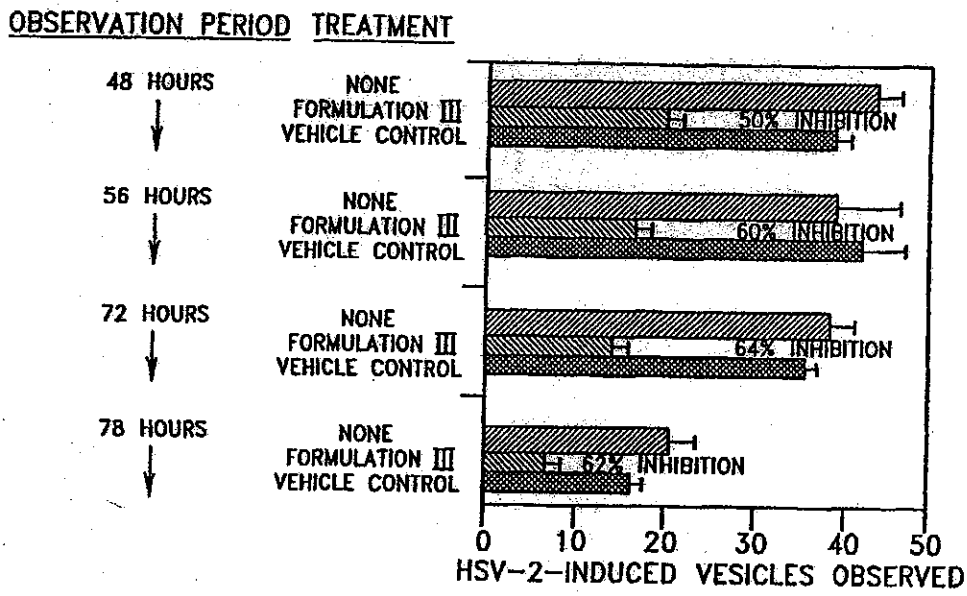

OBSERVATION PERIOD
TREATMENT
48 HOURS
56 HOURS
72 HOURS
78 HOURS
NONE
FORMULATION III
VEHICLE CONTROL
50% INHIBITION
60% INHIBITION
64% INHIBITION
62% INHIBITION
0
10
20
30
40
50
HSV-2-INDUCED VESICLES OBSERVED

FIG.5

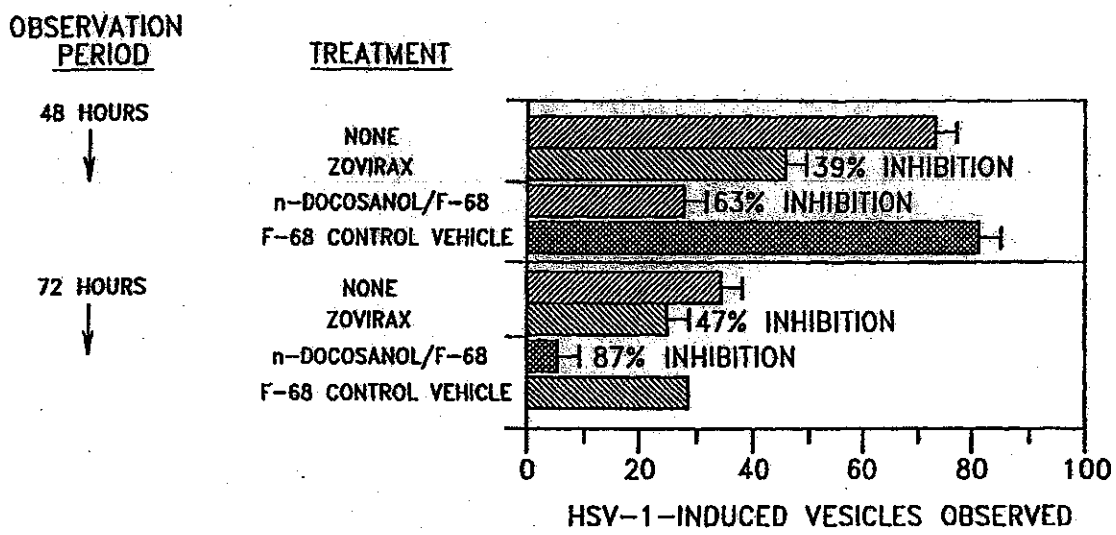

OBSERVATION PERIOD
TREATMENT
48 HOURS
NONE
ZOVIRAX
n-DOCOSANOL/F-68
F-68 CONTROL VEHICLE
39% INHIBITION
63% INHIBITION
72 HOURS
NONE
ZOVIRAX
n-DOCOSANOL/F-68
F-68 CONTROL VEHICLE
47% INHIBITION
87% INHIBITION
0
20
40
60
80
100
HSV-1-INDUCED VESICLES OBSERVED

FIG. 6A

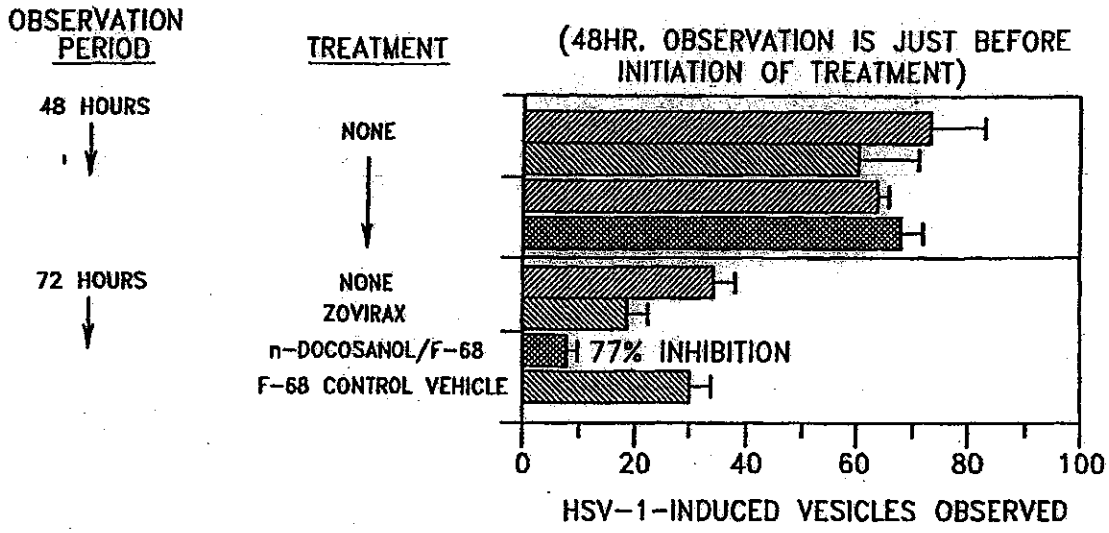

OBSERVATION PERIOD
48 HOURS
72 HOURS
TREATMENT
NONE
NONE
ZOVIRAX
n-DOCOSANOL/F-68
F-68 CONTROL VEHICLE
(48HR. OBSERVATION IS JUST BEFORE INITIATION OF TREATMENT)
77% INHIBITION
0
20
40
60
80
100
HSV-1-INDUCED VESICLES OBSERVED

FIG. 6B

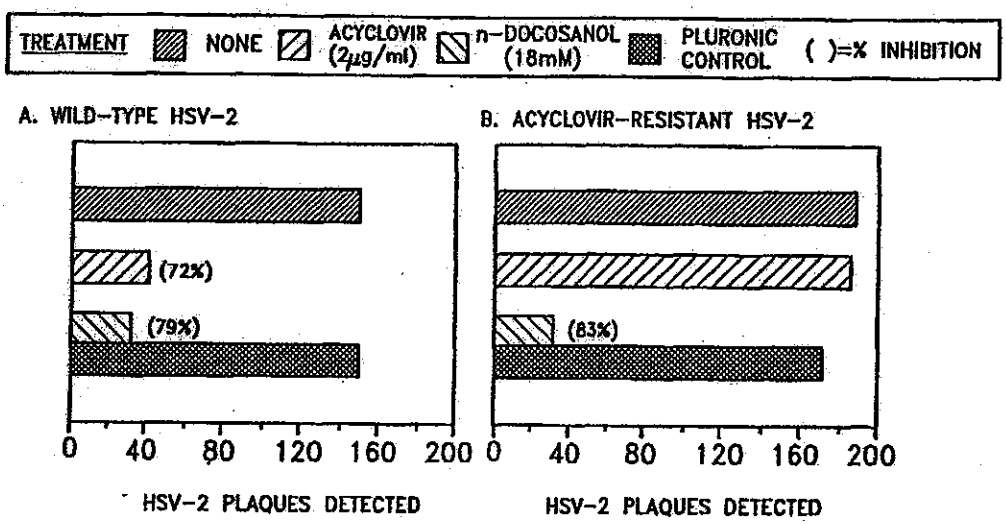

TREATMENT
NONE
ACYCLOVIR (2μg/ml)
n-DOCOSANOL (18mM)
PLURONIC CONTROL
( )=% INHIBITION
A. WILD-TYPE HSV-2
B. ACYCLOVIR-RESISTANT HSV-2
(72%)
(79%)
(83%)
0 40 80 120 160 200
0 40 80 120 160 200
HSV-2 PLAQUES DETECTED
HSV-2 PLAQUES DETECTED

FIG. 7

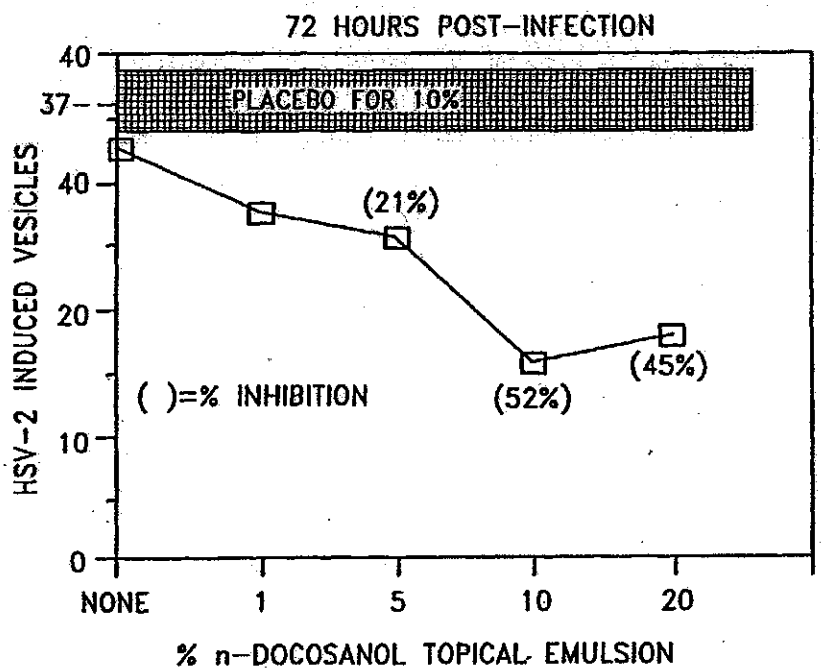

72 HOURS POST-INFECTION
PLACEBO FOR 10%
HSV-2 INDUCED VESICLES
40
37
40
20
10
0
(21%)
( )=% INHIBITION
(52%)
(45%)
NONE
1
5
10
20
% n-DOCOSANOL TOPICAL EMULSION

FIG. 8

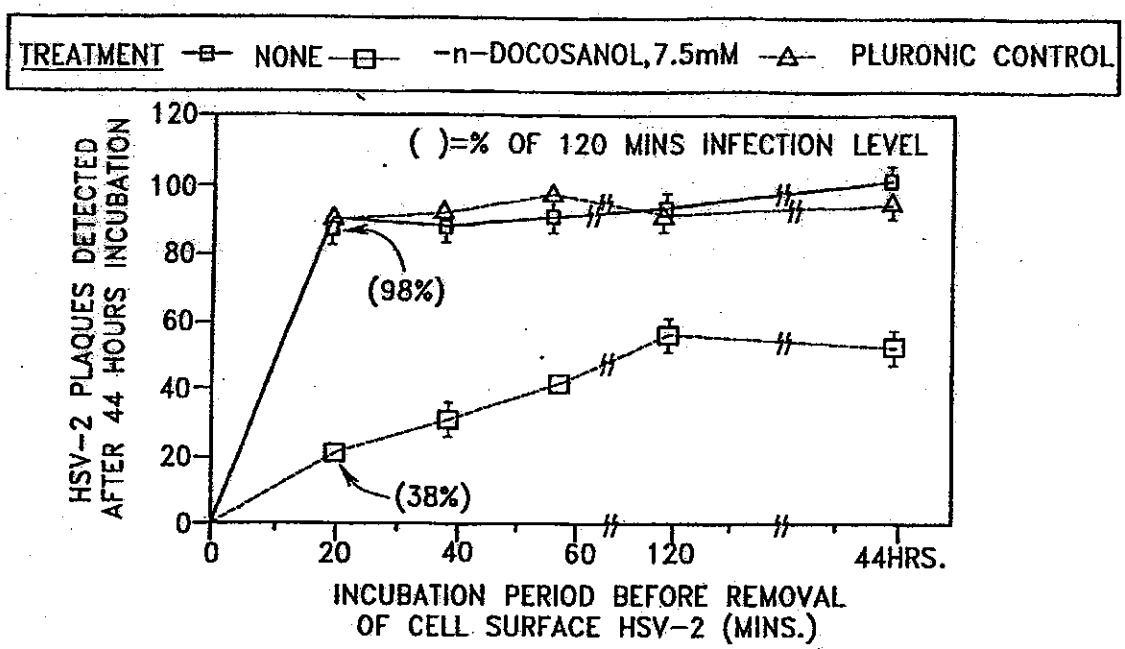

TREATMENT -⊟- NONE -⊡- -n-DOCOSANOL,7.5mM -△- PLURONIC CONTROL
( )=% OF 120 MINS INFECTION LEVEL
HSV-2 PLAQUES DETECTED AFTER 44 HOURS INCUBATION
120
100
80
60
40
20
0
(98%)
(38%)
0
20
40
60
120
44HRS.
INCUBATION PERIOD BEFORE REMOVAL OF CELL SURFACE HSV-2 (MINS.)

FIG. 9

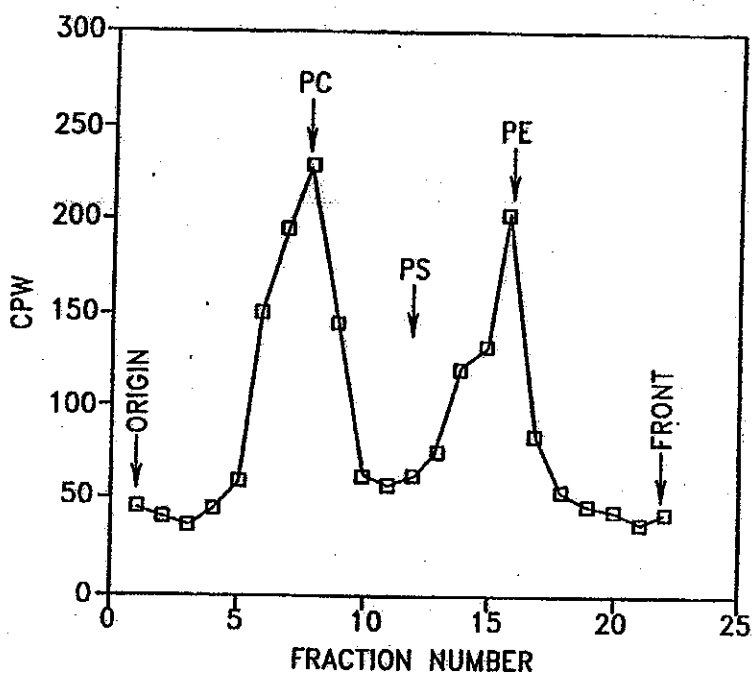

300
250
200
150
100
50
0
CPW
PC
PE
PS
ORIGIN
FRONT
0
5
10
15
20
25
FRACTION NUMBER

FIG. 10

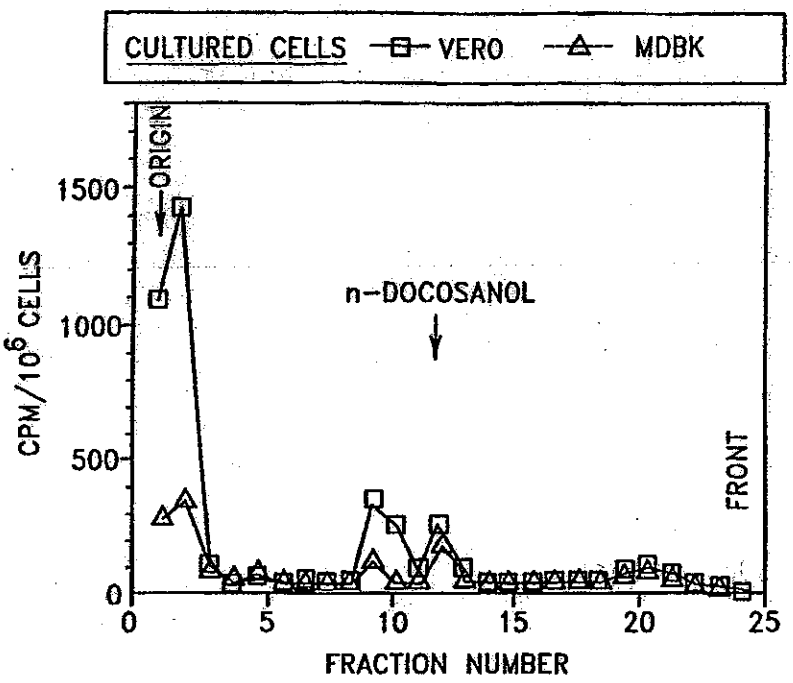

CULTURED CELLS
VERO
MDBK
ORIGIN
n-DOCOSANOL
FRONT
CPM/10^6 CELLS
1500
1000
500
0
0
5
10
15
20
25
FRACTION NUMBER

FIG. 11

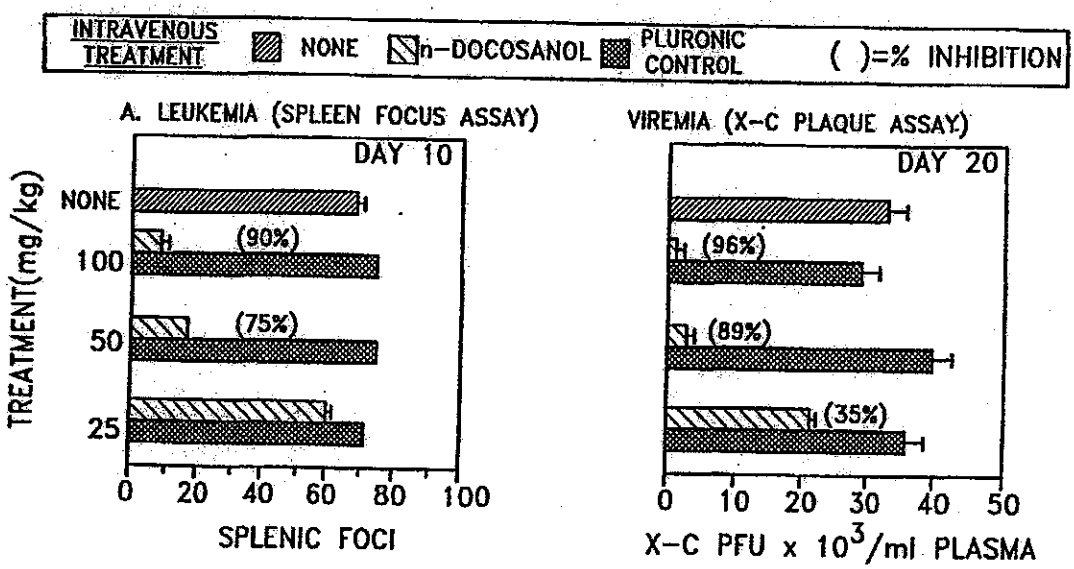

INTRAVENOUS TREATMENT
NONE
n-DOCOSANOL
PLURONIC CONTROL
( )=% INHIBITION
A. LEUKEMIA (SPLEEN FOCUS ASSAY)
DAY 10
TREATMENT(mg/kg)
NONE
100
50
25
(90%)
(75%)
0 20 40 60 80 100
SPLENIC FOCI
VIREMIA (X-C PLAQUE ASSAY)
DAY 20
(96%)
(89%)
(35%)
0 10 20 30 40 50
X-C PFU x 10^3/ml PLASMA

FIG. 12

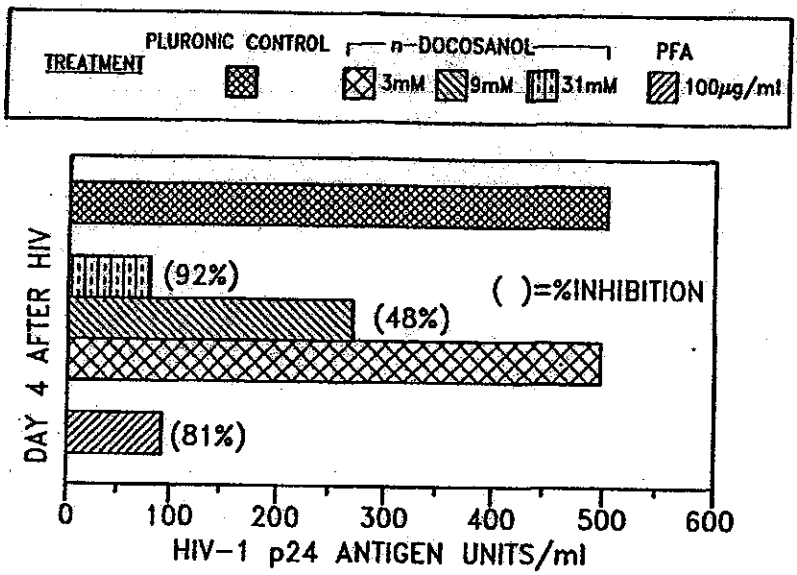

TREATMENT
PLURONIC CONTROL
n-DOCOSANOL
3mM
9mM
31mM
PFA
100μg/ml
DAY 4 AFTER HIV
(92%)
(48%)
(81%)
( )=%INHIBITION
0
100
200
300
400
500
600
HIV-1 p24 ANTIGEN UNITS/ml

FIG. 13

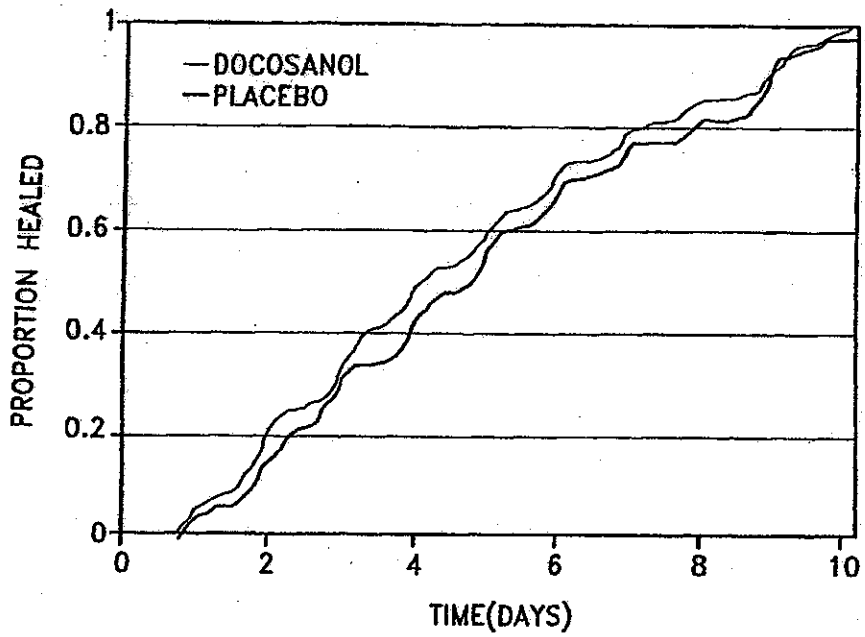
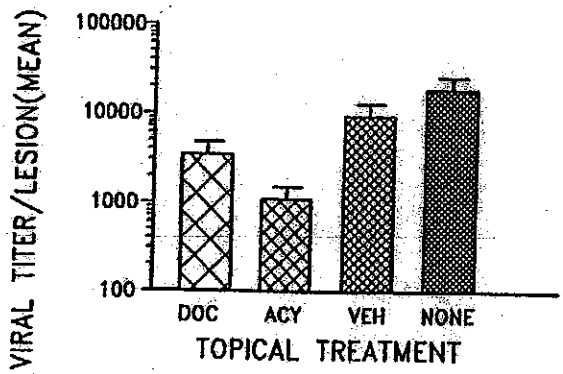
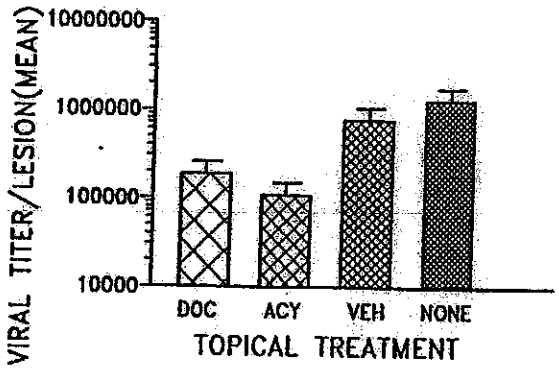

DOCOSANOL
PLACEBO
PROPORTION HEALED
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
TIME(DAYS)

FIG. 14



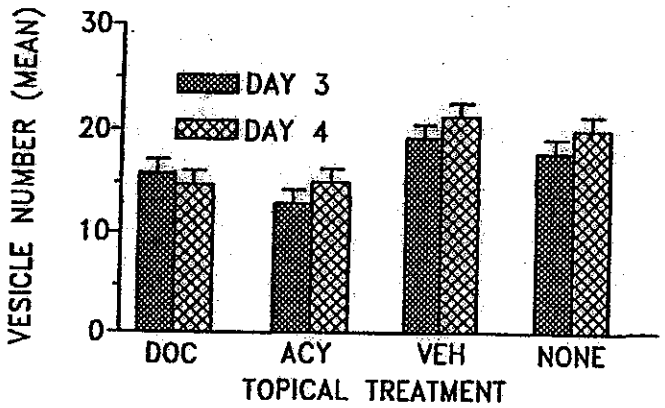
TREATMENT COMPARISON	P-VALUE
DOC vs VEH	0.0241
ACY vs VEH	<0.0001
ACY vs DOC	0.0253

FIG. 15



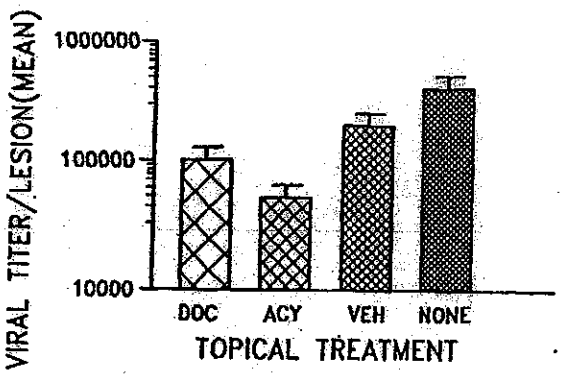
TREATMENT COMPARISON	P-VALUE
DOC vs VEH	0.0032
ACY vs VEH	0.0002
ACY vs DOC	0.2934

FIG. 16



TREATMENT COMPARISON	DAY 3 P-VALUE	DAY 4 P-VALUE
DOC vs VEH	0.0152	0.0011
ACY vs VEH	0.0001	0.0020
ACY vs DOC	0.0678	0.7970

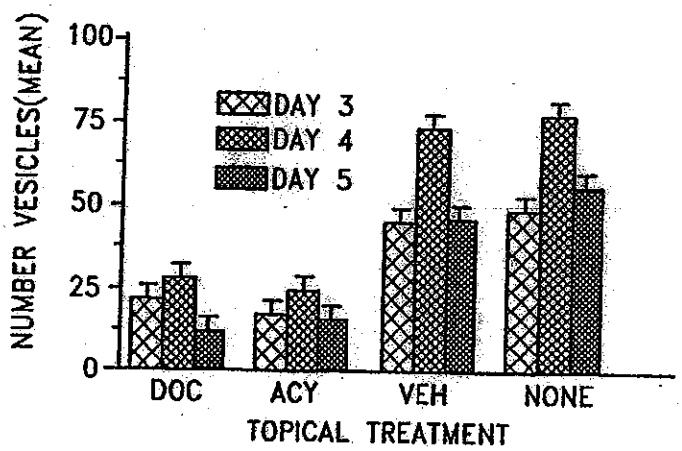
FIG. 17



TREATMENT COMPARISON	P-VALUE
DOC vs VEH	0.2709(0.0091vsNONE)
ACY vs VEH	0.0307
ACY vs DOC	0.2677

TIME(DAYS)

FIG. 18



TREATMENT COMPARISON	P-VALUE DAY 3	P-VALUE DAY 4	P-VALUE DAY 5
DOC vs VEH	0.0008	<0.0001	<0.0001
ACY vs VEH	0.0002	<0.0001	0.0003
DOC vs ACY	0.6105	0.6636	0.5721

FIG. 19

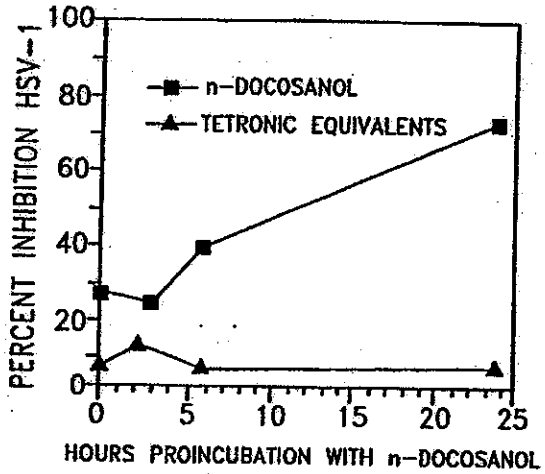


FIG.20A

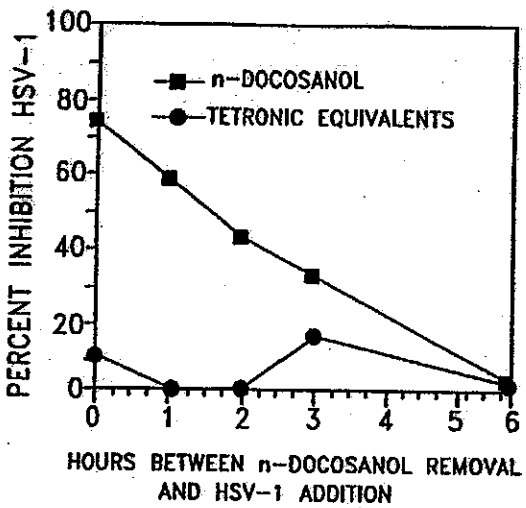


FIG.20B

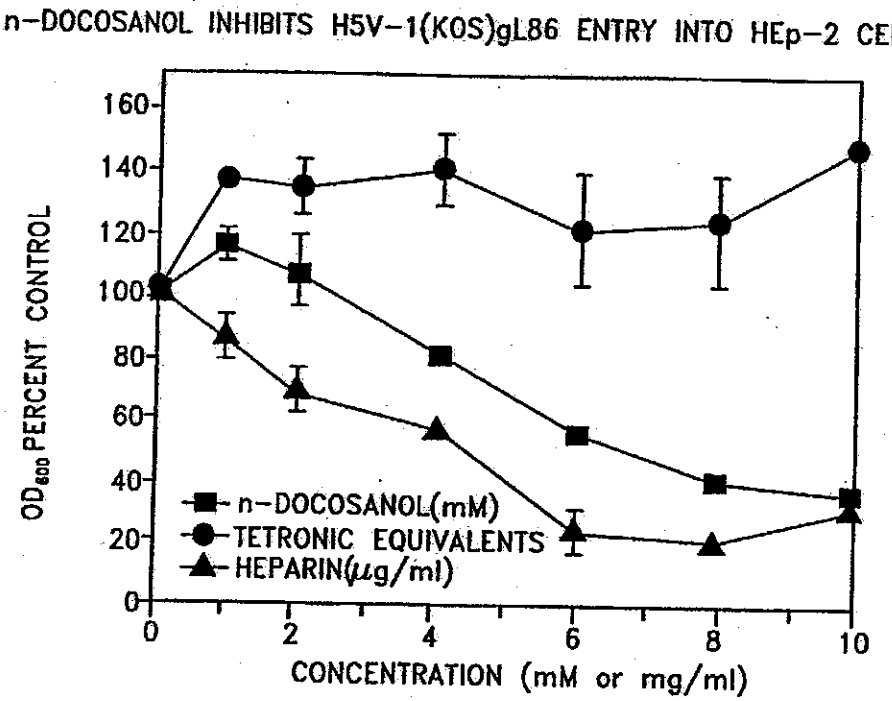

n-DOCOSANOL INHIBITS H5V-1(KOS)gL86 ENTRY INTO HEp-2 CELLS
OD600 PERCENT CONTROL
160
140
120
100
80
60
40
20
0
0
2
4
6
8
10
CONCENTRATION (mM or mg/ml)
n-DOCOSANOL(mM)
TETRONIC EQUIVALENTS
HEPARIN(μg/ml)

FIG.21

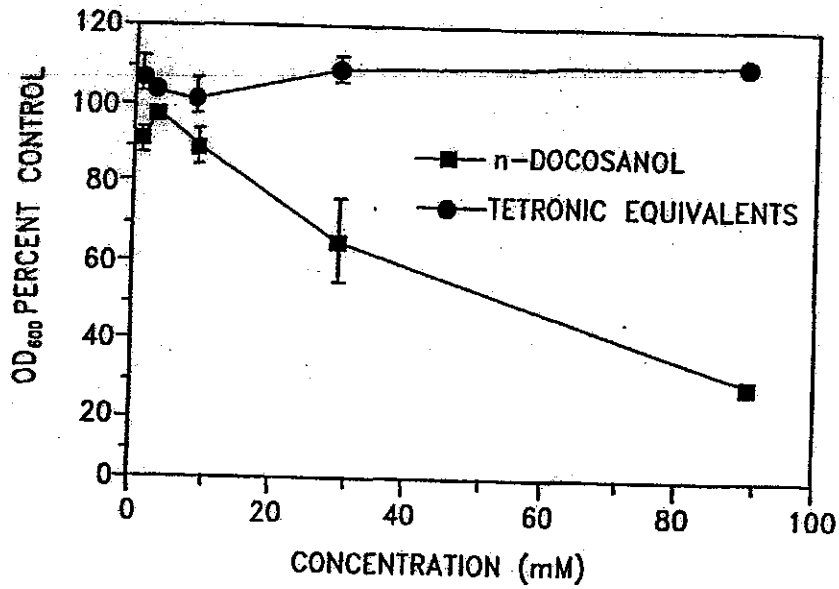

120
100
80
60
40
20
0
OD_{600} PERCENT CONTROL
0
20
40
60
80
100
CONCENTRATION (mM)
n-DOCOSANOL
TETRONIC EQUIVALENTS

FIG.22

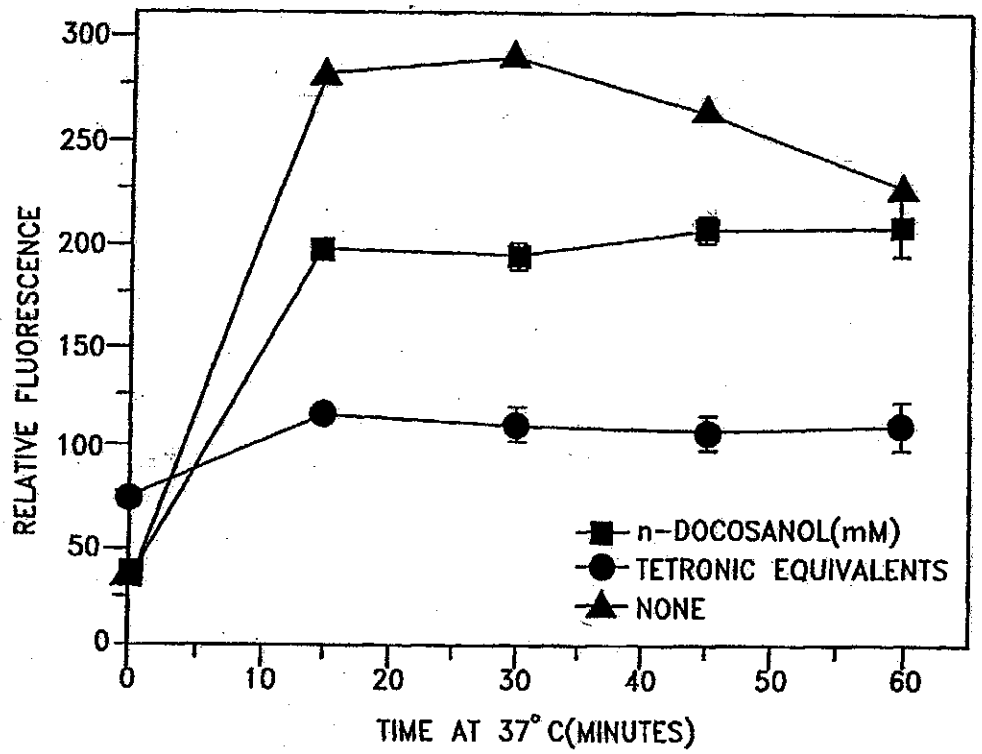

300
250
200
150
100
50
0
RELATIVE FLUORESCENCE
0
10
20
30
40
50
60
TIME AT 37° C(MINUTES)
n-DOCOSANOL(mM)
TETRONIC EQUIVALENTS
NONE

FIG.23