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2000 09 14

OA OAPI

(71) 11388 (: 92121)

(72)

92120	5443
92009	7967
92130	4958
92037	1775
92037	1775

(74)

:

(54)

(phosphonoformic acid)

9

(phosphonoformic acid) (PFA)

n -

(cytomegalovirus), (Epstein - bar), (HSV - 1 HSV - 2),
 (, HTLV - 1), (, HIV - 1)
 . HSV - 1 HSV - 2 , (mucosal membra
 ne) . VZV , EBV
 . HIV
 가 가 가

가 (ACV) , (azidothymidine)(AZT) , (acyclovir)

(2 -) - DNA . ACV , 9 -

(Schaeffer) 4,199,574 , 4,294,831 , 4,360,522 , (Hostetler) 5,580,571 , (Turchetta) 5,756,737 , (Schloemer) 5,567,816 ,

가 /

20 1 4 y - (linolenyl) , 6, 9 12 C18 (Sands et al., Antimicrob. Agents & Chemother. 15:67 - 73, 1979). (C18, (PCT WO9602244A1)).

20 32 4,874,794 , 5,071,879 , 5,166,219 , 5,194,451 5,534,554 ,

4,513,008 C20 C24 , , 5 7 ,

5,276,020 C16, C18 5,216,142 C20

, 1 - D - - sn - - 3 - - ACV ACV C18 (H ostetler et al., Biochem. Pharmacol. 53:1815 - 1822,1997).

(phosphatidylcholine) AL721, (Antonian et al., Neurosci. Biobehav. Rev. 11:399 - 413, 1987). (C10 C8) C15 가 5,208,257 , 5,380,754 (9,12) () 4,025,645

(Katz) (Proc. Natl. Acad. Sci. USA 88:10825 - 10829, 1991; 5,534,554)
 , n - (C22) (), HIV - 1(),
 (), (Friend) (),
 C10 C18
 , n - (Katz et al., Proc. Natl. Acad. Sc
 i. USA 88:10825 - 10829, 199; Snipes et al., Antimicrob. Agents Chemother. 11:98 - 104, 1977).
 가 n -
 n - , n - 70%가
 (Pope et al., J. Lipid Res. 37:2167 - 2178, 1996). n -
 80%
 , (Katz et al., Proc. Natl. Acad. Sci. USA 88:10825 - 10829, 1991).
 (Pope et al., Antiviral Res. 40:85 - 94, 1998).

n - 가
 (Pope et al., J. Lipid Res. 37:2167 - 2178, 1996; Katz et al., Ann. N.Y.Acad.Sci. 724:472 - 488, 1994).
 , n - (Katz et al., Annals N.Y.
 Acad. Sciences, 724:472 - 488, 1994), n - 300mM

가 n - 2 가
 ,
 , ACV
 가 (Spector et al., Proc. Natl.Acad.Sci.USA 86:1051 - 1055, 1989; O'Brien et al., Antimicrob.
 Agents Chemother. 34:1178 - 1182, 1990; Hirsch et al., 1996 Antiviral agents. In Fields Virology Third E
 dition, B.N. Fields, D.M.Knipe, P.M.Howley, eds. Lippincott - Raven Publishers, Philadelphia, pp. 431 - 466).

10% (ZOVIRAX™)
 , n - 가

(PFA) C18 - C28
 , n - , n - ,

0.05% 40%
 ACV, (adefovir), (brivudin), (cidofovir), ddC, ddI,
 (famciclovir), (ganciclover), (idoxuridine), (lamivudin), (lo

bucavir), (penciclovir), (ribavirin), (sorivudine), (trifluridine),
(trimethoprim), (valacicvir) (Ara) A .
PFA가 0.1 10% .

25,000 , 1,000
6,000 12,000
- 10 . - 9

PFA, , - A n - ACV,
0.05% 40% , 0.1 10% , n -

5% , 1% 25% 1% 25% USP, 0.1% 10% , 1% 2

1 5

1 14 1 5 0.01 10g
(transmembranal penetration)

PFA 3 5 , , , ,

- A n - ACV, PFA, ,

1 X n - (C22, ■), n - (,) (C24,), n -
(C26, ●) n - (C28,) HSV - 2
() .

2a HSV - 2 가 12 ,
n - 가 ,
n - 1:1(■), 3:1(), 5:1() 10:1(○) .

2b 2a : 2a
(2a) .

- 3 n - (■) HSV - 2 - , n - HSV - 2 48 가 , HSV - 2 (○) (, 50 /), .
- 4 /n - (■) /n - (▲) HSV - 2 가 12 HSV - 2 .
- 5 DNA ³H - X - , (○) (C18,) (C20,) 48 B - ().
- 6a 6b X - (1,000 / (6a) 30,000 / (6b) 96), (○) , /n - (■) () .
- 7 6a 72 (■) 96 (○) /n - .
- 8 n - ACV 가 HSV - 2 t - (student's two - tailed t - test) .
- 9 n - ACV - HSV . /
- 10 n - ACV HSV - 1 . PFU , 15% ().
- 11 ACV n - / PFU HSV - 1 HSV - 1 EC₉₀ .
- 12 n - PFA HSV - 1 가 PFU .
- 13 n - PFU HSV - 1 EC₅₀ (A) EC₉₀ (B) . , , PFA , PFA , .

18 28 (C18 C28) , n - , n - 가 0.05% 40% 가 , n - 1% 20%

n - (cis - 13 - - 1 -) (, 4,186,211). [: J. Am. Chem. Soc. 78:258 2, 1956]. [: A. Streitwieser, Jr. & C. H. Heathcock, Introduction to Organic Chemistry, 2nd ed., Macmillan Publishing Co., New York, NY, 1981, at pages 160, 243 - 247, 303 - 307, 311 - 312, 315 - 317, 401 - 406, 447 - 453, 515 - 516, 544, 548 - 555, 604 - 605, 670, 753 - 754, 950].

ACV, , ddC, ddl, A PFA 0.1% 10% . 가 , ACV, PFA, - A가 0.1% 10%

haeffer) 4,199,574 , (Schloemer) 5,567,816 , (Turchetta) (Sc 5,756,737 (Nylon), P 가 [: Chemische Berichte 57:1023 - 1038, 1924].

1,000 25,000 6,000 12,000, 8,400 , (188) (, PLURONIC F - 68^R) - 9 / - 10(, TRITON X - 100^R), (1 % 10 % PFA) 0.1 % 50 %, 1:1(w:w) 10:1(w:w), 5:1(w:w)

3,592,930

(myristate),

()
 ()
 , 2 - - 1,3 - - 15 -
 가 가
 (800 20,000) 가 (azone)

(sunscreens)
 B
 (micatin) (tolnaftate) E 가
 (beeswax) 가 (pullulin), (xanthan),
 가 (

agent)()
 가
 14 10mg 10g 1 10 12 4 . 1
 . 가 2 5 , 0.1g 5g
)

HSV - 1, HSV - 2 HSV - 6, CMV, EBV, VZV
 (, HTLV - 1), (, HIV - 1),
 /

any, Inc.) (98% , mw 326) M. (M. Michel and Comp
(Croda Inc.) (Burroughs Wellcome Co.) 9 - β - D -
Research Triangle Park) (St. Louis, MO) (Sigma Chemical Co.) F - 68R(188)
(Parisappany) (BASF)

- HSV - 1 (#VR - 539) (McIntyre) (#VR - 539), HSV - 2 MS
(#VR - 540), (Ellen) (VZV, #VR - 1367), (To
wne) (CMV, #VR - 977) WR (#VR - 119) (Rockville)
(ATCC) . HSV (stock) (
, ATCC #CCL - 81) , VZV CMV MRC - 5
(ATCC #CCL - 171) (PFU)
, - 85

- n - (% w/w
) 10% n - , 5% , 8% , 5% USP, 2.7%
[: Katz et al., InSlow Infections of the Central Nervous System. Ann. N.Y. Acad. S
ci. 724:472 - 488, 1994]. 10% , 10% 가
80 가 30
ACV() 0.3M ℓ n - 2.7M ℓ
5% ACV 9% n - 0.3M ℓ
SPEX SPEX (SPEX Industries, Inc., Metuchen, NJ) 5

, n - F - 68^R (188; Mr 8400) [: Katz et al.,
Proc. Natl. Acad. Sci. USA 88:10825 - 10829, 1991; Pope et al., J. Lipid Res. 37:2167 - 2178, 1996].
F - 68^R 37 12mM , 50 가 . n - 90mM
F - 68^R 가 65W 21 450 (Branson 450 sonifier)
86 가
가 0.1 0.5 [: Katz et al., Proc. Natl. Acad. Sci. USA
88:10825 - 10829, 1991]. F - 68^R

(1) HSV , (2) HSV , (3) (4)
, 가

(250 - 400mg)
, (Parke - Davis, Morris Plains, NJ) (Nemb
utal) (Abbott Laboratories, North Chicago, IL) HSV - 2 . HSV - 2
5x10⁵ PFU (75 $\mu\ell$) 4cm x 4cm , (tattoo instrument)
HSV - 가
[: Spruance et al., Antiviral Res. 9:295 - 313, 1988]. 6 가
200 $\mu\ell$ 2 /

HSV
/M ℓ , 50mg/M ℓ , 5% , 1mM Na (pyruvate), 4mM L - , 50
(2M ℓ) 1.5x10⁵/M ℓ , 10mM HEPES DMEM 16 - mm (1M ℓ) 35 - mm
(n -) . n -
(, ACV) 가 , HSV PFU 가 24 ,
(10% CO₂; 가), (/ 가 44 ,
(fuchsin) 1.25mg/M ℓ), (10) HSV - 2.5mg/M ℓ

HSV 16 - mm HSV
500PFU/ 3
(1 x 10⁵/M ℓ , 0.1M ℓ / 96 -
) PFU 2 72 ,
, HSV 가 .

CMV VZV 16mm HSV PFU MRC - 5
 , 가 2 ,
, MRC - 5 (infectious center assay)
 , 24 - MRC - 5 . 6
, 2 VZV CMV 가 .

1

C21 C28

, n - F - 68^R
37 (DMEM; Whittaker Bioproducts, Walkersvi
lle, MD) 10mg/M ℓ , 50 가 . n - 30mM
가 , (450) 65W 21 ,
88 가 . 가 0.3 μ n -
 . 가 F - 68^R /

(C18), (C20), (C21), (C24), n - (C
26) n - . C22
(C28) 90 가 (C24) 80 , n - (C26) 1 -
 ; M. (New York, NY) (Milwaukee, WI)
(St. Louis, MO) .

2(HSV - 2;from the American Type Culture Collection, Rockville, MD; ATCC No. VR - 540)
MS (Vero cells; ATCC No. CCL81)

37 10% CO₂ , 5%
35 - mm 1.8M ℓ 6x10⁵ , L - / 1mM DMEM
16 - mm 0.8M ℓ 3x10⁵
fu/35 - mm 50pfu/16mm HSV - 2 가 . 24 , 175p

HSV - 2 가 42 ,
(1.25mg/M ℓ) (2.5mg/M ℓ) ,
10% , t -

C21, C24, C26 C28 n - (C22)
HSV - 2 가 1 50%
(mM)(EC₅₀)가 1

HSV - 2 . C21 C28 HSV - 2
(heneicosanol)(C21) C22
(,) . HSV - 2

1

HSV - 2 HSV - 2

<u>탄소쇄 길이</u>	<u>M.W.</u>	50% 억제* <u>농도(mM)</u>
18	284.6	독성**
20	298.6	독성**
21	312.6	16.0
22	326.6	8.6
24	354.6	14.1
26	382.6	8.4
28	410.6	10.5

* 12 가 HSV - 2
가 , 50% (linear regression)

** " " 1.5mM 12

(C18) (C20) n -
가 (0.2 μ M 2 μ
M) , C18 C20

2

가

가

(1:1(w:w) 1) . 1:1 (가
8,400) n - (326.57) 가 26:1 .
가 ,

J. Biol. Chem. 254:2244 - 2249, 1979]. [: Sandra et al.,

n - , F - 68^R n - 3:1, 5:1 10:1(w:w) 가 1 .
가 가 (2) . , 3:1
1 1:1 (4mM n -) 가 , 5:
1:1 (1mM n -) . , 10:1
, n - (2b) .
, n - [1 - ¹⁴ C] 24
가 n - 가 . n -
4:1 7.8x10⁻⁶ µg/ , 1:1
가 3.1x10⁻⁶ µg/
가 4:1 5:1(w:w) .
. , (
TRITON X - 100^R, Rohm & Haas) n - a) n - 2.5g 1.5g 90
, b) 90 500Mℓ 1.15g(PVP) , c)
5 1300psi (microfluidizer) , d)
PVP
. n -
(가 1:1) .
n - 가 HSV - 2 .
가 3 /n - n - 2mM
4.5mM EC₅₀ .
.
50% n - 가 n - (, 15mM 3mM) .
3
, n -
/n - () 1
/n - HSV - 2 /n - , 1
4 , /n - /n -
F - 68^R 1 HSV - 2 . n - (■) n - (▲)
HSV - 2가 가 HSV - 2
). , C22 (,
4
n - 1 -

HSV - 2 /n - () 1
 . C22 n -
 (2). 4mM 15mM n -
 가 , 가 . n - (tolerable)
 (2mM) , n -
 , 4 15mM n - . , C22
 , 가 .

2

**

**

농도*	도코사놀	도코산	도코사노산	에루실 알코올	브라시달 알코올
15	66	58	독성†	독성	ND
8	44	55	독성	독성	48
4	36	42	독성	독성	44
2	40	31	30	독성	35
1	14	28	16	93	27
0.5	ND‡	ND	26	91	ND
0.25	ND	ND	ND	70	ND

*HSV - 2 가 12 , 가
 , 908^R (TETRONIC - 908^R) mM ,
 F - 68R n - (m.w.326.6), n - (m.w. 310.6), n - (m.w. 340.6),
 (m.w. 324.6) mM .

† " " 1 가 24
 .

‡ " ND" .

** 가 . 가
 , 가 가
 5% .

5

C22 -

/ (- 13 - - 1 - ;) 1
 HSV - 2 . / n -
 (2 - 15mM) 가 . , 2
 (1mM) HSV - 2 (93%). , 1m
 M . 50%
 n - 60 (EC₅₀ = 9mM). 6.7 (, 1m
 M/0.15mM).

, C22 - , (- 13 - - 1 -)
 1 HSV - 2 HSV - 1 - 908^R (BASF) 2 ,
 n - .

, C22 13 () 가
 가 가 가 .

/ (virucidal) , HSV - 2
 / 2 .

6

(erucamide)

(- 13 - ; m.w. = 337.59) C
 22 / () - 908^R . C2
 1 HSV - 2 .
 2 n - , 3mM
 가 (2). 3mM 15mM 가 ,
 가 (1.7mM) , n - , n - , n -
 .
 M 44%, 0.59mM 42%, 0.03mM 34% 1.7mM 78%, 1.5mM 68%, 1.2mM 58%, 0.89m
 , C22 , C22 (n -) 가 , C2
 2 - .

7

n - .
 가 : 1)
 ; 2) ³H - (New England Nuclear) 가 DN
 A ³H - DNA , DNA
 ; 3) 96 - 가 (Skehan et al., J. Natl. Cancer Inst. 82:1107 - 1112, 1990)
 (sulforhodamine) .

(1), WI - 38, (ATCC No. CCL 75), HFL1, (ATCC No. CCL 1635), ATCC TIB
 HB 가
 B - (MBI - 9)가
 [: Marcelletti et al., J. Immunol. 148:3857 - 3863, 1992].
 10% , L - /
 DMEM . 1 . 1
 가 9mM n - 72 , 35 - mm
 1.8M $\varnothing$ 6x10⁵ 16mm - 0.8M $\varnothing$ 3x10⁵
 가 3 , 가
 24 72 (ATCC CRL 1900), WI - 38 ,
 B - 가
 n - .
 가

3

n -

처리*	인큐베이션 (시간)	베로 세포		태아포피세포	
		살아있는 수**	%조절***	살아있는 수**	%조절***
n-도코사놀 표면활성제	24	7.48 X 10 ⁵	101	2.41 X 10 ⁵	131
n-도코사놀 표면활성제	48	8.69 X 10 ⁵	137	2.78 X 10 ⁵	118
n-도코사놀 표면활성제	72	8.61 X 10 ⁵	120	2.72 X 10 ⁵	118
표면활성제	24	7.1 X 10 ⁵	95.7	1.55 X 10 ⁵	84
표면활성제	48	7.2 X 10 ⁵	107	1.66 X 10 ⁵	70
표면활성제	72	6.6 X 10 ⁵	89.0	1.0 X 10 ⁵	43

* 1.4mM 1.4mM
 9mM n - n - 4:1(w:w)
 ** (exclusion)

가 n - 72
 , WI - 38 가
 72
 (vacuollized) 72

n - , (C18) C18 C20 (C20) 가 .

DNA ^3H - B

. C18, C20 C22 ^3H - B

DNA 5 . B

(C18) IC_{50} $35\ \mu\text{M}$, (C20) IC_{50} 1.7mM .

, C20 2 IC_{50} 20mM IC_{50} 50 .

5 48 , 24

(C21) , (C24), n - (C26), n -

(C28) n - .

((cytostasis)) n - n - 96 -

n - 가 , n - 6a 6b

가 7 n -

96 - 1,000 / (6a 7) 30,000 / (6b)

. 37 72 96

OD₅₄₀ 72 . 6 96 (1000 /).

3mM n - 96 1,000 /

(6a). , C22 , n -

(6a). (6b) (7) 3mM

, n - () 가 n -

WI - 38, 6 7

C20 72 3mM n -

가

1.5mM C18 35 μM . IC_{50} 's C22 C21 15mM , C20

. C22 4 가

1 908^R (m.w. 284.) HSV -

2 가

908^R 11 μ M 22 μ M 3.5 μ M HSV - 2

44 μ M 908^R 35 μ M 10% 88 μ M 350 μ M

9

n -

HSV - 2

(6 , 200 - 300g; Charles Rivers Laboratories, Wilmington, MA)

HSV - 2(ATCC VR - 540,) . 0 ,

4cm² 6 9.75x10⁶ PFU/Ml 75μl . 24

(1), 2, 3, 4 ,

3 5 2, 3, 4 ,

가 . 0 4 가 , 0, 가

1, 2, 3, 4.

가 (pustule)

n - , (placebo) . n

- 10% w/w n - (Michel and Co., New York, NY), 5% w/w (Croda

a, Inc., New York, NY), 8% w/w NF(Witco Corp., Newark, NJ), 5% w/w USP, 2.7% w

/w (Ruger Chemical Co., Irvington, NJ) 69.3% USP 10% w

/w (Henkel, Cincinnati, OH), 5% w/w (Croda, Inc., New York, NY), 8% w/w

NF(Witco Corp., Newark, NJ), 5% w/w USP, 2.7% w/w NF(Ruger Chemical

Co., Irvington, NJ), 69.3% USP , 8

0 가 , 400 ± 5RPM(Heidolph RZR 2051) , 1900 ±

5RPM 가 85 가 . 80 3 , 30 (8)

PEG 3350 , 30 70% (PEG) 400NF 30% PEG 3350 NF 가

400RPM

4 . 2 48 , 3 72

, 4 96 (6) . 4 2 , . 3 ,

n - . n -

5 3 (saturating)

. 3 , 3

, 5

5 PEG

3 , n - . 4 , . 4 , 5 , n -

n - HSV - 2 . n - 3 5 가 n -

4

HSV - 2

처리	비히클의 수			조사 평가		
	2일	3일	4일	2일	3일	4일
물	45	34	19	0	0	0
n-도코사놀 (3X/일)	40	12	3	0	1.2	0.8
n-도코사놀 (5X/일)	43	5	3	0	1.3	1.3
스테아르산 (3X/일)	49	17	11	0	1.2	0.8
스테아르산 (5X/day)	49	13	5	0	1.7	2
플라시보 (5X/day)	41	30	15	0	0	0

10

n -

12 (, 가 (papule) 648 8.9 (/ 8 10) [: R.J. Whitley, in Fields Virology at p.2316].

9 10% n - 10% 가 5 5

(25 가 , 가 5 , 10 가
(50 가). , , 가
.

가 (episode abortion) ((flaking)
) 가 가 가) ,
(1), , , 가 가
.

5 2 () n -
8.9 5.5
가 n - 35%(P 0.0001
) 6

11

n - HSV - 1
HSV - 1 10 20mg/Ml
5.0mg/Ml n -
USP 5 %, NF 1 NF 5 8 %,
3 %,

가 10 가 , 가
4 2 HSV - 1

5

	n-도코사놀 크림처리됨	스테아르산 크림처리됨	처리되지 않음 ^o
치료시간 (시§)	(1) 123 ± 4.9 (2) 141 ± 5.2	(1) 124 ± 5.2 (2) 143 ± 4.0	(1) 215 ± 0.4 (2) 211 ± 0.4
바이러스 감소 중지 (시§)	(1) 47 ± 2.4 (2) ND**	(1) 49 ± 1.9 (2) ND	74 ± 83*
통증 감소 (시§)	(1) 27 ± 2.3 (2) 55 ± 4.1	(1) 31 ± 3.4 (2) 50 ± 3.8	NR**
통증의 완전한 정지 (시§)	(1) 63 ± 4.4 (2) 96 ± 5.8	(1) 68 ± 4.5 (2) 86 ± 5.0	111 to 178*
가려움증의 중지 (시§)	(1) 58 ± 4.9 (2) 63 ± 5.2	(1) 51 ± 3.4 (2) 76 ± 5.8	NR
딱딱한 가피단계 (시§)	(1) 61 ± 3.2 (2) 87 ± 4.4	(1) 62 ± 2.5 (2) 94 ± 4.9	NR

ed. 297:69 - 75, 1977]

[Spruance et al., New Eng. J.M

§ ±

* 77.5m² 77.5m²

** " ND" " , " NR" "

HSV - 1 20% 60%(4 8) n - 4 n -

, HSV - 1 가 n -

12

USP(0.5 %) NF(2 %) 1.4mM 188
0.15mM
가 (standard flexible nasal spray bottle) , 1.5mM 12
20 ()

(2 4 (1 2) , , , ,) 1 5
 (, , , ,)
 ()
 / /

/ . 5 (1 2) 5
 (2 5) 가 (37.8)
 1 3) (38.9) 가 (37.8)
 1.7 , 3 가 /

가
 / 가
 3 (1 2) 3
 37 가 가 3
 2 / 3
 가

13

HSV - 2

1 5 3mM
 (300 - 400mg/), (300 - 400mg/), (5 - 10mg/) 가
 , (1 - 10g)

/ 15 HSV - 2
 1 4
 (, , , , 가),

12 가

가 .

4 , HSV - 2 7 8 , 5 3

4 가

4

50 80% / 가 60

2 5

1 4 HSV - 2

14

EBV ()

(, , , 10 (14 19) T - , 10mM n -

12,000 18,000)

0.1mg/kg 0.02mg/kg (

1 , 3 1

- EBV EBV

/n - 2

2 3 8

4 T - 가 2

가 n - , n -

EBV -

n - ACV가 - HSV

n - ACV HSV - 2
 HSV - 2
 2 2 3 5
 , 가 2
 5 ,

HSV - 2 - HSV - 2 - 72 (8 A).
 54 . n - ACV 31% ,
 가 (65%) , 19 . n - ACV
 . n - ACV가

HSV - 2 - 96 , 27 .
 가 , n - ACV
 가 가 63% 50% . n - ACV
 , 89% .
 n - ACV , p = 0.003 p = 0.
 0015. , n - ACV가

(hours vesicles) (vesicle time) , (A
 UC) n - ACV AUC 698
 . n - ACV AUC 464(34%) 496(30%) . n -
 ACV 가 AUC 322 (698 x n - [0.66] x ACV
 [0.7]). AUC 206 - , 70% , p=0.01 ,
 HSV - 2 - n - ACV , n -
 ACV가 ,

16

n - ACV - HSV

n - ACV HSV - 2 - 3mM n - 0.4mM F - 68^R (3mM n - , ACV , HSV - 2 50) 24 44 가 . 9 , () 46 , ACV 50% (EC₅₀) 5 μ M . n - ACV EC₅₀ F - 68^R F - 68^R 40% ACV EC₅₀ 0.2 μ M 25 가 . ACV n - 가 ACV n - ACV 17

HSV - 1 n - ACV

HSV - 2 n - EC₅₀ ACV . , 2 - 3mM n - EC₅₀ , 2 - 3mM n - EC₅₀ (iso bologram)() , 가 . ACV가

HSV - 1 n - ACV EC₅₀ (10 A). (n - , HSV - 1 (500 PFU, 0.002PFU/) . 72 , HSV - 1 . HSV - 1 10 μ M ACV EC₉₀ ' 3.3mM PFU 55% , ACV EC₉₀ 17 . 10mM n - 가 30mM (ACV EC₉₀ < 0.1 μ M, (10), EC₉₀ 40).

n - ACV 가 , (10 B). , [: Spe ctor et al., Proc. Natl. Acad. Sci. USA 86:1051 - 1055, 1989]. HSV - 1 PFU ACV

18

MRC - 2 (VZV) (CMV) n - ACV

6 가 . , n - ACV MRC - 5 HSV VZV CMV . VZV - C MV - ACV [: Hirsch et al., In Fields Virology Third Edition, B.N.Fields, D.M.Fields, D.M.Knipe, P.M. Howley, eds. Lippincott - Raven Publishers, Philadelphia,

pp. 431 - 466, 1996].

, n -

ACV

.

6

MRC - 5
ACV

(VZV)

(CMV)

n -

그룹	MRC-5 배양물	바이러스	배양물당 IC x 10 ⁻⁴ () = % 억제	ACV 효능	
				EC ₅₀ (μM)	EC ₉₀ (μM)
I	배지만	VZV	35	3	10
II	n-도코사놀, 30 mM	"	7 (80%)	0.3	2
III	n-도코사놀, 10 mM	"	15 (57%)	0.6	4
IV	n-도코사놀, 3.3 mM	"	21 (40%)	1	6
V	플루로닉 F-68	"	33 (6%)	3	10
VI	배지만	CMV	20	30	250
VII	n-도코사놀, 30 mM	"	3 (85%)	2	6
VIII	n-도코사놀, 10 mM	"	8 (60%)	2	25
IX	n-도코사놀, 3.3 mM	"	16 (20%)	8	35
X	플루로닉 F-68	"	20 (0%)	30	250

MRC - 5

, 30, 10, 3.3mM n -
F - 68(16mm, 10⁵ /MØ, 1MØ/)., 가, VZV(I - V) CMV(-)
. n - , F - 68 가 2

(infectious center analysis) (IC)

가 / (VZV) (CMV) [(Ref. JM 1

290, 460L - 134/9 - 23 - 96)rvsd 4 - 4 - 97].

6 I - V , 350,000 VZV

VZV 500 FPU MRC - 5

4 . ACV 3 μ M EC₅₀ 10 μ M EC₉₀ VZV. VZV 10mM EC₅₀ n - . ACV EC₅₀ EC₉₀ n -

30mM 90% 80% .

가 CMV

(- X, 6). CMV 500PFU MRC - 5 4 ,

200,000 MRC - 5 가 , ACV EC₅₀ EC₉₀ 30 μ M 250 μ M. n - EC₅₀ 10mM CMV . CMV ACV EC₅₀ EC₉₀ n - 10 - 30mM 90% .

19

ACV

HSV - 1

n -

n - ACV 가 n - HSV - 1 PFU F - 68^R

(11). , n - (15mM)

500PFU/HSV - 1

. 3 , HSV - 1 PFU . 19 μ M ACV - HSV

- 1 EC₉₀ , n - 0.9 μ M (21).

(Ara - A) , n - 22 μ M EC₉₀ , n -

1.4 μ M (16) EC₉₀

6.8 μ M EC₉₀ , 가

(rivabirin) , n - 1.35 μ M (5) EC₉₀

0.33 μ M (75) EC₉₀ HSV - 1

HSV (rifampicin)

20

n - (PFA) HSV - 1 가

n - PFA 12

. A , , 3 HSV - 1 10⁷ PFU

, PFA가 18 μ M EC₉₀ PFU . PFU PFA 가

, F - 68^R

10 HSV - 1 PFU , PFA 17 μ M EC₉₀ 가 PFU

n - PFA 가

12 B , PFA가 n -

, 5 - 6x10⁵ PFU가 n - F - 68^R

, n - 가 F - 68^R PFA

21

n - 가

n - , n -

12 B ,

5 - 6 x 10⁵ PFU 3 , n - F - 68^R

13 A , (F - 68^R)

2, 20 25 μ M EC₅₀ , - A

EC₅₀ 15mMn - 10

ACV , n -

13 B EC₉₀ ,

가 n - 가

가 n - ACV -

가 가 , n - AC

V ,

가 ACV - HSV

, n -

HSV n - ACV

n - ACV HSV - 1 HSV - 2 , VZV CMV
가 ACV

[: Hirsch et al., In Fields Virology Third Edition, Third Edition, B.N.Fields, D.M.Knipe, P.
M. Howley, eds. Lippincott - Raven Publishers, Philadelphia, pp. 431 - 466, 1996]. ,
HSV

가 ,
. VAV CVM가 HSV , n -
ACV

n -
n - 가 2
n - 가
n - 가
n - 가

. ACV n -
n - ACV

n -
. PFA n - HSV , HIV AZT
n - 가
/n - 가

n - ACV
n - 가 HIV
가 , HSV n -
ACV , n -
가
n -
가 ,

n-가 (8) HSV ACV n-
 , CMV ,
 , GI ,
 . n-
 . n- 가 , n-
 .
 n- /
 , n- , HSV
 가 HSV - (gan
 ciclovir) [: Oliver et al., Virol. 145:84 - 93, 1985]. n-
 B (Franken et al., Na
 ture Medicine 2:1379 - 1382, 1996) HIV - 1 T (Caruso et al., Virol. 206: 495 - 503, 1995)
 [: Caruso et al., Virol. 206:495 - 503, 1995].

PFA
 , PFA
 가 가 가
 가 가
 .
 1 5
 PFA가 , 1 5
 , 0.05 40% , 1 20%
 .

n- n-
 5 500mg
 0.7 μ g/Ml [: Tyring et al., Arch Dermatol 13
 4:185 - 191, 1998]. 1000mg 4.3 μ g/Ml
 8 5mg/kg 1
 10 μ g/Ml (Blum et al., Am. J. Med. 73:186 - 19
 2, 1982). n- (), 1 5
 가 .

(57)

1.

2.

1 , C18 - C28 , (brassidyl) , n -
 , n - ,

3.

1 , 0.05 40%

4.

1 , 가 (acyclovir), (adefovir),
 (azidothymidine), (brivudin), (cidofovir), ddC, ddI, (fanciclovir), (
 ganciclovir), (idoxuridine), (lamivudin), (lobucavir), (penciclovir),
 (ribavirin), (soribudine), (trifluridine), (valaciclovir) (Ara)
 A

5.

1 , 가 0.1 10%

6.

1 , 가 0.1 10%

7.

1 , 가

8.

7 , 가 1,000 25,000

9.

7 , 가 6,000 12,000

.

10.

7 , 가 - 9 - 10

.

11.

7 , 가 .

12.

1 , , , , , (sunscreens), , ,
, , (agent) 가

.

13.

1 12 ,
, .

14.

13 , 1 5 가 , , ,

.

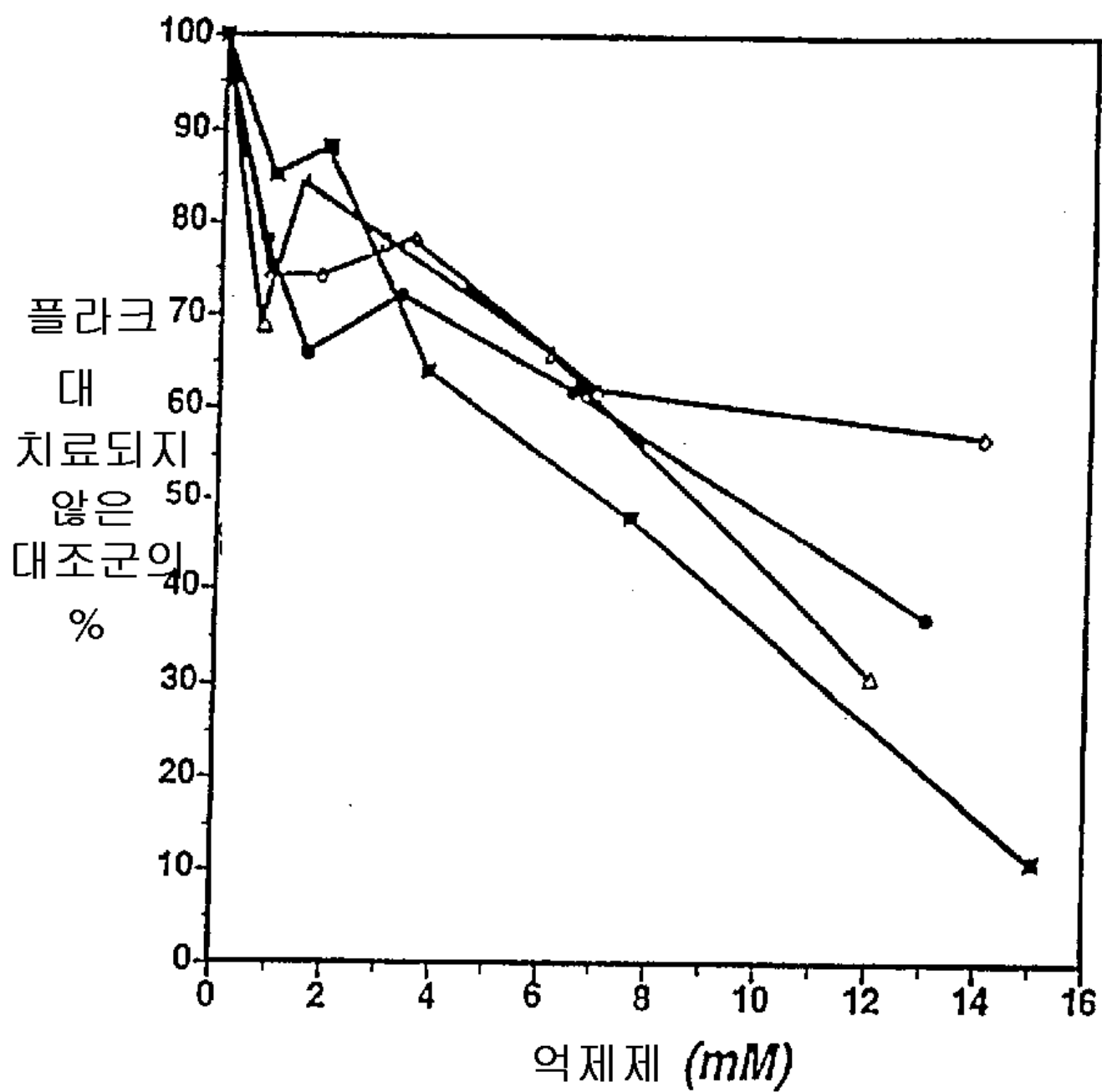
15.

1 14 1 5 0.01 10g
1 12 .

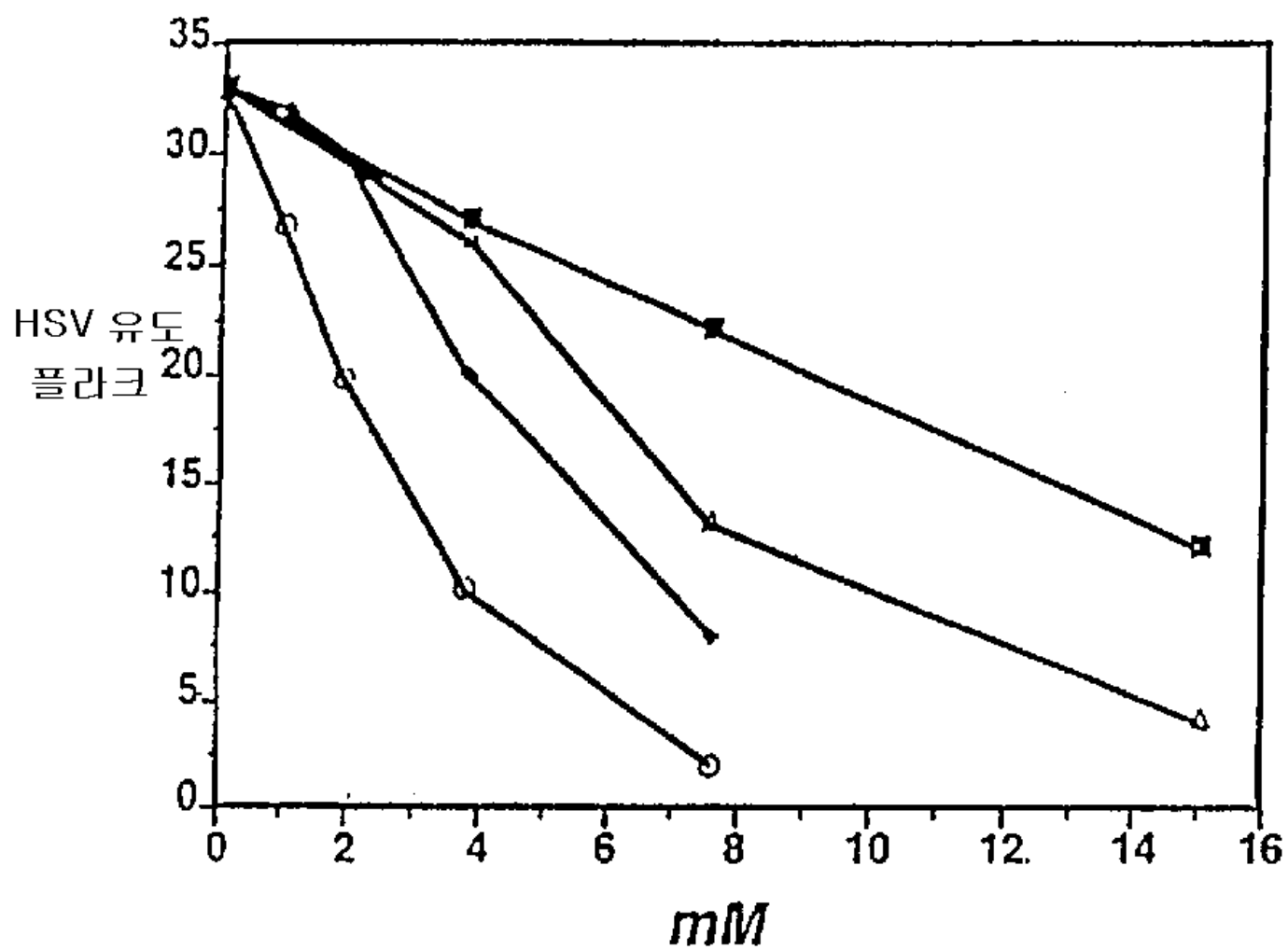
16.

15 , 가 , , ,
.

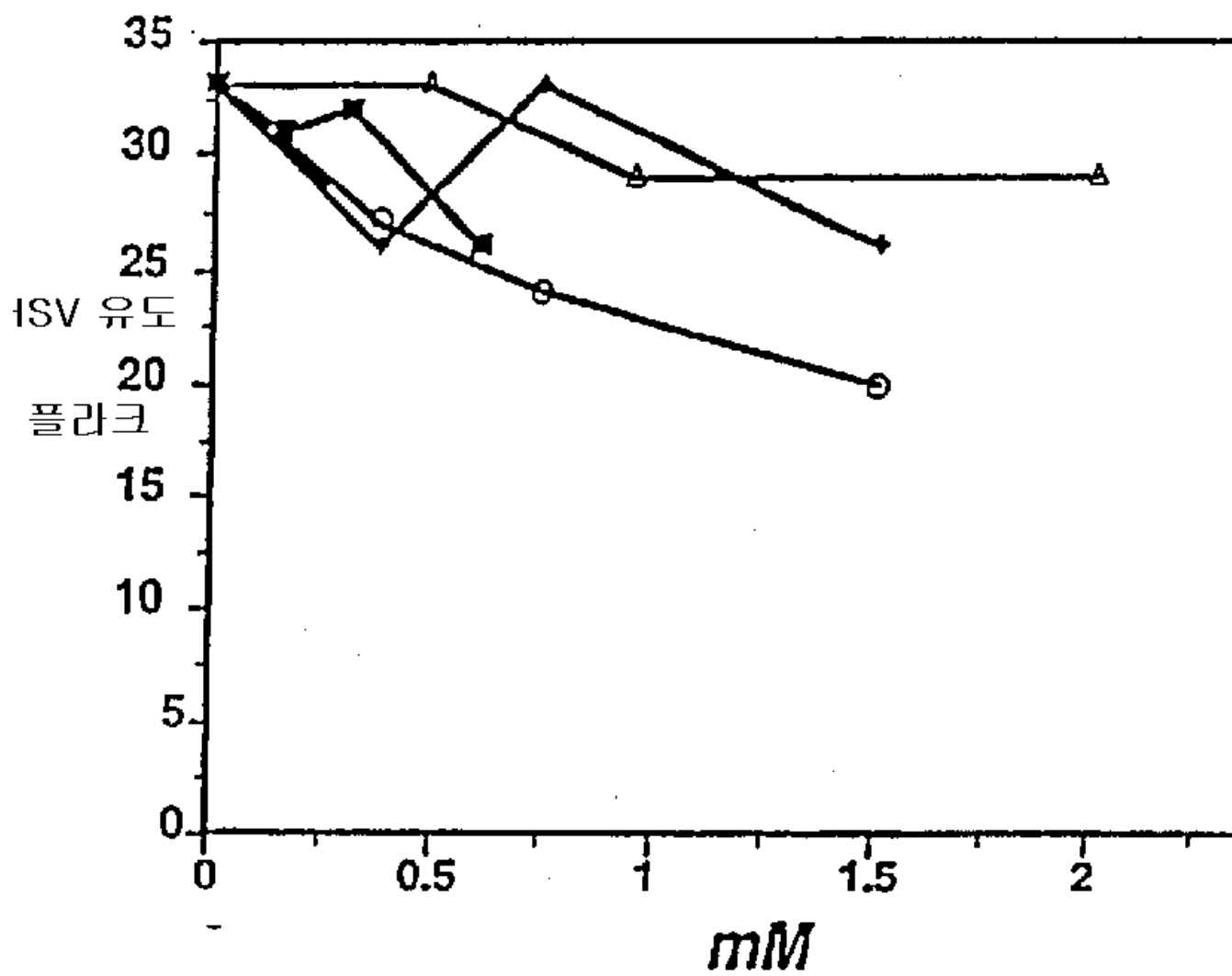
1



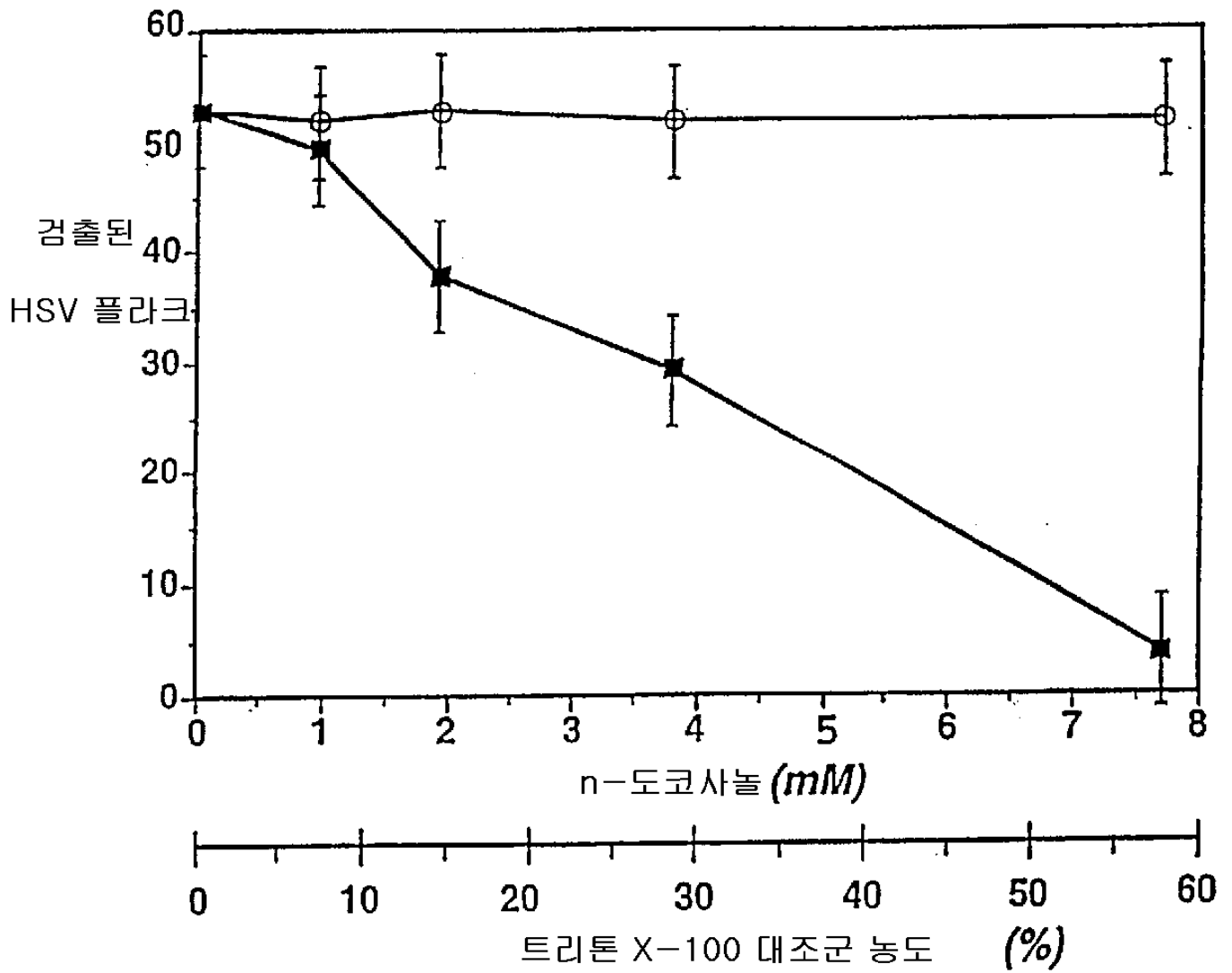
2a



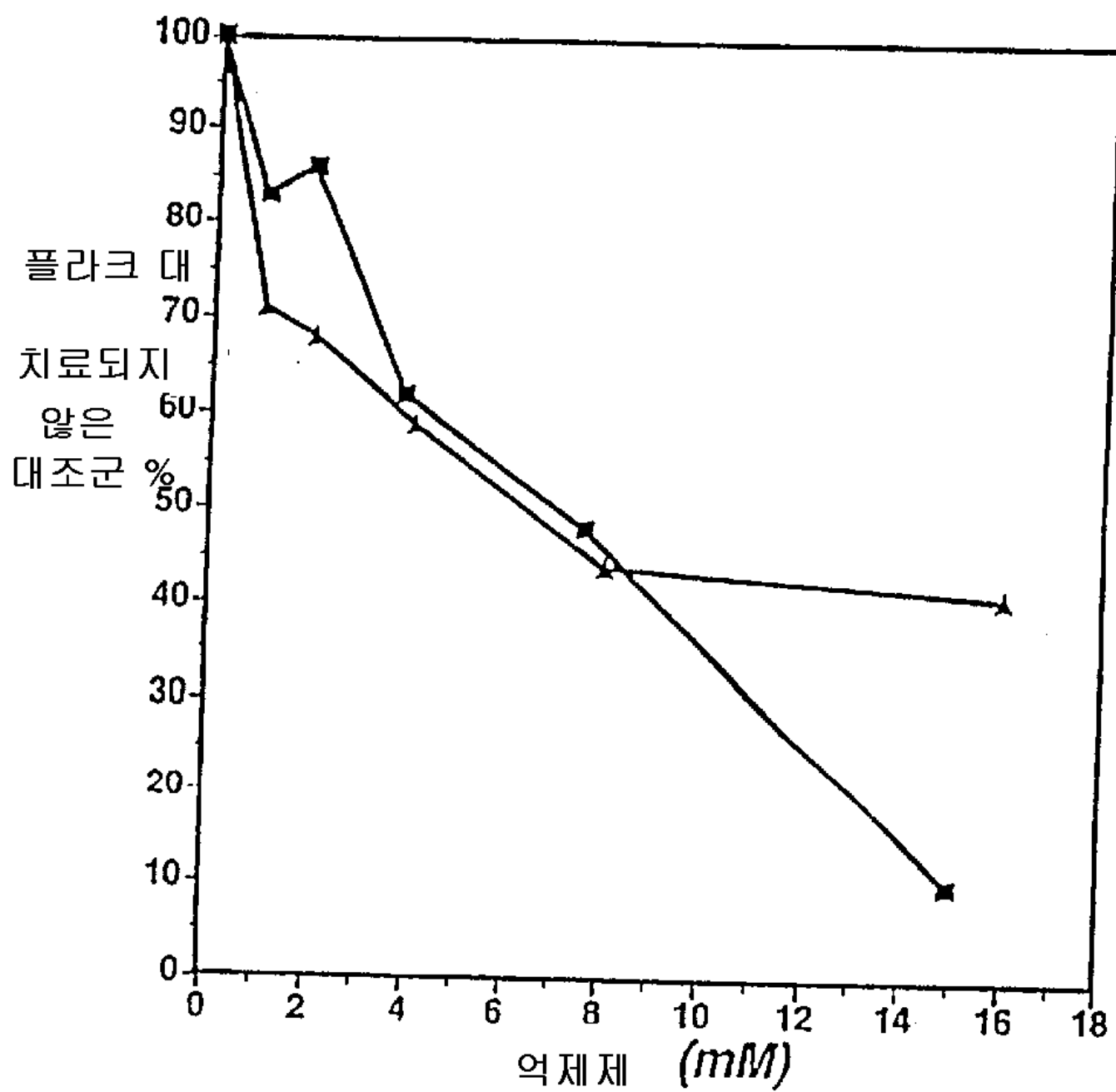
2b



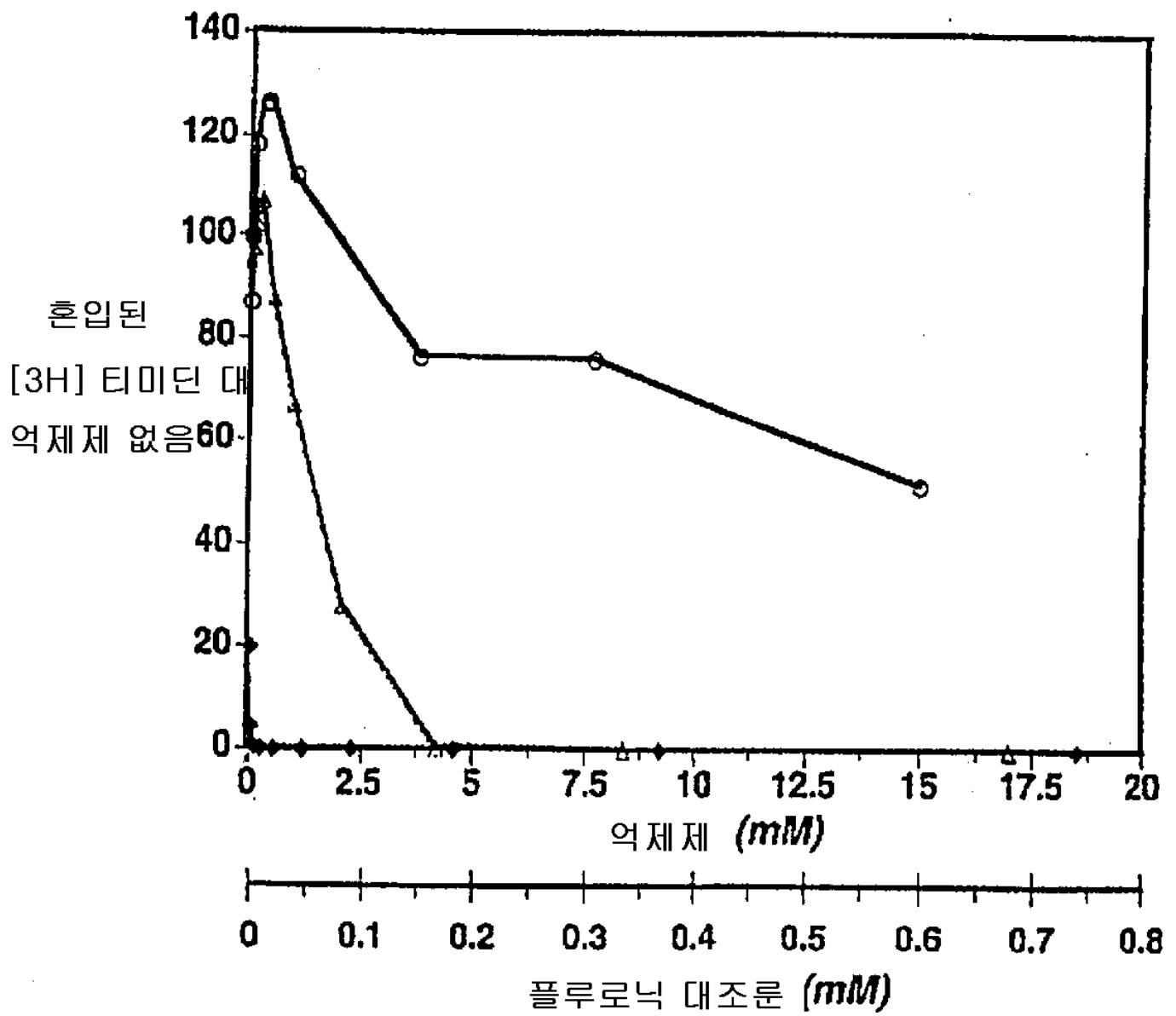
3



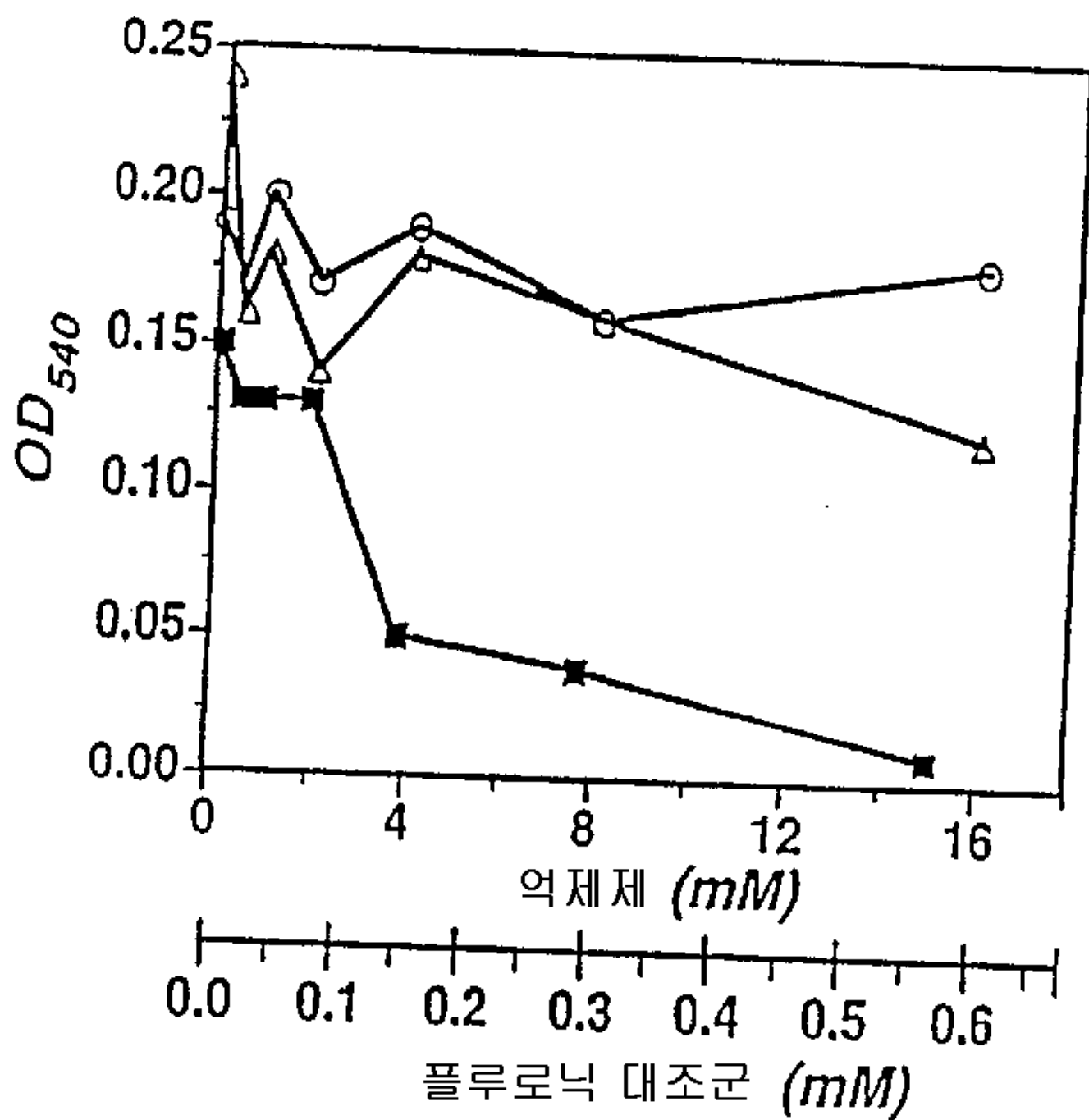
4



5



6a



6b

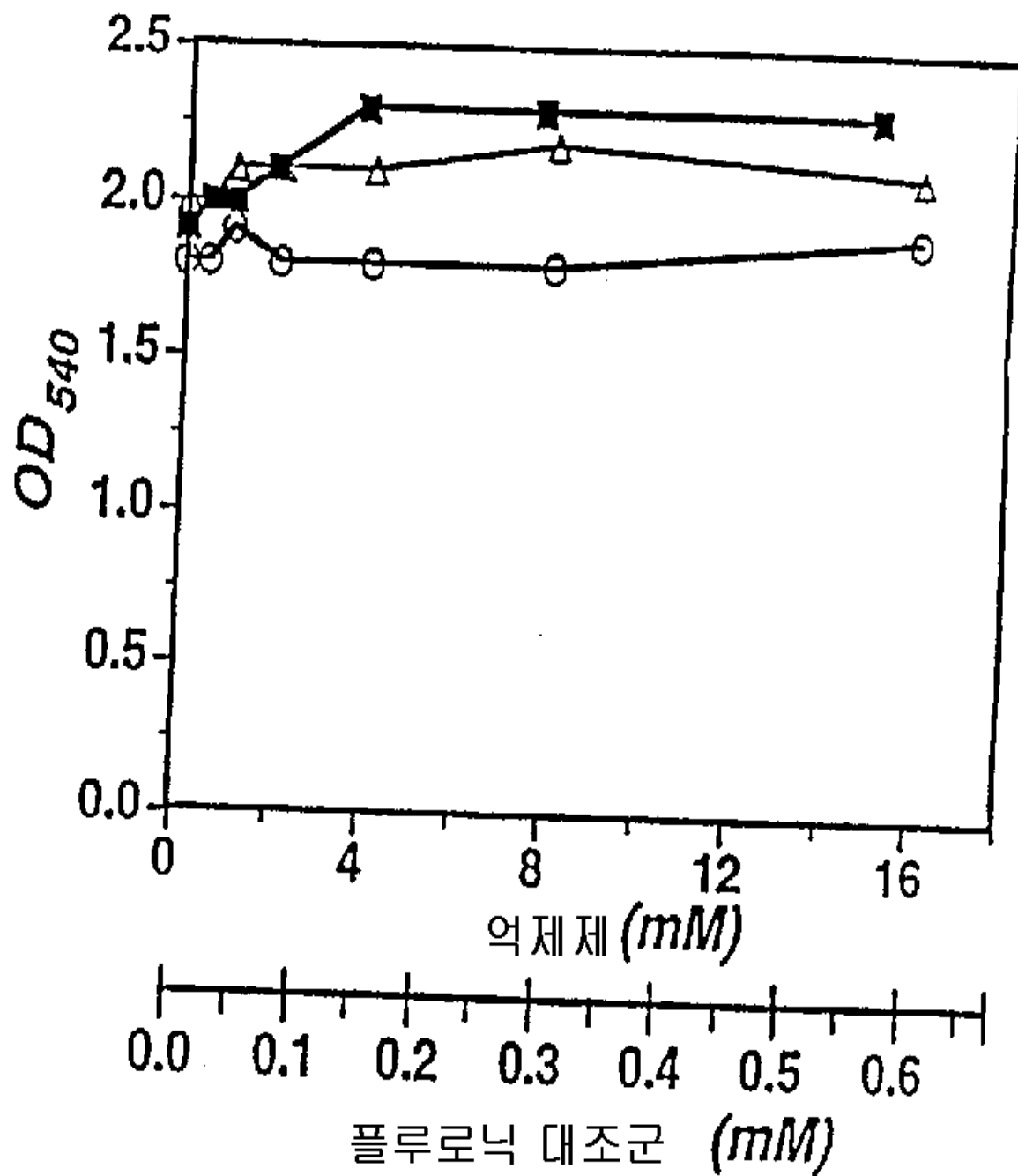
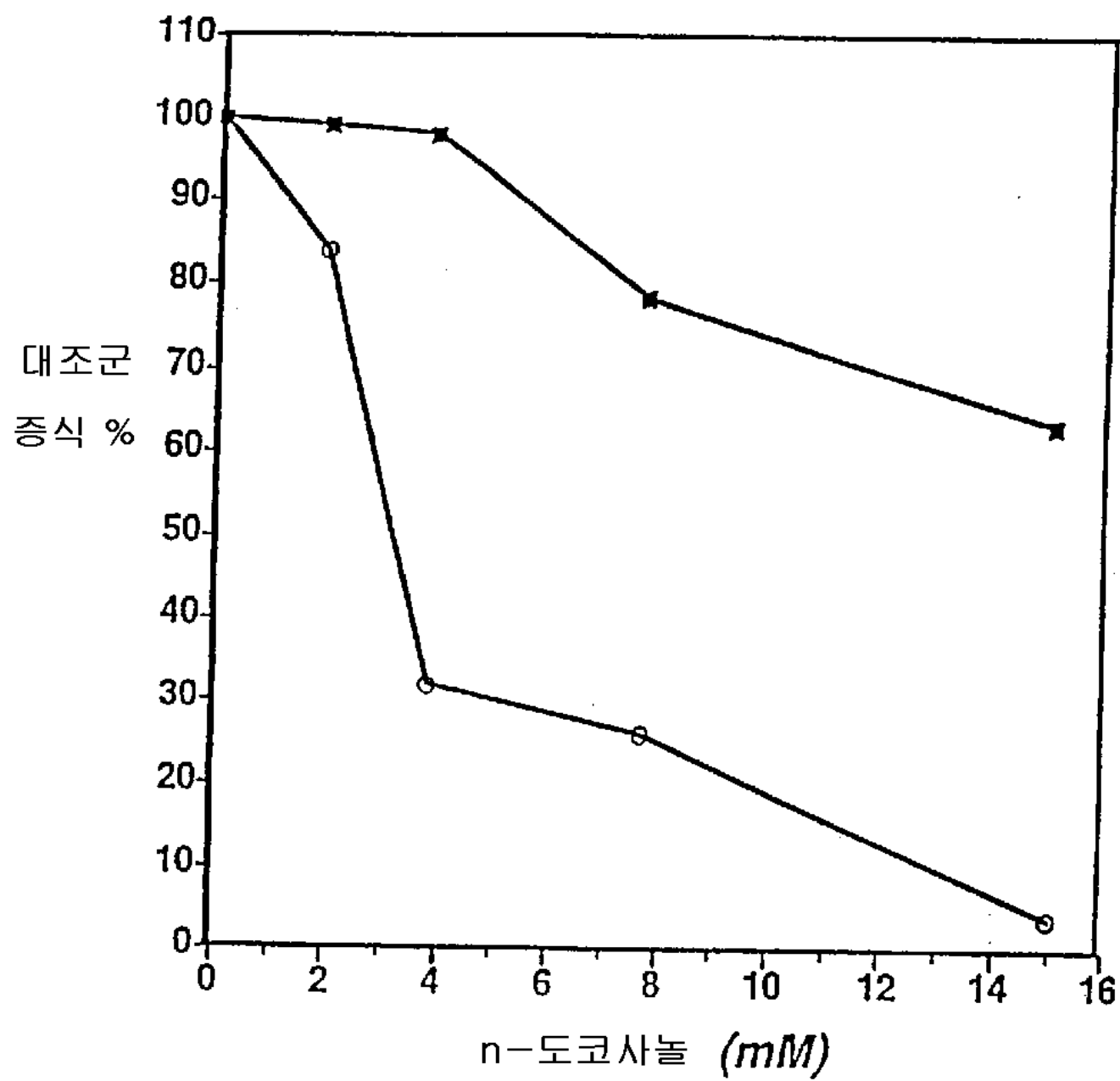


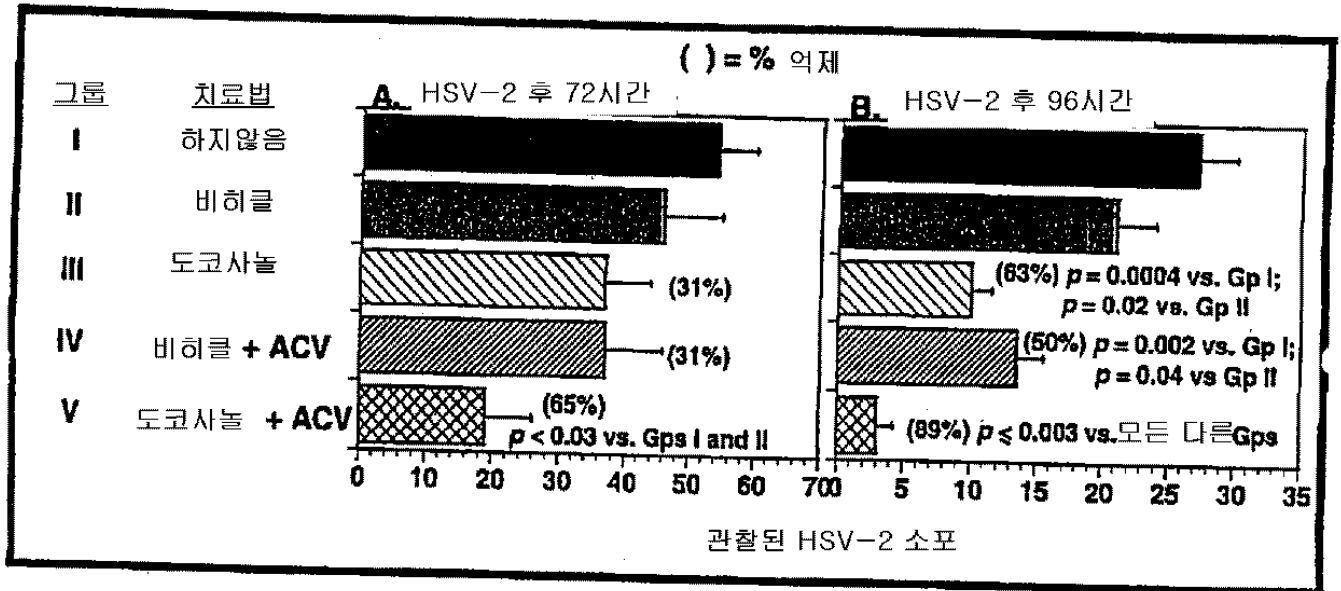
FIG. 6B

7

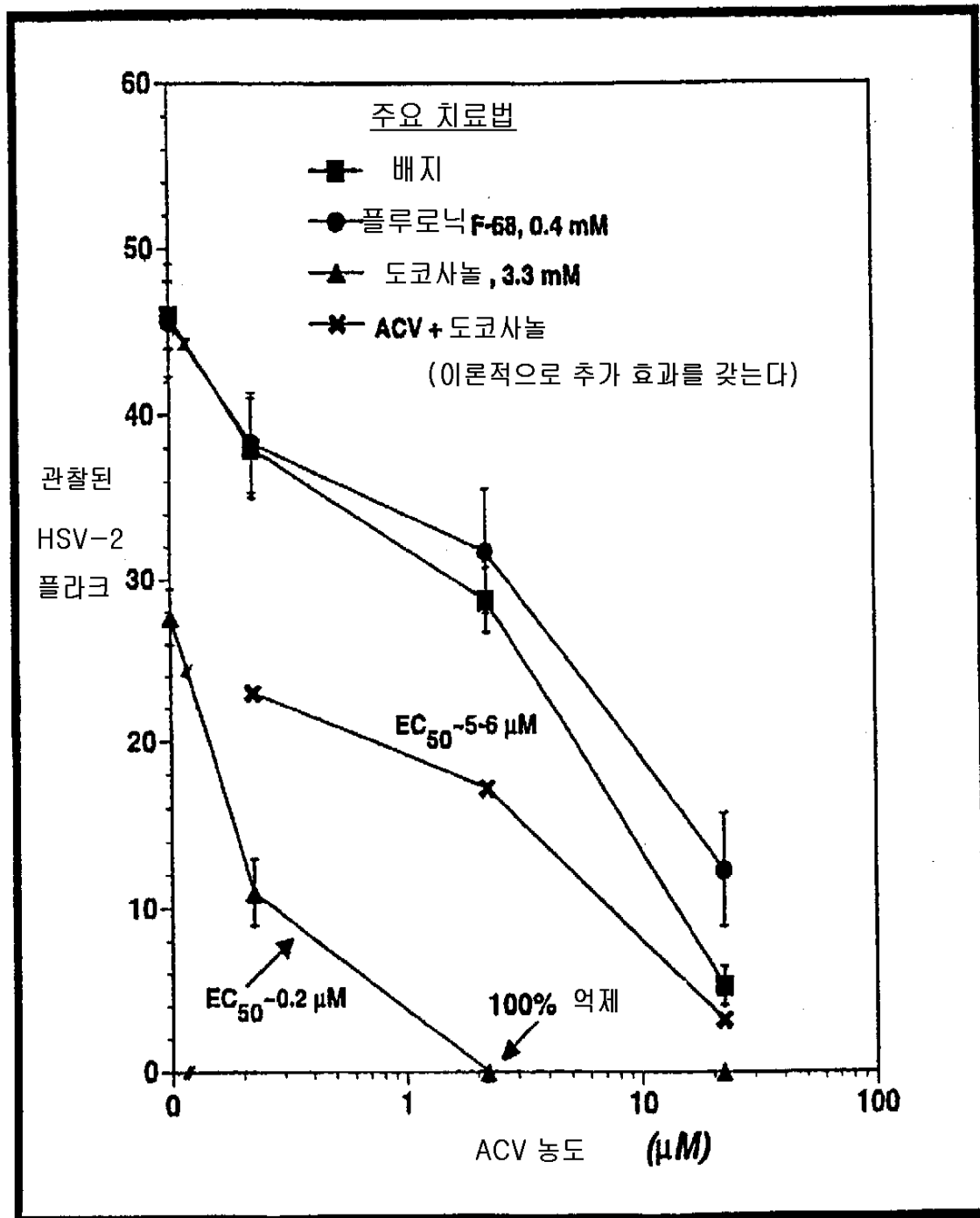


n-도코사놀과 아시클로버(ACV)의 혼합 크림 제형은 하나의 약제를 함유하는 크림보다

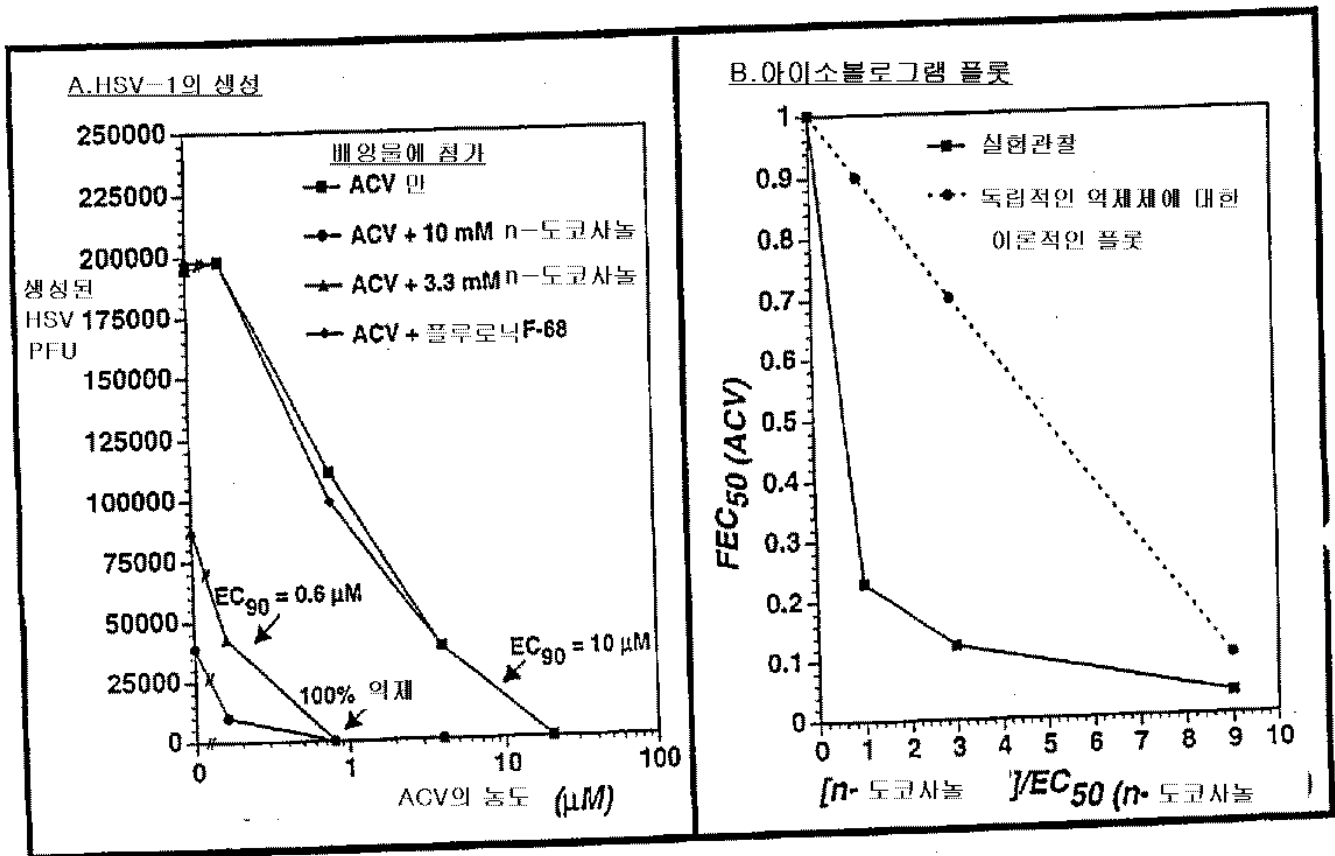
더 잘 탈기니픽의 HSV-2 피부 질환을 억제시켰다



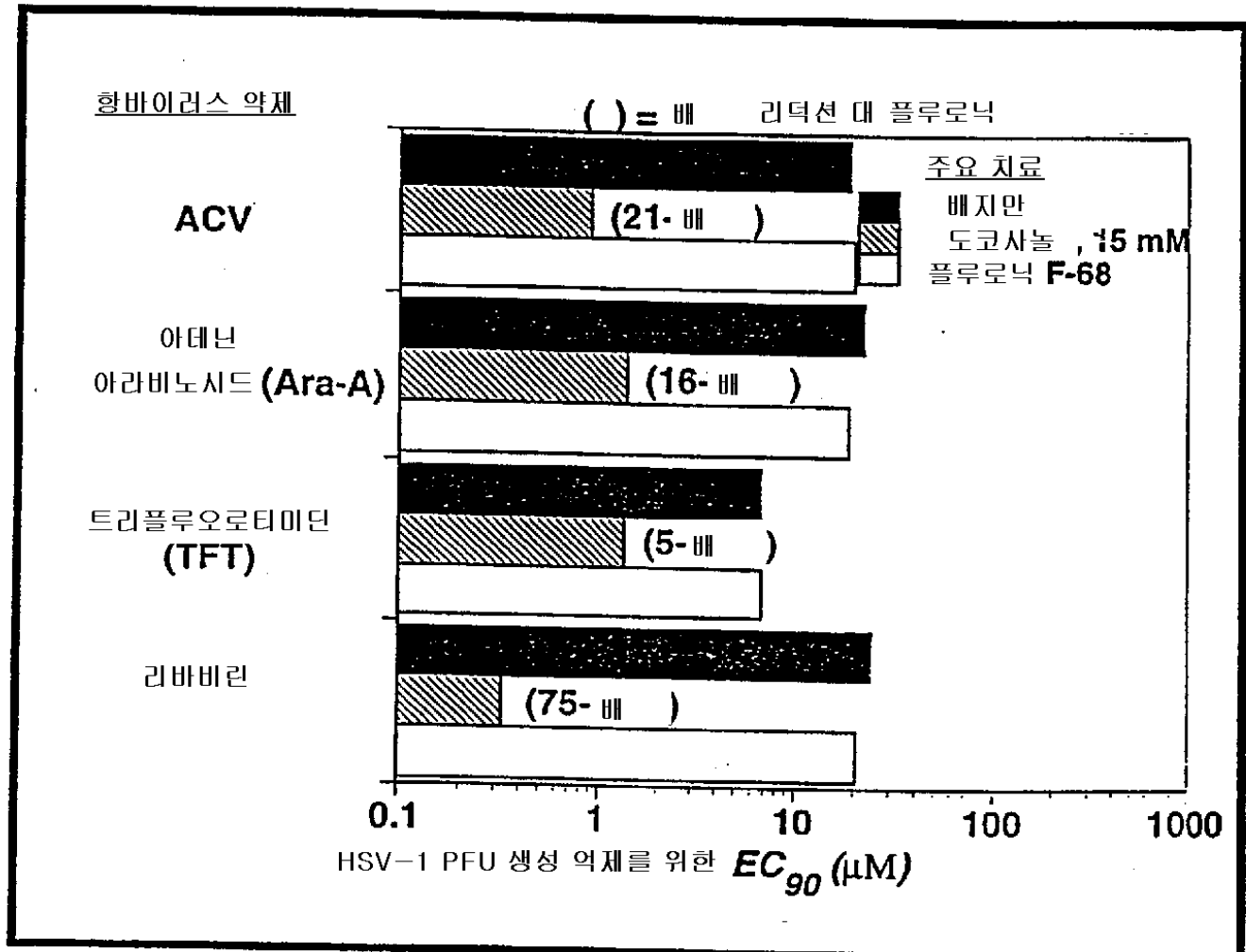
n-도코사놀과 ACV는 베로 세포 배양물에서 상승적인
항-HSV 활성을 나타낼 수 있다.



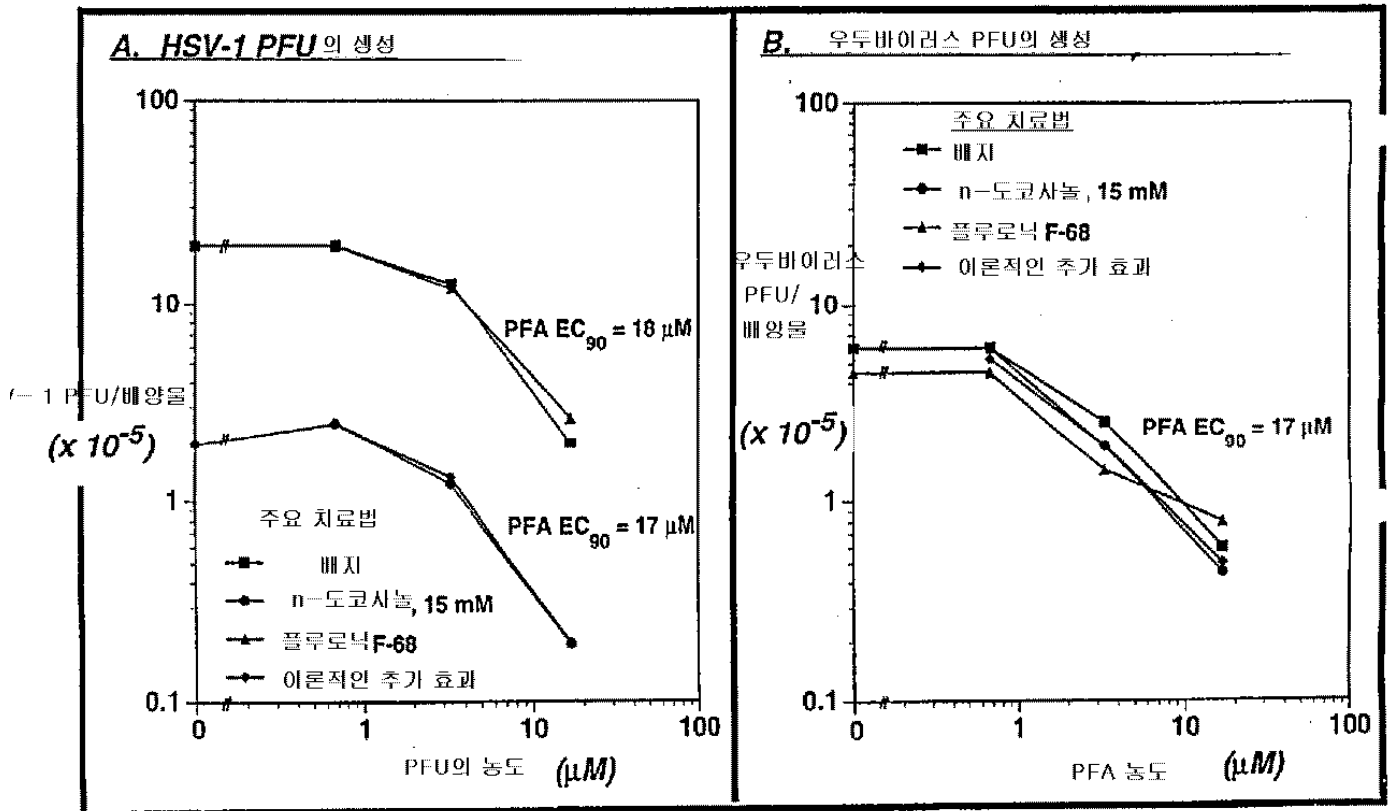
n-도코사놀과 ACV는 배로 세포 배양물에서 SV-1 생성에 대해
상승적인 억제 활성을 나타낸다



ACV 이외의 뉴클레오시드 유사체는 생체외 HSV-복제를 억제하도록
n-도코사놀과 상승작용할 수 있다



n-도코사놀과 포스포노포르메이트(PFA)는 HSV-1에 반하여 추가 항바이러스 활성을 나타내고
우두바이러스에 반하여 상호반응하지 않는다



n-도코사놀은 우두바이러스 복제에 대해 뉴클레오시드 유사체의 항바이러스 활성을 증가시킨다.

