

1

(Age - related macular degeneration, ARMD)

(Retinitis pigmentosa, RP)

ARMD

(Sur Ophthal,1988, 32, 252 - 269).

(photo - oxidative stress)

(model)

: (photoreceptor)

(retinal pigment epithelium)

(Invest Ophthal & Vis Sci.,1996, 5, 450 - 472;Sur Ophthal,1988, 32, 375 - 413);

(Trans AM Ophthal Soc.,1996, 94, 411 - 430;Res Commun Mol Pathol Pharm

acol,1996, 92, 177 - 189);

ARMD RP

(Arch Ophthal,1

992, 110, 99 - 104;Invest Ophthal & Vis Sci.,1996, 37, 775 - 782);

(Proc Nat Acad Sci.,1992, 89, 11249 - 11253;N

ature,1990, 347, 83 - 86).

: (ascor

bate),

(dimethylthiourea),

(- tocopherol)

(- carotene)

(Invest Ophthal & Vis Sci.,1985, 26, 1589 - 1598;Invest Ophthal & Vis Sci.,1992, 33, 450 - 472

;Nippon Ganka Gakkai Zasshi, 1994, 98, 948 - 954; Cur Eye Res,1995, 15, 219 - 232);

(flunarizin

e) (calcium antagonists)(Exp Eye Res.,1993, 56, 71 - 78;Arch Ophthal,1992, 109, 554 - 6

22); (bFGF),

- 1 -

(Proc Nat Acad Sci., 1992, 89, 11249 - 11253);

(Graefes Arch Clin Exp Ophthal,1993, 231, 729 - 736);

(Cur Eye Res.,1

991, 2, 133 - 144).

(excitatory amino acid antagonist)가

가

(Exp Brain Res.,1995, 106, 93 - 105;Vis Neurosci.,1992, 8, 567 - 573).

RPE

(dextrom

ethorphan treatment)

가

(Arch Ophthal, 1993, 111, 384 - 388).

, MK - 801

60

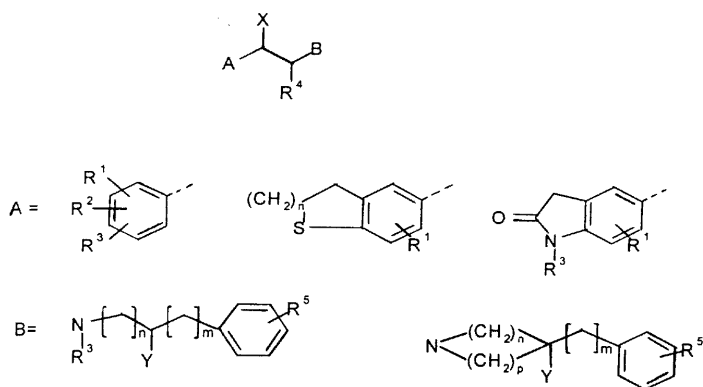
3 20

(Invest Ophthal & Vis Sci., 1997, 38, 138

0 - 1389).

MDA, NMDA (NMDA receptor channel complex); (NMDA (NMDA (redox) (" RPE ") (PDT) (excitotoxicity) /

1



1, Y, X, OH, H,

m 0 - 3,

n p 1 2,

R¹, R² 4-OH, C1-C4, R³ 4-OH, R¹, C1-C16, C1-C4

R², C1-C4, OH, C1-C4,

R³ R⁴, C1-C4,

R⁵, C1-C4, OH, C1-C4, C1-C16

1

) / R S 2 - [4 - (4 -) -] - 1 - (4 -) (

가 (5,547,963).
lin and Exp Ophthal,1996, 234 supplement 1, S96 - 100), (Graefes Arch C
가

1 100 mg 0.01 500 mg
(transdermal patch), (parenteral) (iontophoresis) (intravitreal) (retrobulbar)
U

S 5,604,244
0.001 - 10 μ M 0.01 - 5 μ M

가 , 가 ,
가,
가
- 940
가

pH 4 8
.001% 5 % .01 2
% 4 1 - 2 1

(R S)
(Drugs of the Future,1994, 19, 905 - 909), 가
4,690,931

가
RPE

1 1

가

가

(apoptosis)

(Shahinfar, S., Edward, D. P., Tso, M.O. (1991),

Current Eye Research, 10:47 - 59; Alber, A. S., Chang, C.J., Fu, J., Tso, M. O. (1994),
Investigative Ophthalmology & Visual Science, 35(supple):1517).

(C

hang, C. J., Lai, W. W., Edward, D. P., Tso, M. O. (1995),
Archives of Ophthalmology, 113:880 - 886; Portera - Cailliau, C., Sung, C. H., Nathans,
J., Alder, R. (1994), Proceedings of National Academy of Science(U.S.A), 91, 974 - 978; Buchi, E. R. (1992),
Experimental Eye Research, 55: 605 - 613
; Quigley, H. A., Nickells, R. W., Kerrigan, L. A., Pease, M. E., Thibault, D. J., Zack, D. J. (1995),
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(Noell, W.K., Walker, V.S., Kang, B.S., and Berman, S.(1996),
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(Lawwill, T. (1973), Investigative Ophthalmology & Visual Science, 12:45 - 51),
(Colier, R.J. and Zigman, S. (1989), UV 가
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UV Investigative Ophthalmology & Visual Science, 30:631 - 637),
(Tso, M. O. M. (1973),
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: Vision Research, 20:1105 - 1111; Sperling, H. G., Johnson, C. and Harwerth, R.S. (1980),
Vision Research, 20:1117 - 1125; Sykes, S. M., Robison, W.G., Jr., Waxler, M. and Kuwabara, T. (1981),
Investigative Ophthalmology & Visual Science, 20:425 - 434; Lawwill, T., (1982),
3가
: Transactions of the American Ophthalmology Society, 80:517 - 577), (Marsh
all, J., Hamilton, A.M. and Bird, A.C. (1975),
British Journal of Ophthalmology, 59:610 - 630; Green, W. R. and Robertson, D.M.(1991),
American Journal of Ophthalmology, 112:520 - 527).

(Young, R.

W. 1998), Surrey of Ophthalmology, 32:252 - 269; Taylor, H. R., West, S., Munoz, B., Rosenthal, F.S., Bressler, S.B. and Bressler, N.M. (1992), 가
Archives of Ophthalmology, 110:99 - 104; Cruickshanks, K. J., Klein, E.K. (1993),
Beaver Dam Eye , Archives of Ophthalmology, 111:514 - 518).

SD (Sprague Dawley rat) 1 MK - 801, 2
(memantine) 1 2 , (~
0, 24 48 , (~

220fc) 6
 (electroretinogram, ERG) . a - b -
 ERG , a -
 , b - (muller) . 75 m
 g/kg - (ketamine - HCl) 6 mg/kg (xylazine)
 5 ERG (ganzfeld)
 가 ERG (voltage)
 (log intensity)

가 : 6 , 5 ERG
 (ANOVA, P < 0.001; Bonferroni t - test, P < 0.05)
 (1A). a - b - 70% 가

1 1:

MK - 801,

1.) MK - 801. 20 mg/kg MK - 801

. a - 734.05 μV (SEM = 36.79 μV)
 20 mg/kg MK - 801 537.93 μV (SEM = 34.42 μV) (1A) . , b -
 , MK - 801 1449.77 μV (SEM = 68.12 μV) . 2 1807 μV (SEM = 74.32 μV)
 01 10 mg/kg MK - 8

2.) .20 mg/kg ()
 (1A). ERG a - b - 57% 53%
 2.4 2.2 가 . 2 10 mg/kg
 ERG
 32%

3.) . 1A , 2 mg/kg
 . 20 mg/kg , 20 mg/kg
 ERG

2 2: R S

1.) () 20 40 mg/kg
 (1B). 20 40 mg/kg
 a - 2.4 2.25
 5 a - 20 mg/kg 395.82 μV (SEM = 46.
 4 μV) , 40 mg/kg 419.85 μV (SEM = 63.88 μV) . 20 40 m
 g/kg , 60%

2.) R - 1B , R - 0.5
 . 20 mg/kg R - 5
 38% 36% , a - b -
 , 40 mg/kg R - (1B).
 2 50% . a - b -
 397.25 μV (SEM = 77.14 μV) 812.87 μV (SEM = 160.13 μV) . 80 mg/kg R -
 , a - b -
 40%

3.) S - .5 mg/kg S - ERG
 1B , 2 . 10 mg/kg
 S - 5
 , a - b - 64% 76% ,
 20 mg/kg S -
 , 2 , 5
 62% . a - b - 418.04 μV (SEM = 56.18 μV)
 1015.95 μV (SEM = 141.49 μV) .

가 RPE

S - 가 MK - 801
 2

(,) - , 가

(CNS) 20%가 6 6 18%가

(cytokine) 가 RPE

가
 LE(Long Evans) 64, 48, 2
 4 2 , (: 200 micrones, : 100 mW,
 : 0.1) 2 4 3, 19 24 . 48
 (resin) 가
 가

(image analysis system)

:

48

가

(bruch)

, RPE

RPE

50,627.07 55,243.

65 μ^2 (2 3).

1.) (2 3).

mg/kg

7 μ^2 (SEM = 2555.47 μ^2)

가

22,406 μ^2 (SEM = 3559.3 μ^2)

60% 가

.10 55,411.6

2.) R - .40 mg/kg R -

. R -

28%

가

36,016 μ^2 (SEM = 4779.49 μ^2)

(3). 20 mg/kg R -

16%

가
가

3.) S - .20 mg/kg S -

94 μ^2)

15%

43,098.5 μ^2 (SEM = 2992.

(3).

R -

R -

2

2

S -

NMDA

R -

NMDA

3 3

1.0%	w/v%	
		1%
		0.5%
2 -		0.2%
		0.75%
2 -	EDTA	0.01%
	80	0.05%
		0.01% + 5%xs
		pH 5
		pH 5
		q.s to 100%
	(290mOsm/kg)	pH = 5

4 4

3.0%	w/v %	
		3.3%
		0.9%
	80	0.1%
		q.s to 100%

5 5

10 mM IV	w/v %	
		0.384%
L -		2.31%
		pH 3.8
		pH 3.8
		q.s to 100%

6 6

0.3%	w/v %	
		0.33%
		0.07%
		4.3%
2 -	EDTA	0.1%
		0.01%
		pH 4.0
		pH 4.0
		q.s to 100%

7 7

R - 5 mg		
	mg/ (221 mg)	% w/w
R -	5.53	2.5%
	206.67	93.52%
	6.6	2.98%
	2.2	1.00%

8 8

S - 50 mg		
	mg/ (221 mg)	% w/w
S -	55.25	25%
	156.95	71.02%
	6.6	2.98%
	2.2	1.00%

9 9

R - 10 mg		
	mg/ (221 mg)	% w/w
R -	11.05	5%
	201.15	91.02%
	6.6	2.98%
	2.2	1.00%

10 10

20 mg		
	mg/ (221 mg)	% w/w
	22.1	10%
	109.1	86.02%
	6.6	2.98%
	2.2	1.00%

(57)

1.

2.

1 , 가

3.

1 , 가 1

1

7 , R S

9.

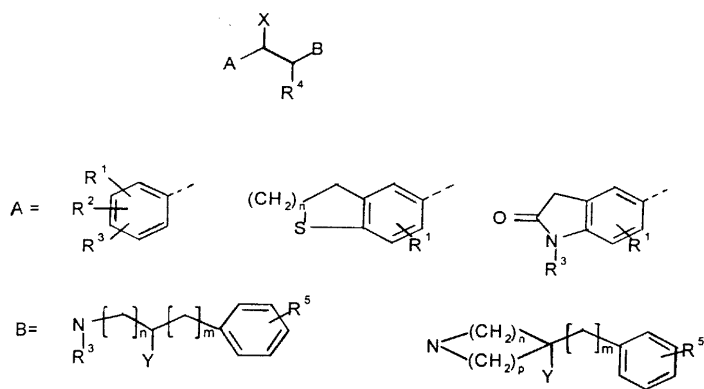
10.

9 , 가

11.

9 , 가 1

1



1 , Y X OH H ,

m 0 - 3 ,

n p 1 2 ,

R¹ , , , C1 - C4 , OH, C1 - C4 , , C1 - C16 , C1 - C4

R² 가 4 - OH

OH

, C1 - C4

, OH, C1 - C4

R³ 가

, C1 - C16

, C1 - C4

R² , , C1 - C4 , OH C1 - C4 ,

R³ R⁴ C1 - C4 ,

R⁵ , , , C1 - C4 , OH, C1 - C4 , , C1 - C16

12.

11 ,

2

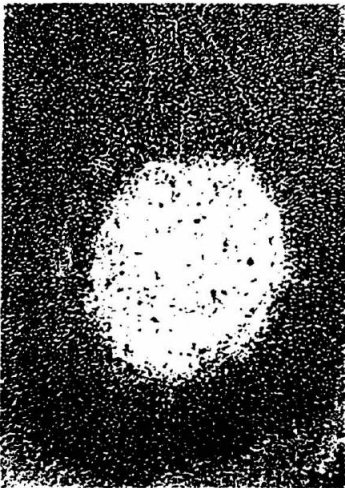
레이저 손상 중심부



손상 부위 주변



담체

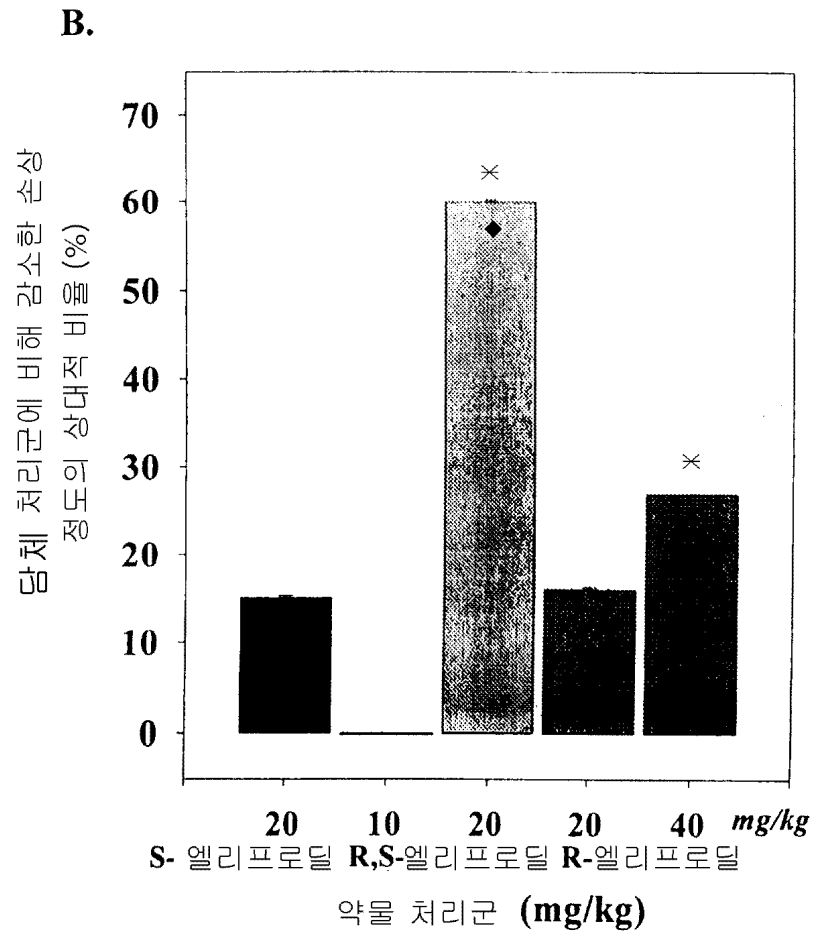
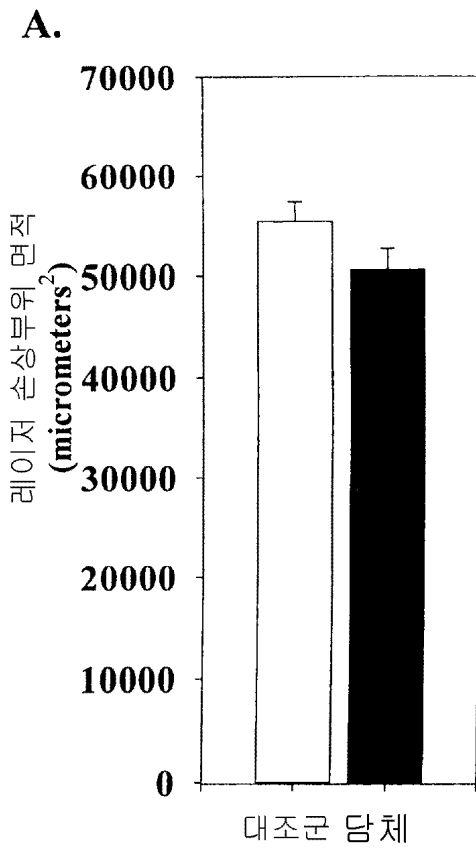


AL04043 - 10mg/kg



AL04043 - 20mg/kg





* 담체에 비교되는 상당히 좁은 손상면적 (P<0.05)

◆빛에 의한 망막질환에 대한 현저한 예방을 제공하는 복용량