

(19)
(12)

(KR)
(A)

(51) 。 Int. Cl. 7
A61K 35/78

(11)
(43)

2003-0035974
2003 05 09

(21) 10-2002-0065744
(22) 2002 10 28

(30) 1020010066810 2001 10 29 (KR)

(71) 2 39-1

(72) 3 107 105-1701

89 318-3 03

288 2 210-204

639 203-905

781-3 312

104-1 LG

57 1-505

(74)

:

(54)

1 / - ,
 2 - ,
 3 / - ,
 4 - ,
 5 / - ,
 6 ,
 7 DPPH ,
 8 / ,
 9 , 3- ,
 10 , 3- ,
 11 , 3- ,
 12 , 3- .

가 (myocardial infarction) (cell death) (brain infarction)
 가 (glycolysis)
 , (cerebral ischemia) (cardiac arrest) 가
 가

가

(free radical)

(reactive oxygen species, ROS)

(Koroshetz amp; Moskowitz, *Trends Neurosci* . 17:227, 1996).

가

가 (xanthine oxidase)

(Fe²⁺)

(Fenton)

(superoxide anion radical)

(hydroxyl radical)

ATP

(polyunsaturated fatty acid)

(Halliwell and Gutteridge, *Trends Neurosci* . 8:

22, 1985).

2

(senile plaque)

(A)

(peroxynitrite)

(Behl, *Prog. Neurobiol* . 57:301, 1999).

가

가

(Ebadi , *Prog. Neurobiol.* 48:1, 1996).

(Choi, *Neuron* 1:623, 1988).

(Tirilazad), U-74389G,

(ebselen)

MDL 74,722

21-

(Clemens, *Free Radic. Biol. Med* . 28:1526, 2000).

noamine oxidase)-B

(Ebadi , *Prog. Neurobiol* . 48:1, 1996).

(selegiline)

(mo

II.)

(*Opuntia ficus-indica* (Linne Mi

(Trejo-Gonzalez , *J. Ethnopharmacol.* 55:27-33, 1996; 497, 1998; Galati , *J. Ethnopharmacol.* 76:1-9, 2001).

(31:412, 2000)

70%

(2000 11 15)

44:613, 2000)

6683836

가

가

가

가

1 3
3-methyl ether),

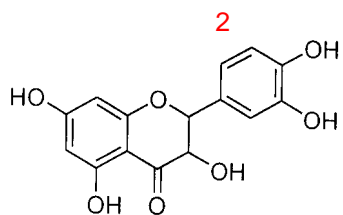
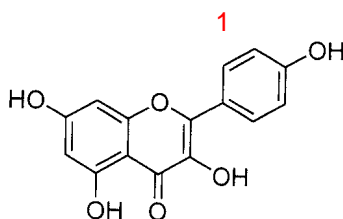
(*Opuntia ficus-indica*)
(kaempferol),

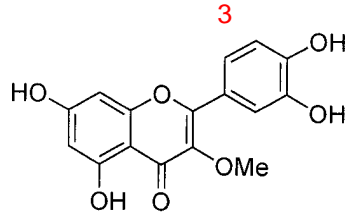
(dihydroquercetin),

3-

(quercetin

:





1 3

가

(: , ,), (: , ,),
 가 (: , ,) 1 , 2 3

(MeOH)

1 kg 0.1 10 ,
 1 kg 0.1 3 10 ,
 (EtOAc) 0.1 5 , 0.5 2

DPPH (1,1-diphenyl-2-picrylhydrazyl)
 /

, DPPH

가

가

가

oyopearl) XAD

, RP-18,

(T

, RP-18

가

3- - - -D-

1

6

3-

3-

-D-

3-

3-

3

3-

/

DPPH

3-

가가

,

/

,

,

,

,

3-

3-

, NMDA

/

(Growth factor withdrawal apoptotic cyto

xicity)

3-

3-

NMDA

3-

NMDA

가

가

3-

17

3-

1

3

/

3-

, NMDA

DPPH

/

가

mg,
mg,

50
150

1,000 mg
3,000 mg

가

3-
10 50,000
10 5,000

1

(N-acetylcysteine), (nimodipine),
(tissue plasminogen activator),

가 N
C E,

< 1> DPPH

(Blois, *Nature* 181:1199, 1958) (Electron
donating ability, EDA) 99.9%
10 $\mu\ell$ 100 μM DPPH (1,1-diphenyl-2-picrylhydrazyl) (99.9 %) 190
 $\mu\ell$ 5 37 30 515 nm
50% (IC₅₀)

< 2>

(Xanthine) (xanthine oxidase, XOD) (superoxide
anion) 가 (Toda, et al., *Planta, Med.* 57:8, 1991)

, 0.1 mM , 0.1 mM EDTA, 50 $\mu\text{g}/\text{M}\ell$ (Bovine serum albumin, BSA), 25 mM
(Nitroblue tetrazolium, NBT) 40 mM Na₂CO₃ ,
7 \times 10⁻³ XOD 가 200 $\mu\ell$ 25 20
6 mM CuCl₂ 6.6 $\mu\ell$ 가 (formazan) 560 nm
(IC₅₀) 50%

< 3>

(*Life Sci.* 68:1567, 2001)
16 18 (-)
25 mM , 5% , 5% , 2 mM L- (MEM, Gib
co BRL)
(poly-L-lysine) 24- (well) 4 5 \times 10⁻⁵
37 95% O₂ /5% CO₂ 2
7 9 10 μM (cytosine arabinoside) 24 72
10 14

< 4>

10 mU/M ℓ) HEPES- (HCSS) 3 (0.5 mM) ()
(serum-free MEM; 25 mM , 2 mM 가 MEM) 10
MEM HCSS MEM
37 95% O₂ /5% CO₂ 20 24
100 μM HCSS 5
MEM 20 24
가 , 20 24

5

< 5>

4

(lactate dehydrogenase, LDH)

가 (Sigma) LDH, 50%

(IC₅₀) 1 2 2 4 (Prism; Graphpad software Inc., USA)

< 6>

(hippocampus) 17 SD

5x10⁴ 가 (poly-L-lysine) 96 2.5x10⁴ 가 B-27 (Life technologies) 2%, 25 M, 0.5 mM 가 (Life technologies) 200 μl 가 37 7 10

< 7> NMDA

200 μM NMDA (Sigma) 6 2 (2) LDH NMDA 24 LDH (Boehringer Mannheim)

< 8>

6 DMEM B27 2% 가 가 B-2 7 DMEM .24 L DH LDH (Boehringer Mannheim)

< 9> (middle cerebral artery occlusion, MCAO)

250 300 g (Sprague-Dawley,) 70% (N₂O) 30% (O₂) 1.5% (isoflurane,) 37 ± 0.5 가 (Nagasawa and Kogure, *Stroke* 20:1037, 1989)

17 mm (Nitcho Kogyo Co., Ltd., Japan) 4-0 17 mm (Bayer Dental, Xantopren) (Optosil-Xantopren) Activator, Bayer Dental) 7 9 mm 0.3 0.4 mm가 25 30 가

가 .120 10 mm 1

(vehicle) 0.9% (1 Ml/kg), 10 mg/kg , 3-

< 1>

가 4 5 () 7.8 kg 40
 .3
 498 g 1
 (CH₂Cl₂, 600 Mℓ×3) (EtOAc, 600 Mℓ×3)
 (BuOH, 600 Mℓ×3)
 1 5 DPPH
 , / - ,
 , 1 2 1 (GM),
 (GD), (GB), (GH) /
 (GE) 60.0 μg/Mℓ IC₅₀ 115.
 9 μg/Mℓ IC₅₀ / - 67.7 μg/Mℓ

< 2>

가 () 15 kg 20 가 41
 4 5 40
 6.0 g 412 g 1.5 (800 Mℓ×3)
 (800 Mℓ×3) DPPH
 / - , 1 5
 , 1 가 (SH)
 8.0 μg/Mℓ, / - 22.2 μg/Mℓ, 가 5
 μg/Mℓ IC₅₀ 21.2

< 3>

() 32.6 kg 20 가 4 5
 .3 40
 819.9 g 1 (600 Mℓ×3)
 (600 Mℓ×3) DPPH
 , / - , 1 3
 , 3 4 1 (FH),
 (FD), (FB), (FH) /
 (FE) 60 μg/Mℓ, / -
 15.2 μg/Mℓ, 17.5 μg/Mℓ IC₅₀
 (FE) 가 ,
 (SE) 가 (GE)
 (oxidative injury)

활성 용매분획	DPPH 라디칼 소거능 (IC ₅₀ , µg/ml)	잔틴/잔틴 옥시다제-유발 신경세포독성 억제효과 (IC ₅₀ , µg/ml)	과산화수소-유발 신경세포독성 억제효과 (IC ₅₀ , µg/ml)
열매의 메탄올 추출물 (GM)	>500	>1,000	>1,000
열매의 디클로로메탄 분획 (GD)	145.4	>1,000	>1,000
열매의 에틸 아세테이트 분획 (GE)	60.0	67.7	115.9
열매의 부탄올 분획 (GB)	142.2	>1,000	>1,000
열매의 물 분획 (GH)	>500	>1,000	>1,000
가공한 열매의 메탄올 추출물 (SM)	312.6	600.8	457.6
가공한 열매의 디클로로메탄 분획 (SD)	367.5	277.1	202.2
가공한 열매의 에틸 아세테이트 분획 (SE)	58.0	22.2	21.2
가공한 열매의 부탄올 분획 (SB)	206.3	570.6	803.9
가공한 열매의 물 분획 (SH)	>500	>1,000	852.1
줄기의 메탄올 추출물 (FM)	>500	>1,000	>1,000
줄기의 디클로로메탄 분획 (FD)	448.2	>1,000	>1,000
줄기의 에틸 아세테이트 분획 (FE)	60.0	15.2	17.5
줄기의 부탄올 분획 (FB)	>500	>1,000	>1,000
줄기의 물 분획 (FH)	>500	>1,000	>1,000

< 4 >

, 가 , 가

<4-1>

4.98 g (Cat. No. LH-20-10)
 0, Sigma) (4×5 cm)
 TLC (: =5:1) TLC (: =40:60
) , 17 (1 17)
 . No. 13900, Merck) 12 (LiChroprep RP-18, 40 63 µm, 2.5×35 cm, Cat
 가 40% 60%
 12 (12A 12L)
 (2.5×35 cm) 3- - - 12B (90 mg) 5
 (12E) -D- (30.7 mg) 12C
 (2.5×35 cm) (77.5 mg)
 12I 50%
 (LiChroprep RP-18, 40 63 µm, 2×35 cm, Cat. No. 13900, Merck)
 3- (59.3 mg) 가 12K
 Merck, 50% MeOH) UV , TLC (10×10 cm×0.25 mm, Cat. No. 15423,
 mg) 3- (5.2
 , TLC 15
 Merck, 60% MeOH) (2.0×30 cm,) TLC (10×10 cm×0.25 mm, Cat. No. 15423,
 (10 mg) (10 mg)

<4-2>

가
 1.82 g (4.0×26.5 cm,
) TLC TLC
 가 13 (1 13)
 11 2.4 mg 12 3.6 mg
 . 8 (2×30 cm) (1/2)
 (20/1)
 (6.1 mg) 9 (1
 ×18.5 cm) (20/1)

(0.6 mg), 3- (5/1) (3.0 mg) (2.2 mg), 3- 가 가 3- - -

< 5 >

4 ¹H-NMR (300 MHz) ¹³C-NMR (75 MHz)
 (chemical shift) (3.3 ppm, 49.8 ppm)
¹H-NMR (300 MHz), ¹³C-NMR (75 MHz) ¹³C- ¹H
 2 3

[2]

H			3-			3-
2		4.99 (11.59)			4.39 (11.54)	
3		4.55 (11.59)			4.80 (11.54)	
4						
5						
6	6.07 (1.72)	5.89 (2.09)	6.10 (1.41)	6.07 (1.79)	5.77 (1.79)	6.09 (1.82)
7						
8	6.29 (1.82)	5.93 (2.13)	6.30	6.29 (1.72)	5.81 (1.79)	6.28 (1.82)
9						
10						
1'						
2'	7.98 (8.81)	7.36 (8.57)	7.89 (8.67)	7.63 (1.75)	6.85 (1.22)	7.52 (1.96)
3'	6.79 (8.83)	6.84 (8.60)	6.82 (8.82)			
4'						
5'	6.79 (8.83)	6.84 (8.60)	6.82 (8.82)	6.78 (8.49)	6.69 (8.11)	6.80 (8.38)
6'	7.98 (8.81)	7.36 (8.57)	7.89 (8.67)	7.53 (8.45, 1.83)	6.74 (8.16, 1.52)	7.43 (8.46)
OMe			3.67			3.68
* (Hz)						

[3]

C		3-			3-	
			HMBC			HMBC
2	85.4	158.5		85.5	158.4	
3	74.0	139.9		74.1	139.9	
4	198.8	180.4		198.8	180.4	
5	169.4	163.5		169.2	163.5	
6	97.8	100.2	C5, C7, C8, C10	97.7	100.1	C5, C7, C8, C10
7	165.7	166.5		165.7	166.3	
8	96.8	95.2	C6, C7, C9, C10	96.7	95.1	C6, C7, C9, C10

9	164.9	158.9		164.9	158.8	
10	102.2	106.3		102.2	106.2	
1'	129.7	123.0		130.3	123.3	
2'	130.7	131.8	C2, C4', C6'	116.5	116.8	C2, C3', C4', C6'
3'	116.5	117.0	C1', C5', C4'	146.7	148.8	
4'	159.6	162.1		147.5	150.3	
5'	116.5	117.0	C1', C3', C4'	116.3	116.8	C1', C3', C4'
6'	130.7	131.8	C2, C2', C4'	121.3	122.7	C2, C2', C4,
OMe		60.9	C3		60.9	C3

(Okuyama, *Chem. Pharm. Bull.* 26:3071, 1978), (Grande, *Planta Medica*, 51:414, 1985), (Shen, *Phytochemistry* 24:155, 1985), (Nonaka, *Chem. Pharm. Bull.* 35:105, 1987), (Grande, *Planta Medica*, 51:414, 1985), (Barbera, *Phytochemistry* 25:235, 1986), (Pabst, *Phytochemistry* 31:1649, 1992).

< 6 > , 가
 DPPH, NMDA
 1 8
 3- -D- 3- 3- /
 3 DPPH 3- 3- 3- /
 3- 4 5 5 6 (4).
 가 NMDA 3-

[4]

	DPPH (IC ₅₀ , µg/Ml)	(IC ₅₀ , µg/Ml)
	>50	>50
	>50	>50
3-	>50	>50
	2.89	>50
	4.49	2.48
3-	3.76	4.77

[5]

	/ (IC ₅₀ , μg/Mℓ)	(IC ₅₀ , μg/Mℓ)	NMDA-	-
	24.9	29.7	-	-
	>300	>300	-	-
3-	-	>300	-	
	5.5	4.1	-	-
	16.6	7.8	33% (9 μg/Mℓ) 47% (30 μg/Mℓ)	-
3-	0.65	0.60	21% (9 μg/Mℓ) 54% (30 μg/Mℓ)	31% (9 μg/Mℓ) 86% (30 μg/Mℓ)

< 7> 3-

120 TC (2,3,5-triphenyltetrazolium chloride) (Bederson et al., *Stroke* 17:1304, 1986) 가 T
 Warren, MI, USA) (ASI Instruments, 1 mm 2 mm
 0.9% 2% TTC 가 37 60 . TTC
 10% (phosphate-buffered formalin) CCD
 (mm³) (mm³) (Optimas, Edmonds, WA, USA)
 () ()

1

$$\text{부종율}(\%) = \frac{A-B}{B} \times 100$$

A: (mm³)

B: (mm³)

3- 30 10 mg/kg
 .6, 45.6 54.7%

55.3, 49

6

[6]

	n					(%)
()	6	36.7 ± 2.0	181.8 ± 11.4	218.6 ± 12.5	150.0 ± 7.1	12.8 ± 1.0
	9	30.1 ± 4.9	130.5 ± 18.6	161.1 ± 21.4	110.6 ± 15.8	9.1 ± 1.1 *
3-	11	28.9 ± 3.1	81.2 ± 20.8 *	110.1 ± 22.9 *	81.6 ± 17.8 *	5.8 ± 0.7 *
	8	30.1 ± 4.3	169.4 ± 12.7	199.5 ± 16.5	130.7 ± 13.1	11.9 ± 0.5
n: *						
(Duncan's multiple range test)				(p<0.05)		

< 8> 3-

7 (Relton) (n
 neurological score) (*Stroke* 28:1430, 1997)
 , (forelimb flexion,) ,
 (duration of forelimb flexion, 10) () ,
) () 7

[7]

	0	1	2	3	4
					-
	8-10	6-8	4-6	2-4	0-2
					-

8 (7 ±) , 12 가 . 10

[8]

	()		3-	
30	2.33 ± 0.24	2.44 ± 0.24	2.36 ± 0.15	2.33 ± 0.16

24	2.50 ± 0.41	4.56 ± 0.53 *	4.81 ± 0.44 *	3.00 ± 0.33
* 24		(p<0.05)		

8 가 , 12 가 , 3- , 3-

3- , NMDA , DPPH - , /

(57)

1. (*Opuntia ficus-indica*)

2. 1 , 3-

3. 1 , 가

4. 3 ,

1) 가 1 kg 0.1 10 가 4 5 ;

2) 1) ;

3) 1 kg 0.1 10 가 , (EtOAc) 0.5 2

5. 4 ,

1) 가 , 60%

6.

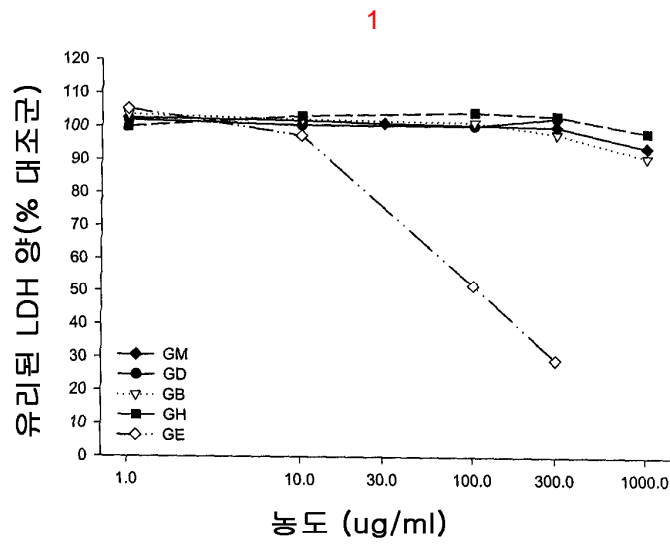
1

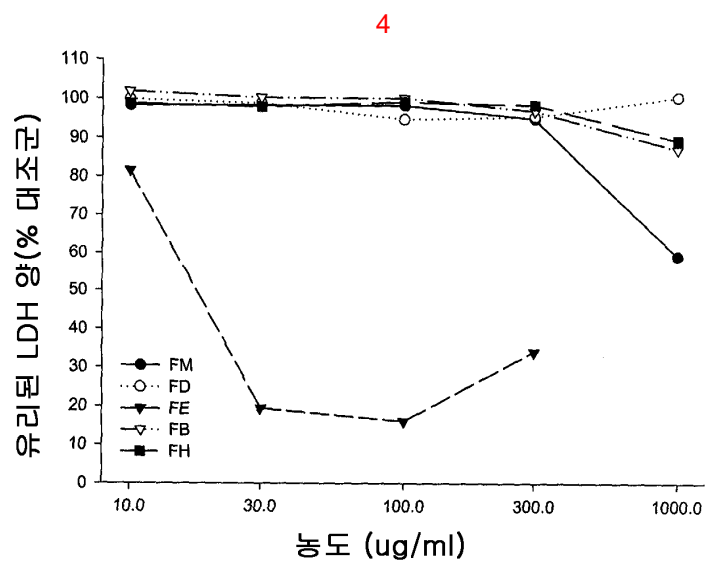
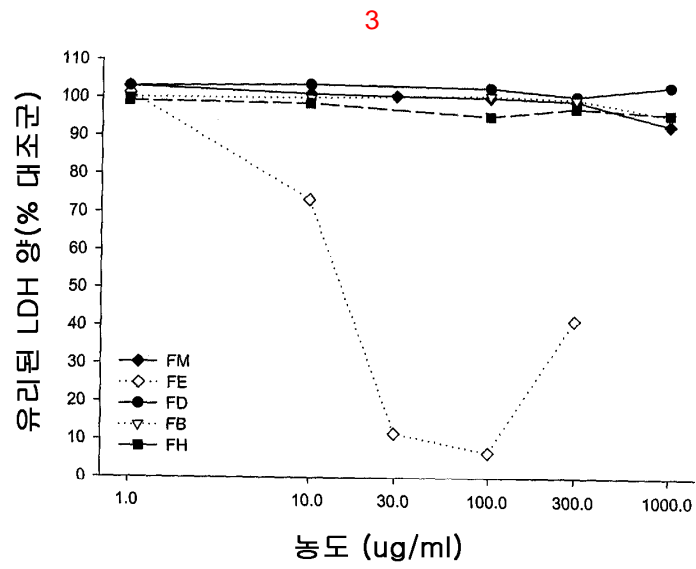
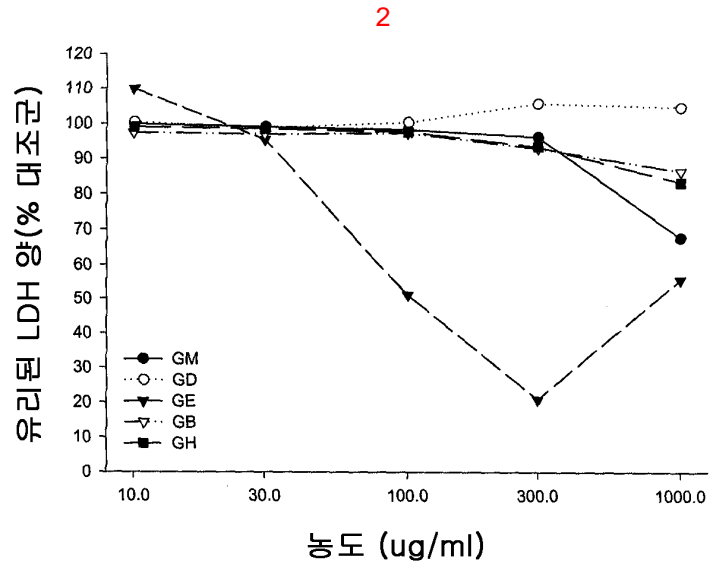
7.

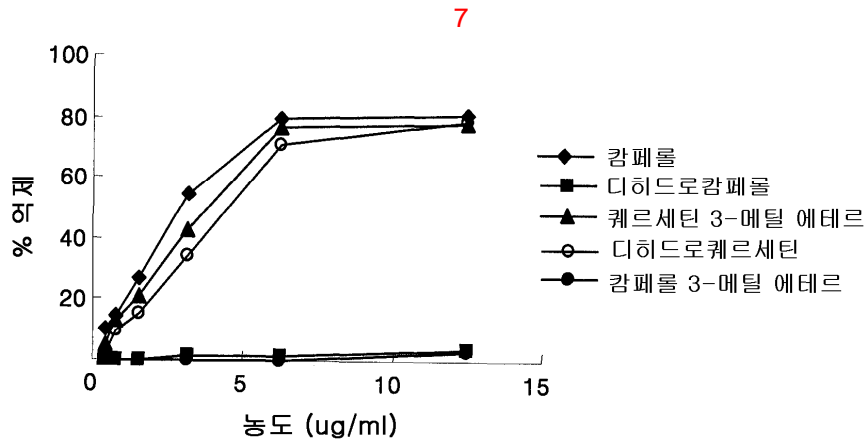
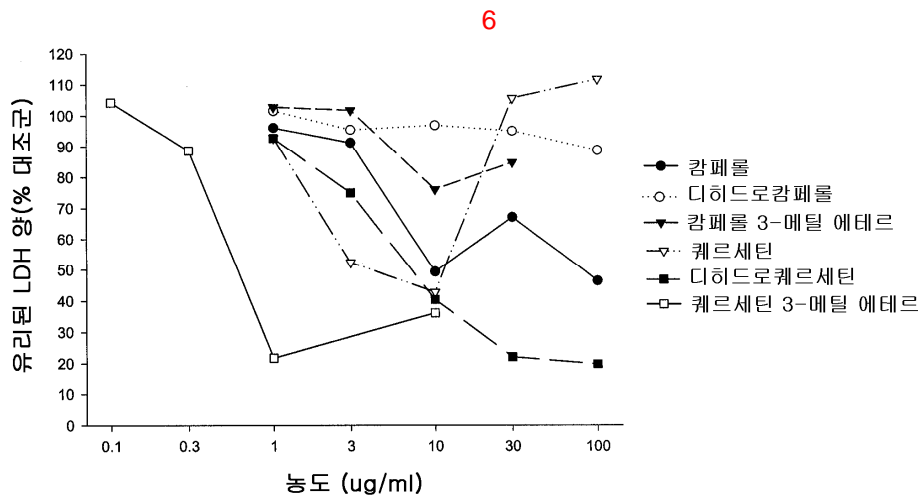
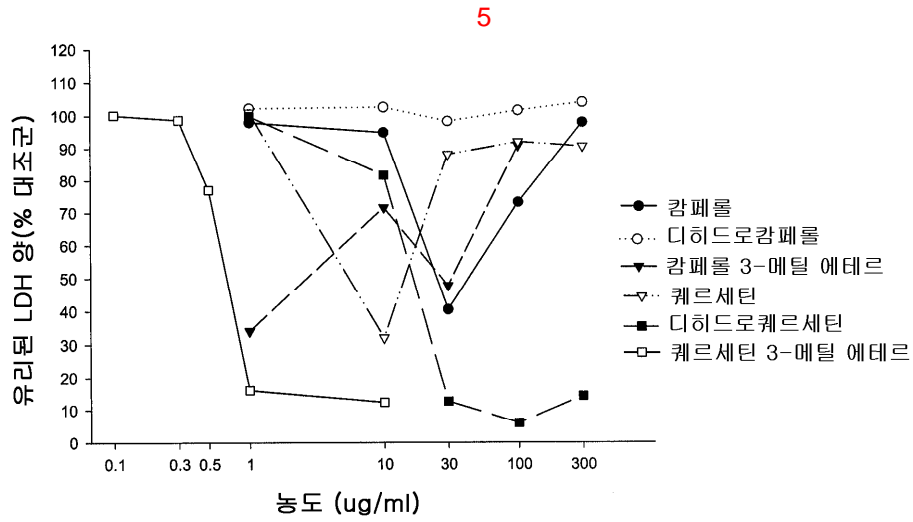
3-

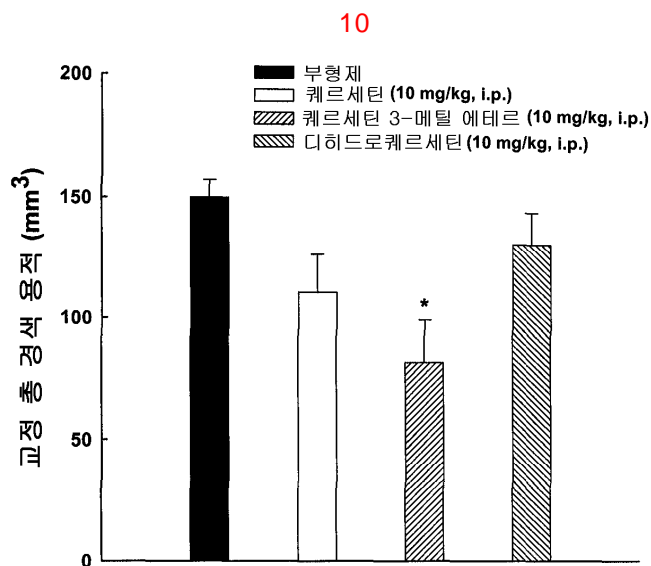
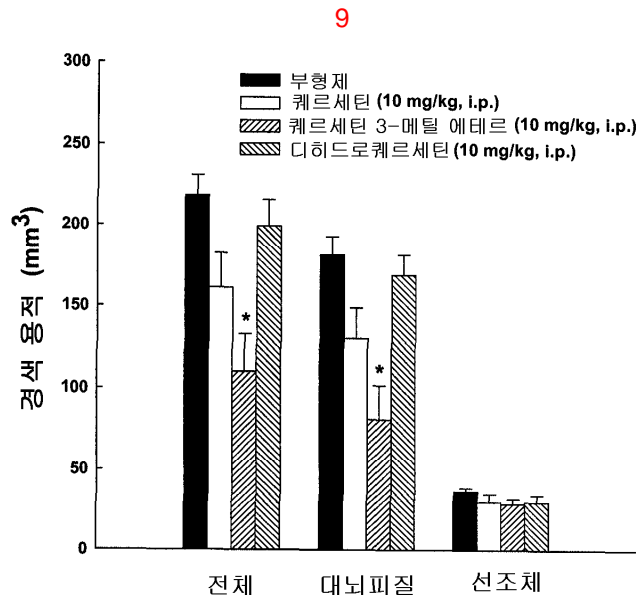
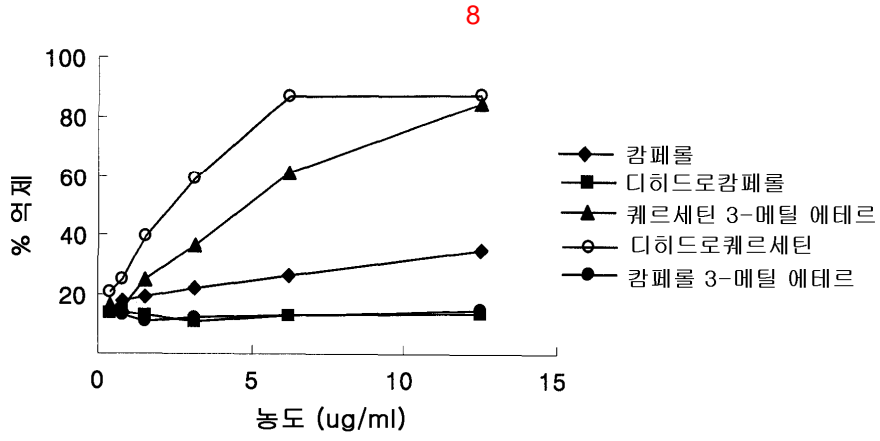
8.

7

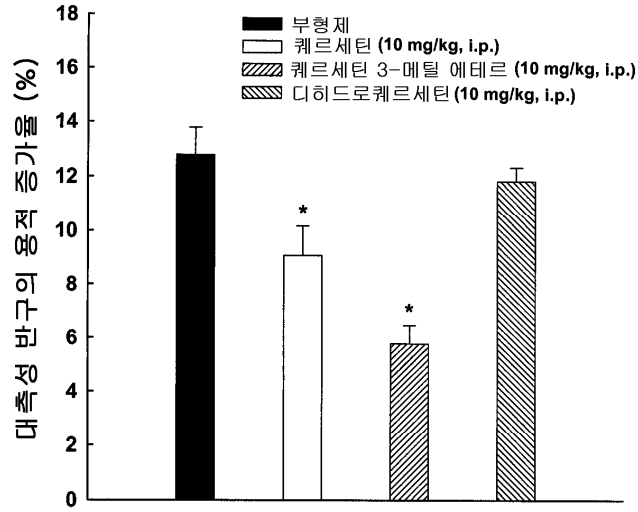








11



12

