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(12) (A)

(51) 。 Int. Cl.7  
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A61K 9/52

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(43)

10-2004-0111348  
2004 12 31

(21) 10-2004-7011457

(22) 2004 07 23

2004 07 23

(86) PCT/US2003/002206

(87)

WO 2003/065982

(86) 2003 01 24

(87)

2003 08 14

(30) 60/351,808

2002 01 24

(US)

10/351,291

2003 01 23

(US)

(71)

95051

3410

(72)

94403

3336

94062

45

94022

511

(74)

:

(54)

1 4(MCT 1 MCT 4)  
가

- (SMVT)  
가

( , ) .

2 4

2003 1 23  
351,808 -가 )

Attorney Docket 019282-001610US(2002 1 24

USSN 60/

가 1 1 가 1  
 가 가 ) ( , 가 ); ( )  
 ( , ALZA , OROS( ) )

(conjugate moiety)

$V_{max}$  가

$V_{max}$   $V_{max}$  2 10

pH

가  $V_{max}$  가 2

$V_{max}$  2 가

2 가 가  $V_{max}$

가 , 가 , 가 가 , 가  
 1 2 L- , ATBO, CAT-1, FATP4, MCT1, MCT4, NADC  
 1, NADC2, OCTN2, PEPT1, PGT, RFC, SAT-1, SAT-6, SMVT, SUT2 SVCT1

MCT1, MCT4 SMVT

$V_{max}$  가

$V_{max}$  가

,  $V_{max}$  2 10 . , .

, , pH , , 가

, 가  $V_{max}$  가 . , .

, 2 가 ,  $V_{max}$  . ,

2 가 , 2 가 가  $V_{max}$  .

max .

, 가 , 가 , , L-

, 1 2

ATBO, CAT-1, FATP4, MCT1, MCT4, NADC1, NADC2, OCTN2, PEPT1, PG  
T, RFC, SAT-1, SAT-6, SMVT, SUT2 SVCT1 . , .

, . , ,

가 ,  $V_{max}$

가 ,  $V_{max}$   $V_{max}$  2 10 . ,

, , pH , .

, 가 , ,

가  $V_{max}$  가 . ,

, 2 가 ,  $V_{max}$  . ,

2 가 , 2 가 가  $V_{max}$  .

max .

, 가 , 가 , 가 , 가

, L- ,

1 , ATBO, CAT-1, FATP4, MCT1, MCT4, NADC1, NA  
DC2, OCTN2, PEPT1, PGT, RFC, SAT-1, SAT-6, SMVT, SUT2 SVCT1 .



(OAT),

$10^{-6}$  cm/

$1 \times 10^{-6}$  cm/

(, Caco-2)

5 x

1

2

1

가

가가

가

가

가

(, )

가

가

가

가

가

가

가

50

100

(, )

$V_{max}$  가 2, 5, 10, 20,

L-

).

가

가

가

$$\frac{V_{max}}{K_m} \cdot K_m \cdot V_{max} \cdot \frac{1}{2}$$

$$\frac{V_{max}}{K_m} \cdot V_{max}$$

$$\frac{V_{max}}{K_m}$$

$$\frac{V_{max}}{K_m}$$

$$V_{max}$$

$$V_{max}$$

A 0.01%  
%

-3-

(, )

GAPDH  
GAPDH가

mRNA  
가 mRNA

(GAPDH) mRNA 0.2%  
0.1%, 1% 10

mRN

GAPDH 0.01% GAPDH 0.1%

가  $10^5 M^{-1}$ ,  $10^6 M^{-1}$ ,  $10^7 M^{-1}$ ,  $10^8 M^{-1}$ ,  $10^9 M^{-1}$ ,  $10^{10} M^{-1}$ ,  $10^{11} M^{-1}$ ,  $10^{12} M^{-1}$   
 PEPT1 MCT ELIS

A Lane (1998) [Antibodies, A Laboratory Manual, Cold Spring Harbor Publications, New York] Harlow

Smith amp; Waterman [Adv. Appl. Math. 2:4  
 82 (1981)] Needleman amp; Wunsch [J. Mol. Biol. 48:443 (1970)] Pea  
 rson amp; Lipman [Proc. Nat'l. Acad. Sci. USA 85:2444 (1988)]  
 (575)  
 GAP, BESTFIT, FASTA, TFASTA) (Ausubel)

Altschul [J. Mol. Biol. 215: 403-410 (1990)] BLAST . BLAST  
 (http://www.ncbi.nlm.nih.gov/)  
 T W (HSP)  
 T (Altschul). 가 가  
 HSP M(  
 ; > 0) N( ; < 0)  
 X ; 가  
 ; 가 0  
 BLAST 가 . BLASTN ( )  
 (W) = 11, (E) = 10, M = 5, N = -4 가  
 , BLASTP (W) = 3, (E) = 10 BLOSUM62 . TB  
 LATN ( ) (W) = 3, (E) = 10  
 , BLOSUM 62 ( : Henikoff amp; Henikoff, Proc. Natl. Acad. Sci. USA 89:1091  
 5 (1989)).

BLAST ( : Karlin amp; Altschul, Proc. Nat'l. Acad. Sci. USA 90:5873-5787 (1993)). BLAST  
 가 (P(N)) 가 가 0  
 .1 , 0.01 , 가 , 0.01 ,

( , )

가

I.

가 5  
4 가 1 6  
20  
2 4 S  
가 8 18

( , ).  
( , ).

가 1  
2 가  
가 1 2 가  
가 1 2 mRNA가  
-3- mRNA 0.2%

ATBO, CAT -1, FATP4, MCT1, MCT4( ), NADC1, NADC2, OCTN2,  
PEPT1, PGT, RFC, SAT -1, SAT -6, SMVT( ), SUT2 SVCT1  
MCT1, MCT4, ATBO, OCTN2, NADC1 NADC2  
SMVT

가 가 5  
( , PEPT1).

(GenBank) 가 가  
90%

II.

가 ) 가 ( , 가  
가  
가 /  
K<sub>M</sub> ( , ) 가 가



III.

가

DNA

CHO (HEK) CaCo-2 가

가

가

PMT

CCD

LC/MS

가

(repertory)

가

$V_{max}$  가  $V_{max}$  1%, 5%, 10%, 20% , 가 50%  
 $V_{max}$  가  $V_{max}$  50%, 100%, 150% 200% ( , 2 ) ,  $V_{max}$   
 $V_{max}$  가 ( ,  $V_{max}$   $V_{max}$  가 0.1% 1%).  
 $V_{max}$  가 2  $V_{ma}$

x

IV.

(alga),



가  
( : 5,382,513 ).  
WO 02/44324; 188,256 ; 4,671,958 ; 4,659,839 ; 4,414,148 ;  
4,669,784 ; 4,680,338 , 4,569,789 4,589,071

가

1 2

-2- -2R,4R- ]-2,3- -2S- -2- , N-  
-N-[3-[(2,2- -1- ) ]-2- -1- ] , (2R,4R)-2-  
)-3-(3- )-4- , (S) -4- -6- -2-  
[2S-1[R\*(R\*)]]2 ,3 ,7 ]-1[2-[[1- -3- ]- ]-1- ]  
-1H- -2- , [3S-1[R\*(R\*)]],3R\*]-2-[2-[[1- -3- ]- ]-1- ]-1,2,3  
,4- -3- ;

BCX-1812;

( ), 4-

- ) , 2-(8- -10,11- -11- [b,f] -2  
, O-( ) ;  
, 16- -16- -16- E<sub>2</sub>, 6,16- E<sub>2</sub>,  
E<sub>1</sub>, E<sub>2</sub> F<sub>2</sub> A<sub>2</sub> ;

가

가

가

, N-[3(R)-[2- -4- )

]-2- -1- ] -3(R)- - - , L-  
, 1- -6- -1,4- -4- -7-(1- )-1,8- -3- , 1-  
-6- -1 4- -4- -7-( )-3- .

-5-

, 7-

A,

C, Fd4C, FddC, FMAU, FTC, 2'-  
, 5- -2'-

, d4C, ddC, DMD  
, SddC,  
EB-1053,

, YH-529

8-

2-

B,

( ), ( ), ( ), ( ), ( ), ( ),  
(CNS), ( ) ( ) ( ) .

, CGP-24592, CGP-37849, CGP-39551, CGP-40116,

, AR-C69931MX, BMS-187745,  
, EB-1053,

, WAY-126090, YH-529

, GP-668,

3TC,

, AZT, BVDU, ddC, ddl, FMAU, FTC,

, H2

G,







(bore),  
 ( ) ( )  
 3,845,770 ; 3,916,899 ; 4,063,064 ; 4,088,864 ; 4,816,263  
 4,200,098 4,285,987

0.1 2 mg

가  
 1 kg

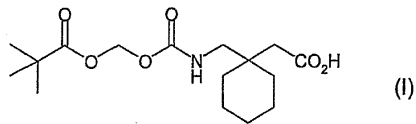
(NF) 가 (GMP)

I. PCR

DNA  
 가 55  
 PCR( YBR- ) ( PCR ; MJ PCR ; S  
 ) (Thermoscript)(  
 ) 1  
 cDNA mRNA PCR mRNA  
 (threshold) mRNA GAPDH  
 GAPDH

II.

1. 가



p- (4.2 g, 30 mmol) (300 mL)  
 (2.7 mL, 30 mmol) 가 (4.2 mL, 30 mmol) 가  
 ( )가 , 30  
 mL) , (200 mL) 2 p- (250  
 Cl(200 mL) 1 , 1 N H

p- (90 99%) LC-MS  
 1 H NMR(CDCl<sub>3</sub>, 400 MHz): 5.86 (s, 2H), 7.44 (d, J = 9 Hz, 2H), 8.33 (d, J = 9 Hz, 2H).

p- (4.5 g, 30 mmol) (4.7 g, 20 mmol) (250 mL)  
 60 가 (3.4 g, 40 mmol) 가 12 24  
 1 H NMR  
 (200 mL) 2 (100 mL) (200 mL)  
 p- LC-MS  
 1 H NMR (CDCl<sub>3</sub>, 400 MHz): 6.06 (s, 2H), 7.42 (d, J = 9 Hz, 2H), 8.30 (d, J = 9 Hz, 2H). <sup>13</sup>C N  
 MR(CDCl<sub>3</sub>, 100 MHz): 155.1, 151.0, 146.0, 125.8, 125.7, 121.9, 33.5.

(1.0 g, 10 mmol) (20 ml) (1.6 g, 7 mmol) 가 60  
 4 (350 ml)

( : 40 80%).

p- (325 mg, 1.0 mmol) (15 ml) (27  
 0 mg, 1.3 mmol) 가 60 12  
 ml) 1 (100 ml) (100 ml) 2 , 1 N HCl(100  
 (100 ml) 1 (50 ml) 1

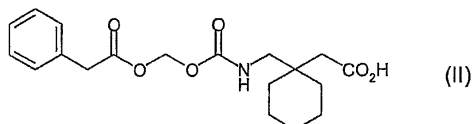
(8:1 :EtOAc) p-  
 1 H NMR(CDCl<sub>3</sub>, 400 MHz): 1.25 (s, 9H), 5.88 (s, 2H), 7.40 (d, J = 9 Hz, 2H), 8.29 (d, J  
 = 9 Hz, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): 177.0, 155.3, 151.6, 145.8, 125.6, 121.9, 83.1, 39.1, 27.0.

가 (100 mg, 0.5 mmol) (25 mL)  
 가 , 가 (750 μl, 0.6 mmol) 가 (1.4 mL, 1.0 mmol)  
 가 , 가 15 30 p-  
 (150 mg, 0.5 mmol) 가 , (LC-MS )  
 18 (200 mL) , 1 N HCl 2  
 HPLC

-78

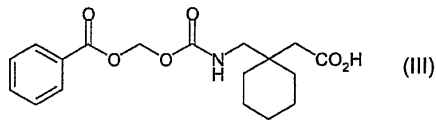
가 ( I) . MS (ESI)m/z 328.36(M-H<sup>-</sup>), 330.32(M+H<sup>+</sup>), 352.33(M+  
 Na<sup>+</sup>). 1 H NMR(CDCl<sub>3</sub>, 400 MHz): 1.21(s, 9H), 1.3-1.5(m, 10H), 2.32(s, 2H), 3.26(s, 2H), 5.33(m, 1H), 5,  
 73(s, 2H). <sup>13</sup>C NMR(CDCl<sub>3</sub>, 400 MHz): 178.0, 176.8, 155.9, 80.6, 39.2, 38.2, 38.2, 34.3, 27.3, 26.2, 21.7.

## 2. 가



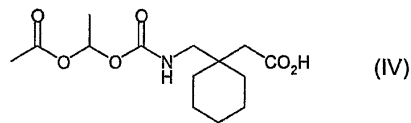
가 ( II)  
 . MS (ESI) m/z 362.4(M-H<sup>-</sup>), 364.4(M+H<sup>+</sup>).

3. 가



가 ( III)  
 . MS(ESI) m/z 348.4(M-H<sup>-</sup>), 350.4 (M+H<sup>+</sup>).

4. 가



(60 mL) p- (1.39 g, 10 mmol) (0.81 g, 10 mmol)  
 1- (1.2 mL, 11 mmol) 가 0 30  
 1 , 0.5%(v/v)  
 NaHCO<sub>3</sub> (2.4 g, 97%) Na<sub>2</sub>SO<sub>4</sub>  
 , CH<sub>3</sub>), 6.55 (q, 1H, CH), 7.42 (d, 2H, ), 8.28 (d, 2H, ).  
 1 H NMR(CDCl<sub>3</sub>): 1.93 (d, 3H

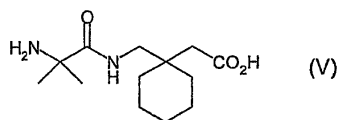
1- -p- (0.5 g, 2 mmol) NaI(0.6 g, 4 mmol) 40 3  
 , 1- -p-  
 (480 mg, 72%)

NaHCO<sub>3</sub> (0.336 g, 4 mmol), (0.68 g, 2 mmol), (0.122 g, 2 mmol), (5 mL) (10 mL) 1 (10 mL) 1  
 - -p- (0.674 g, 2 mmol) 가 , 16  
 (95:5) , Na<sub>2</sub>SO<sub>4</sub> :  
 (0.11 g, 21%) . 1 H NMR(CDCl<sub>3</sub>): 1.58 (d, 3H, CH<sub>3</sub>), 2.11 (s, 3H, Ac), 6.84 (q, 1 H, CH), 7.39 (d, 2H, ), 8.26 (d, 2H, ).

, - -p- (15 mL) 1- -p- 1- -p- (0.5 g, 2 mmol)  
 2 (1.5 g, 4.4 mmol) , 0.5%(v/v) NaHCO<sub>3</sub> , Na<sub>2</sub>SO<sub>4</sub>  
 (0.45 g, 84%) : (95:5)

(20 mL) 가 (633 mg, 3.7 mmol) (1.03 mL, 7.4 mmol)  
 (0.93 mL, 7.4 mmol) 가 , (1 g, 3.7 mmol) 가 , 30 (1  
 0 mL) - -p- NaHCO<sub>3</sub> (20 mL) , (3 x 1  
 0 mL) 가 MgSO<sub>4</sub> :  
 (4:1) 가  
 ( IV)(700 mg, 63%) . 1 H NMR (CDCl<sub>3</sub>): 1.27-1.60 (m, 10H ), 1.55 (d , 3H, CH<sub>3</sub>), 2.08 (s, 3H, Ac), 2.38 (s, 2H, CH<sub>2</sub>), 3.25 (m, 2H, CH<sub>2</sub>), 5.31 (t, 1H, OH), 6.81 (q, 1H, CH);  
 MS (ESI) m/z 302.2 (M+H<sup>+</sup>). (5 mL)  
 0.5 N NaHCO<sub>3</sub> 가

5. 가



40 mL N-Boc-L-phenylalanine (5 mmol), (1.24 g, 6 mmol), N-tert-butyl-L-glutamate (1.04 g, 6 mmol),  
 (0.7 g, 6 mmol), (20 mL) 가 . 가  
 6 mmol) (0.4 g, 10 mmol) (30 mL) 가 . 가  
 (100 mL) , 0.5 M 22 25 16  
 00 mL) (MgSO<sub>4</sub>), (2 x 100 mL) (2 x 1  
 (4 mL) , 0.25 μm HPLC (Phenomenex 250 x 2  
 1.2 mm, 5 μm LUNA C18 , 100% , 5 , 0.5% 0 60%  
 , 20 , 20 mL/ ) 가 ( V) ( 70%).

MS (ESI) m/z 255.26 (M-H<sup>-</sup>), 257.28 (M+H<sup>+</sup>).

### III. HEK

HEK

pH \_\_\_\_\_ :

: HEK

:

1

1 mM CaCl<sub>2</sub>

1 mM MgCl<sub>2</sub>

150 mM NaCl

3 mM KCl

1 mM NaH<sub>2</sub>PO<sub>4</sub>

5 mM

50 mM 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES)

pH 7.4

2

, 50 mM HEPES 50 mM 2-[(2-aminoethyl)amino]ethanesulfonic acid (ACES)

pH 6.7

3

120 mM KCl

30 mM NaCl

0.2 mM MgSO<sub>4</sub>

1 mM CaCl<sub>2</sub>

1 mM NH<sub>4</sub>PO<sub>4</sub>

5 mM

10 mM HEPES

10 mM -1,4- (2- ) (PIPES)

pH

96 100,000 , 100 μl 1  
2 .

(50:50 1 1 μM 2,7- (2- )-5- ) 50 μl 가 37 (BCECF AM 15

가 50 μl 2 2 50 μl 가 , 5 FLEX / 440/335 490/535  
0.5 mM 2 50 μl 가 , 5 FLEX FLEX 2  
FLEX (T0). 2 50 μl/ 2 가 .  
3(pH 9.7; 8.4; 7.4; 7.0; 6.5; 6.0; 5.5 (T1). 10 μM .

\_\_\_\_\_:

, A, B C T0 T1 :

A = / 440/535 -

B = / 490/535 -

C = B/A.

T0 T1 C T0 T1 (%) .  
T0 , (%) .

C (%) pH .

1 HEK 가 I .  
MCT , HEK ( ) .

IV. PEPT1 PEPT2

(a) Gly-Sar \_\_\_\_\_

PEPT1 PEPT2 CHO PCT WO 01/20331 .가

가 , PCT WO 01/20331 . PEPT1 PEPT2  
(*Xenopus*) .

(b) \_\_\_\_\_

RNA : PEPT1 PEPT2 cDNA - RNA 5' 3' 가  
pGEM .  
cDNA , (GTP)).  
, 4:1 :

\_\_\_\_\_ : (*Xenopus laevis*) ( 1.5 g/mL) 15  
, 1 mg/mL (Worthington Type 3) (9  
0 mM NaCl, 2 mM KCl, 1 mM MgCl<sub>2</sub>, 10 mM Na HEPES, pH 7.45, CaCl<sub>2</sub> ) 80 100  
6 , CaCl<sub>2</sub> (1.8 mM)  
16 , 45 μl  
10 20 μg RNA

\_\_\_\_\_ : 2 14 2- ( 500 , 1320/P  
CLAMP ADInstruments )  
(2 4 mQ) 3 M KCl . ( )  
bath) ( 0.3 μA ). (ALA

nstruments , -60 -90 mV , (PowerLab) ADI  
4 8 Hz . 20 Hz (lowpass)  
가 CaCl<sub>2</sub> 가 .  
( 60 )  
, 30 40 .  
, 1/2  
(1 mM)

V<sub>max</sub> ( , ) .  
1 mM V PEPT1 Gly-Sar V<sub>max</sub> 50% V<sub>max</sub>  
, PEPT1 Gly-Sar V<sub>max</sub> 66% V<sub>max</sub>  
PT Lys( - )-Leu V<sub>max</sub> PEPT Gly-Sar V<sub>max</sub> <5% PE

**V. SMVT ATBO+**

ATBO+ . ATBO+ Na/Cl  
(GABA) , 20 . SMVT  
(Asp, Glu)  
- SLC5A6 , , , , ,

**1. \_\_\_\_\_**

ATBO+(SLC6A14) SMVT(SLC5A6) mRNA c  
DNA . PCR , (AF151978 NM-021095)  
pcDNA3 , (pMO ) 5' 3'  
, HEK293 SMVT 가 ( ) . 3 H 3 H  
ATBO+ SMVT 가 ( ) .

2. \_\_\_\_\_

cRNA cDNA T7 (Collins ,  
 PNAS 13:5456-5460 (1997)), 10 30 ng RNA  
 aCl<sub>2</sub>, 1 mM MgCl<sub>2</sub> 10 mM Na HEPES, pH 7.4; Na<sup>+</sup> , NaCl 90 mM (90 mM NaCl, 2 mM KCl, 1.8 mM C  
 D ) 7 가 (ATBO+ 3 mM) (SMVT 0.5 mM) Hill 1  
 . ATBO+ SMVT Na<sup>+</sup> , Na<sup>+</sup>

3. \_\_\_\_\_ IC<sub>50</sub> \_\_\_\_\_

CHOK1 , G418 , FACS( , Cytomation) 가  
 . ATBO+ SMVT CHOK1 96  
 30 2 3 4 , ( )  
 ( ) (IC<sub>50</sub>) ( )

4. LC/MS/MS \_\_\_\_\_

SMVT ATBO+ 100,000 , 24 48  
 96 ( 0.1 3 mM) (HBSS) 가 , 0.1 ml 가  
 . 가 20 60 (0.04 mL/ ) 10 , HBSS 4  
 0.03 mL LC/MS/MS Na<sup>+</sup>

5. \_\_\_\_\_

hSMVT

	IC <sub>50</sub> (μM)	(%)( )
가	>500	0
I	450	21
IV	80	ND
V	320	36
SMVT CHO 0.5 mM	IC <sub>50</sub>	(%)( ). ND:

VI. Caco-2

Caco-2 , .

PEPT1 PEPT2 Lys( - )-Leu

, PEPT1 / PEPT2가  
PT2 Lys( - )-Leu

. PEPT1 / PE

1. \_\_\_\_\_

1. Caco-2 12 24 , 19 30 . 21  
가 .
2. Lys( - )-Leu (pH 6.0) .
- a. 1 mM , 600 μM Lys( - )- .
- b. 20 μM 가 .
3. Lys( - )-Leu 500  
μℓ 가 (24 125 μℓ).
4. HBSS , pH 7.4 가 (12 1.5 mL, 24 875 μℓ).
5. , 50 μℓ LC/MS ( , PP ) .
6. , , 125 μℓ 500 μℓ 50/50% /  
LC/MS , 2,500 rpm 5 . 5  
50 μℓ
7. PepTI (pH 6.0) 1:2 1:4 .
8. -20 .

2. \_\_\_\_\_

2 PEPT1/PEPT2 Lys( - )-Leu 가 V  
Caco-2 V Lys( - )-Leu , PEP  
T1 / PEPT2 가 . V

VII.

가 . 가 ,  
3 4 . ,  
( ), 가 , 가  
, 가 ,  
가

1. \_\_\_\_\_

) 1 kg 25 mg 가 4 ( 400  
(0.5 mL) / 가 . 8

2. \_\_\_\_\_

1. 1.5 mL 가 / 50/50 300 µℓ p- 20 µℓ
2. 100 µℓ 가
3. 가 (0.04, 0.2, 1.5, 25, 100 µg/mL) 10 µℓ 90 µℓ (blank) 가  
 (0.004, 0.02, 0.1, 0.5, 2.5, 10 µg/mL) / 50/50 300 µℓ  
 가 , p- 20 µℓ 가
4. , 14,000 rpm 10
5. LC/MS/MS

LC/MS/MS :

10ADVp 가 API 2000 LC/MS/MS (CTC Analytics A  
 G, -PAL) Zorbax XDB C8 4.6 x 150 mm 45 가  
 0.1% (A) , 0.1% (B) : 5%  
 B 1 , 98% B 3 , 2.5 , 5% 2 . API 2000  
 TurbolonSpray , 가 MRM 172/1  
 37 ( I 330/198, III 350/198, II 364/198). 20 µℓ  
 (Analyst) 1.1

3.

3A I, II III 가 가 가  
 가 가 I  
 3B 'F' 가 I 가  
 가  
 4 가 24 V ( 5 ) 가  
 7 가  
 가 ,

[ 1 ]

\*\*\* 인간에서는 발현되지만  
다른 종에서는 발현되지 않음

유전자 명	SLC 명	진뱅크	***
ATBO		XM_010112	
BAT		AF141289	***
CAT-1	SLC7A1	XM_029358	
CAT-2	SLC7A2	NM_003046	***
CNT1	SLC28A1	NM_004213	***
CNT2	SLC28A2	NM_004212	***
CNT3		NM_022127	***
FATP4	SLC27A4	XM_005658	
GLUT-2	SLC2A2	NM_000340	***
GLUT-3	SLC2A3	NM_006931	***
GLUT-5	SLC2A5	NM_003039	***
MCT1	SLC16A1	NM-003051	
MCT4	SLC16A4	NM-004207	
NADC1		NM_003984	
NADC2		NM_022444	
NPT-4	SLC17A4	XM_030208	***
OCT_3	SLC22A3	NM-021977	***
OCTN1	SLC22A4	NP_003050	***
OCTN2	SLC22A5	O76082	
PEPT1	SLC15A1	NM_005073	
PGT	SLC21A2	U70867	
RBAT	SLC3A1	L11696	***
RFC	SLC19A1	U19720	
SAT-1	SLC26A1	AF297659	
SAT-3	SLC26A3	XM_004952	
SAT-6	SLC26A6	AF416721	
SERT	SLC6A4	XM_047486	***
SGLT-1	SLC5A1	M24847	***
SMVT	SLC5A6	AF081571	
SUT1	SLC13A4	NM_012450	***
SUT2	SLC26A2	XM_003788	
SVCT1	SLC23A2	AF170911	
SVCT2	SLC23A1	AF164142	***

[ 2 ]

4F2HC	SLC3A2	AB018010	
AE1	SLC4A1AP	XM_031667	
AE2	SLC4A2	NM_003040	
CAT-4/LAT4	SLC7A4	XM_036892	
ENT1	SLC29A1	AF079117	
ENT2	SLC29A2	NM_001532	
ENT3	SLC29A3	AF326987	
GLUT-1	SLC2A1	NM_006516	***
GLUT-8	SLC2A8	XM_011828	
GLUT-13	SLC2A13	NM_052885	
GLUT-14	SLC2A14	XM_016498	
LAT1	SLC7A5	AF104032	
LAT2	SLC7A8	NM_012244	***
MCT11	SLC16A10	NM_018593	***
MCT2	SLC16A7	NM-004731	***
MCT5	SLC16A5	NM-004696	
MCT6	SLC16A6	NM-004695	
MCT7	SLC16A7	NM-004694	
NAATB	SLC1A5	U53347	
NaMI-1		L38500	
NNaI-2		XP_089960	
NNT-5		NM_014037	
NNT-a		BC006252	***
NNT-xt3		NM_020208	***
nSGLT-2		AY044906	
nSGLT-3		AL109659	
OAT-B	SLC21A9	AB026256	
OAT-D	SLC21A11	AB031050	
OAT-E	SLC21A12	AB031051	
ORCTL2	SLC22A1L	AF037064	
OST-1		NM_012264	
OST-2		BI770976	
OST-4		AI640188	
PHT1	SLC15A3	W53019	
PHT2		AB020598	
SAT-2	SLC26A2	NM_000112	
SGLT-2		AF307340	
SGLT-3		NM_006933	
SGLT-4	SLC5A4	SLC5A4	***
XCT	SLC7A11	NM_014331	***
Y+LAT1	SLC7A6	D87432	***
Y+LAT2	SLC7A7	NM_003982	***

(57)

1.

, (conjugate moiety),

$V_{max}$  가

2.

1,  $V_{max}$   $V_{max}$  2

3.

1,  $V_{max}$   $V_{max}$  10

4.

1,

5.

1,

6.

5, pH,

7.

- 5 , .
- 1 8. , 가 .
- 1 9. , .
- 1 10. , 가 .
- 1 11. ,  $V_{max}$   
가 .
- 1 12. , 2 가  $V_{max}$  가 .
- 1 13. , 2 가 , .
- 1 14. , 2 가  $V_{max}$  가 가 .
- 1 15. , , , .
- 1 16. , 가 , 가 .
- 16 17. , 가 , 가 가 .
- 1 18. , L- , .
- 1 19. , 1 2 .
- 1 20. , ATBO, CAT - 1, FATP4, MCT1, MCT4, NADC1, NADC2, OCTN2, PEPT1, PGT, RFC, SAT - 1, SAT - 6, SMVT, SUT2 SVCT1 .
- 1 21. , MCT 1 MCT 4 .
- 1 22. , SMVT, ATBO, OCTN2, NADC1 NADC2 .

23.

1 ,

24.

1 ,

25.

MCT1, MCT4 SMVT

$V_{max}$  가

26.

$V_{max}$  가 ;

27.

26 ,  $V_{max}$

$V_{max}$  2

28.

26 ,  $V_{max}$

$V_{max}$  10

29.

26 ,

30.

26 ,

31.

30 , pH ,

32.

30 ,

33.

26 , 가

34.

26 ,

35.

26 , 가

36.

26 ,  $V_{max}$  가

37.

26 , 2 가  $V_{max}$  가

- 26 38. , 2 가 , .
- 26 39. , 2 가  $V_{max}$  가 가 .
- 26 40. , , , .
- 26 41. , 가 , 가 .
- 26 42. , L- , .
- 26 43. , 1 2 .
- 26 44. , ATBO, CAT - 1, FATP4, MCT1, MCT4, NADC1, NADC2, OCTN2, PEPT1, PGT, RF C, SAT - 1, SAT - 6, SMVT, SUT2 SVCT1 .
- 26 45. , MCT 1 MCT 4 .
- 26 46. , SMVT, ATBO, OCTN2, NADC1 NADC2 .
- 26 47. , , .
- 26 48. , .
- 49 49. , , 가 ,  $V_{max}$  가 .
- 49 50. ,  $V_{max}$   $V_{max}$  2 .
- 49 51. ,  $V_{max}$   $V_{max}$  10 .
- 49 52. , .
- 49 53. , .

- 49 **54.** , pH , .
- 49 **55.** , .
- 49 **56.** , 가 .
- 49 **57.** , .
- 49 **58.** , 가 .
- 49 **59.** ,  $V_{max}$  가 .
- 49 **60.** , 2 가  $V_{max}$  가 .
- 49 **61.** , 2 가 , .
- 49 **62.** , 2 가  $V_{max}$  가 가 .
- 49 **63.** , , , .
- 49 **64.** , 가 , 가 .
- 49 **65.** , 가 , 가 가 .
- 49 **66.** , L- , .
- 49 **67.** , 1 .
- 49 **68.** , ATBO, CAT -1, FATP4, MCT1, MCT4, NADC1, NADC2, OCTN2, PEPT1, PGT, RF C, SAT -1, SAT -6, SMVT, SUT2 SVCT1 .
- 49 **69.** , MCT 1 MCT 4 .

- 49 **70.** , SMVT, ATBO, OCTN2, NADC1 NADC2 .
- 71.** ; , ; , 가 , , .
- 71 **72.** , 가 .
- 73.** , , , ( ) ( ) .
- 73 **74.** , ; ; , 가 , .
- 73 **75.** , .
- 73 **76.** , pH , .
- 73 **77.** , .
- 73 **78.** , ( ) .
- 73 **79.** , ( ) 가 .
- 73 **80.** , , , .
- 73 **81.** , 1 .

82.

73 , ATBO, CAT-1, FATP4, MCT1, MCT4, NADC1, NADC2, OCTN2, PEPT1, PGT, RFC, SAT-1, SAT-6, SMVT, SUT2 SVCT1

83.

73 , MCT 1 MCT 4

84.

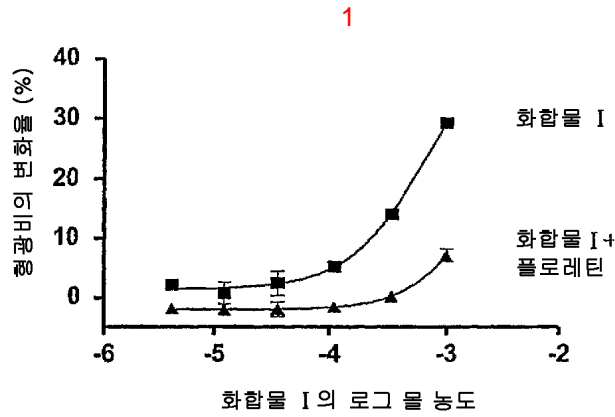
73 , SMVT, ATBO, OCTN2, NADC1 NADC2

85.

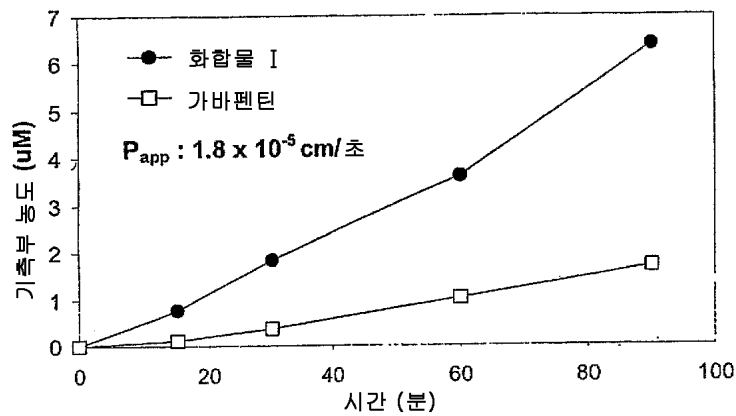
73 ,

86.

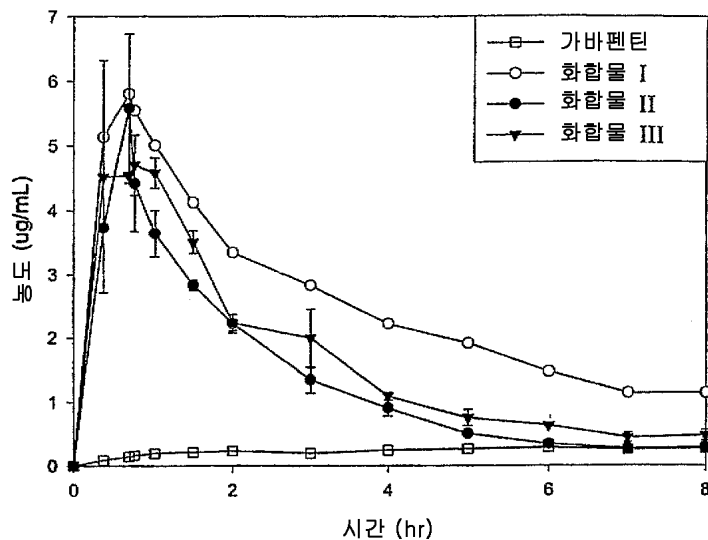
73 ,



2



3a

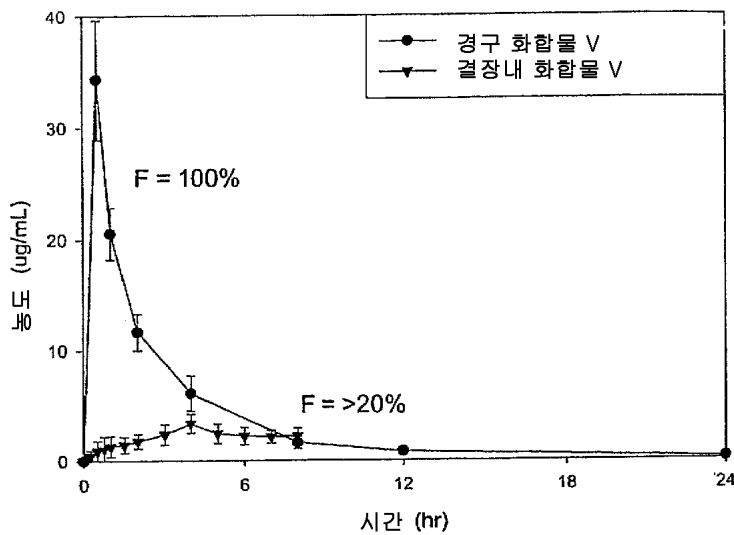


3b

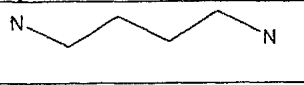
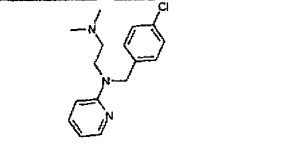
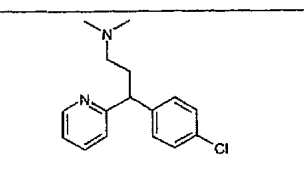
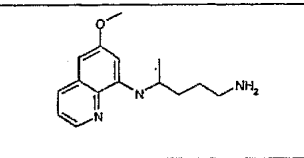
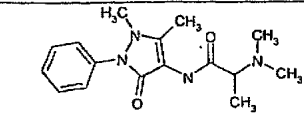
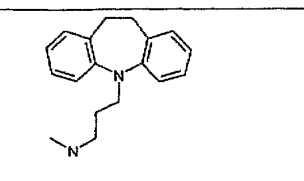
가바펜틴 또는 프로드럭을 래트의 결장내에 투여한 후의  
혈장내 가바펜틴에 대한 약동학 매개 변수

처리	Cmax (ug/mL)	Tmax (hr)	반감기 (hr)	AUC(0-8) (ug.hr/mL)	F (%)
가바펜틴	0.3	6.0	ND	1.8	2.7
화합물 I	5.8	0.5	3.4	20.6	38.9
화합물 II	5.7	0.6	1.7	11.1	17.6
화합물 III	5.3	0.7	2.4	13.6	22.5

4



5

화합물 스퍼미딘	IC50 ( $\mu\text{M}$ )		
	푸트레신	스퍼미딘	
	70	510	800
	580	1500	1900
	1600	4300	6200
	680	1600	4400
	48	120	170
	80	1500	2400