

(19)  
(12)

(KR)  
(A)

(51) 。 Int. Cl. <sup>7</sup>  
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(11)  
(43)

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(81)

:  
- 가  
가 가  
가  
가  
AP ARIPO : , 가  
EA :  
EP :  
OA OAPI : , 가

(30)	99401605.3	1999 06 28	EP(EP)
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(71) - ( :75013) 174

(72)	,	- 78650		33
	,	- 92160	14	
	,	- 64600	15	
	,	- 91410	39	

(74)

:

(54)

0 ) 1 (pulse) (30 ) 2 ( 50 20  
(timed dual release) .

1

, , , , , , , ,

(timed dual release) .

:

- ( : ) ,
- ( : (R) - ) ,
- ( : , ) ,
- ( : ) ,
- ( : ) .

.

, , " " , 가 , , , .

, 2 (pulse)가 .

, 1 , 1 2  
 ,  
 .  
 " " .  
 ( ) 30 pH 1 7.5, 37  
 , 1 , 50rpm 가  
 .  
 30 90% 20 , 15 .  
 , 1 , 30  
 .  
 ,  $T_1$   $T_2$  .  
 $T_1$  2 , 10%  
 .  
 $T_2$  , 85%  
 .  
 , ( $T_2 - T_1$ ) 30 200  
 .  
 , " " 50 200 , 60 150 ,  
 .  
 , ,  $T_2$  2 6 8 ,  
 2.5 5 .  
 40 70% .  
 가 1 , 60% , 2  
 90 ( $T_1$ ) ,  $T_2$  150 .  
 2 , 2 (30 )  
 , 2 ( )  
 .  
 , 가 30 ,  
 30  
 ,  
 .

30 , 30 0 20%, 0 90% 5% .

2

10 30mg 7.0 15mg .

6 12mg 4 16mg, 가

2 pH

가 가

가

( ) ( )

(1) , 0.2 2mm

:

(spheronisation),

가

(i) (iii) :

(i) 1 ( : , B , )

- 1 ( : , , A ) .
- (ii) 4 ( ) , (i) ( A B ) .
- (iii) , , 1 , . , 1 가 (zwitterionic) 가 가 . , 가 가 , . (CTAB), (DDAB(12)), N - , C - , N - ( : ), N - 2, 3 5 . 1 가 ( ) , 가 1 가 , pH (2) : (1) (3) (1)



가 .

가 ,

가 .

가 ( )

(spirits), (liqueurs),

50 1250kDa), ( 10 1500kDa), (

가

가

S, AC,

V, FCF, S, BN, 2G,

FK HT, BK

3 가

( , )

가 ,

가 .

- 1 40% , 90 150 . 60% , 2
- 2 1 (pH 2.0).
- 3 2 (pH 2 6.8).
- 4 3 (pH 2 6.8).
- 5 1 7.5mg ) 3 4 ( , (pH 2.0).
- 6 1 (pH 2 6.8).
- 7 2 (pH 2 6.8).
- 8 5 .

1:

(nonpareil) 16/18 1000g :



[ 1 ]

	11.54%	78.125g
K30 <sup>1</sup>	11.54%	78.125g
	76.92%	520.8g
<sup>1</sup> BASF (Kollidon, )		

GPCG1 - ( (Glatt))  
 50rpm 37 ± 0.5 0.01M 900Mℓ  
 310nm  
 2

2: : , ,

16/18 1000g :

[ 2 ]

	6.0%	78g
<sup>1</sup>	4.0%	53g
	3.0%	39g
	43.5%	567g
	43.5%	567g
<sup>1</sup> - (Pharmacoat, ) 603		

, GPCG1 - , 가  
 :

[ 3 ]

	8.3%	78g
K30 <sup>2</sup>	8.3%	78g
	83.4%	784g
<sup>2</sup> BASF		

:

[ 4 ]

B <sup>3</sup>	11.40%	83.4g
A <sup>4</sup>	0.93%	6.8g
<sup>5</sup>	1.37%	10.0g
	51.80%	379.0g
	34.50%	252.0g
<sup>3</sup> (Rohm Pharma) (Eudragit, ) RS100 <sup>4</sup> RL100 <sup>5</sup> (Eudraflex, )		

1 0.01M 0.1M 0.02M pH 6.8

3

3: : , ,

16/18 1000g

:

[ 5]

	6.0%	78.0g
1	4.0%	53.0g
	3.0%	39.0g
2	1.4%	18.2g
	42.8%	557.0g
	42.8%	557.0g
1 - 603 <sup>2</sup>		

, GPCG1 - , 가 ,

2 . 4 .

4:

15mg :

[ 6]

	/	
1	112mg	7.5mg
3	131mg	7.5mg
3		-
( )		15.0mg

2 0.01M 5 .  
 $T_1 = 2.0h$   $T_2 = 5.0h$  .

1:

GPCG1 - 1 850g  
 :

[ 7]

B <sup>1</sup>	11.41%	129.6g
A <sup>2</sup>	0.92%	10.5g
3	1.37%	15.6g
	51.78%	588.0g
	34.52%	392.0g
3 RS100 <sup>4</sup> RL100 <sup>5</sup>		

35 24 , 2 0.01M 0.1M  
 pH 6.8 0.02M  
 . 0.01M ( 12 )가 , pH 6.8 .

2:

16/18 735g :

[ 8]

	10%	58.4g
K30 <sup>1</sup>	2%	11.5g
95%	88%	505.0g
<sup>1</sup> BASF		

, GPCG1 - :

[ 9]

	11.54%	78.125g
K30 <sup>2</sup>	11.54%	78.125g
	76.92%	520.8g
<sup>2</sup> BASF		

, - - 748g :

[ 10]

B <sup>3</sup>	11.40%	62.5g
A <sup>4</sup>	0.93%	5.1g
<sup>5</sup>	1.37%	7.5g
	51.80%	283.5g
	34.50%	189.0g
<sup>3</sup> RS100 <sup>4</sup> RL100 <sup>5</sup>		

35 24 2 0.01M 0.1M  
pH 6.8 0.02M pH 7  
pH

가가 pH pH 가

5: : , ,

GPCG1 - , 16/18 1000g  
:

[ 11]

	5.0%	78.0g
1	2.5%	39.0g
VA 64 <sup>2</sup>	5.0%	78.0g
	5.0%	78.0g
	41.25%	643.5g
95 °	41.25%	643.5g
1 (Seppic) (Amonyl, ) 380LC 2 BASF VA 64		

, 가 :

[ 12]

	8.3%	78g
VA 64 <sup>3</sup>	8.3%	78g
95 °	83.4%	784g
2 BASF VA 64		

1000g :

[ 13]

B 4	11.40%	83.4g
A 5	0.93%	6.8g
6	1.37%	10g
	51.80%	379g
	34.50%	252g
3 RS100 <sup>4</sup> RL100 <sup>5</sup>		

30 16 , 100rpm  
0.01M 37 ± 0.5 0.01M 900  
MØ 310nm 8  
6: 6.5mg - 6mg  
3  
20 % - , :

[ 14]

	3.0%
	20.0%
<sup>1</sup>	68.0%
606	3.0%
<sup>2</sup>	5.0%
	1.0%
<sup>1</sup> FMC (Avicel, ) <sup>2</sup> BASF CL	

, 가 . 130mg 217mg

(57)

1.

, 37

1 (pulse)

2

(timed

dual release)

2.

1 , 1 가 30 가 .

3.

1 2 , 50 200 .

4.

3 , 60 150 .

5.

1 4 , 40 70%가 .

6.

1 5 , 가 30 200 .

7.

1 6 , 85%가 2 6 .

8.

9.

8 , , , , .

10.

8 9 , 1 1 .

11.

8 9 , .

12.

8 9 , .

13.

8 9 , (i) 가 , (ii) , (iii) , (iv) 가 .

14.

10 13 , 가 1 .

15.

10 13 , 가 1 (zwitterionic) .

16.

14 , - 가 - , - , - , - , - .

17.

15, 가 N -, C -, N -, N -, .

18.

16. 가 .

19.

20.

18

21.

1 20 , 가 , , , .

22.

21. 가, , (R) - , ,  
 , 가 .

23.

21, 가 가 .

24.

23 , .

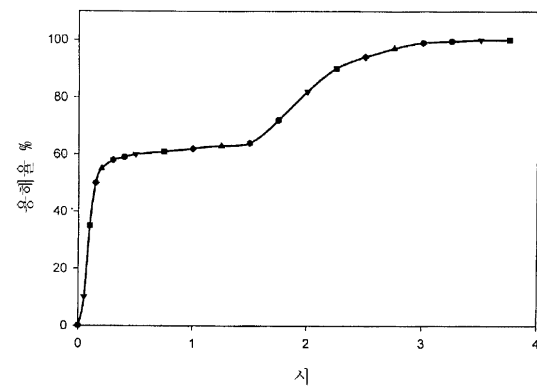
25.

1 24 , .

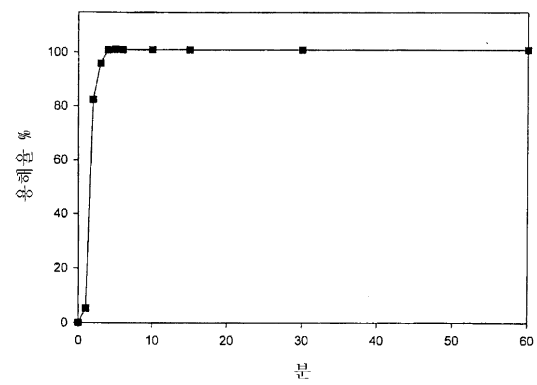
26.

25 ( ) , , , , 가 , .

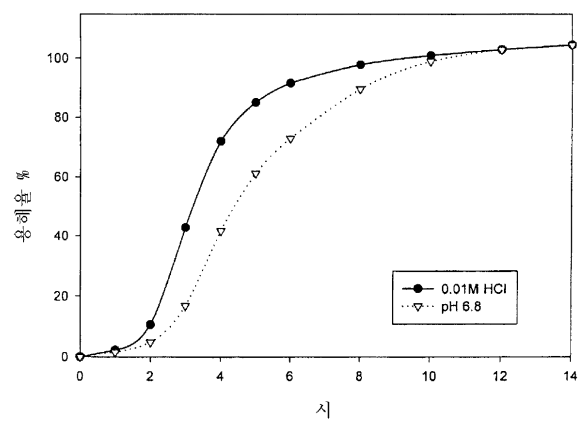
1



2

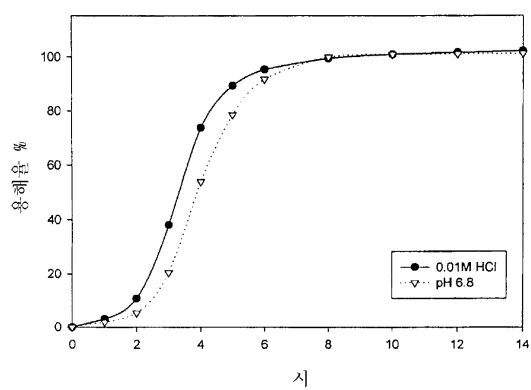


3

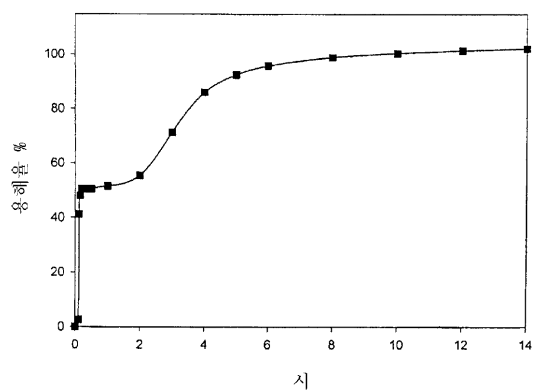




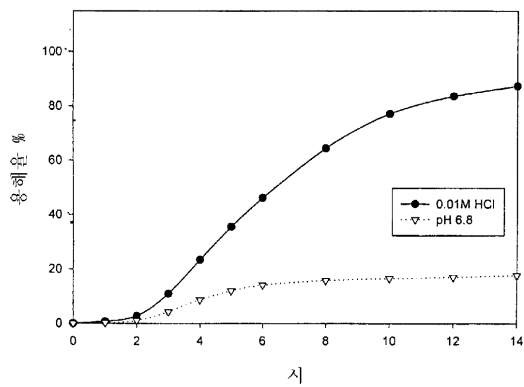
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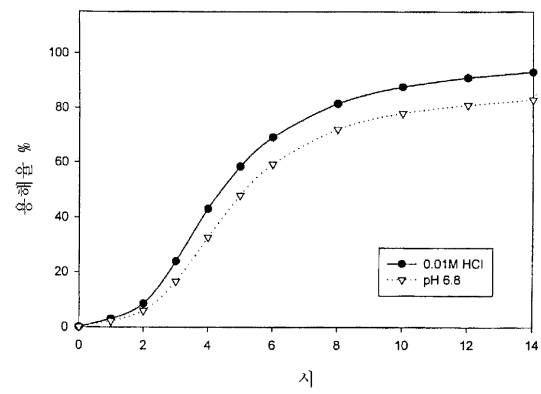
5



6



7



8

