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2004 02 03

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(43)

10-2002-0041712
2002 06 03

(73) 373-1

(72) 211-1501

373-1

(74)
:

(54)

(PEG)

가

1

1
2

3
4
5

(micelle)

가 (FDA)

(polyglycolic acid, PGA), (D,L- -co- (poly(D,L-lactic-co-glycolic acid, (poly(lactic acid, PLA), PLGA), (), (), PLGA)

, PLGA 가

, 가 가

(microsphere), 가 (nanoparticle), (micelle) 가 가 가

가 , 가

, 가 , 50

, (taxol), 5- (doxorubicin), (adriamycin), (cisplatin), (5-fluorouracil) 가 가 가

가 가 가

(: T. Minko, et al., J. Control. Rel., 54:223-233, 1998; A. Colin de Verdiere, et al., Cancer Chemother. Pharmacol., 33:504-508, 1994).

가 가 가

가

가
가
가

(stannous octoate) 가 160 200 가 2 (PEG) 6
가 ;
가 ;
가 (: 1).

1 :
160 200 가 2 (PEG) 6 (stannous octoate) 가
(PLA), (PGA), (D,L- -co- , PLGA),
(PLGA), (PLGA), (PLGA) 50:50() PLGA 가
(methoxypolyethyleneglycol, mPEG)

2 :
p- (DSC) p- (CDI), N,N'-
1:2:2 1:2:6() 2

3 :
가 : ,
, 5-

4 :
가 : 1 ,
가 가
:

가 ; , 가
가 ; , 가
(renal exclusion) (pharmacokinetics) :
(vascular permeability) (passive diffusion) 가 (multi-dr
ug resistance, MDR) (endocytosis) 가 가
PLGA -PLGA

가

가

1 : mPEG가 (D,L- -co-)(PLGA) 26g mPEG-PLGA 700 (mPEG) 2g, 3350 mPEG 8g 8000 mPEG 16g 140 가 (stannous octoate) 가 0.05% (methylenchloride) 가 180 3 (diethylether) 가 mPEG-PLGA (gel permeation chromatography, GPC) mPEG-PLGA (differential scanning calorimetry, DSC) (: 1).

[1]

mPEG-PLGA

	(Mn)	GPC (Mn)	GPC (Mw)	DSC()
PLGA - PEG750	8300	11000	26000	21.63
PLGA - PEG3350	9600	13000	23000	1.15
PLGA - PEG8000	9000	9000	20000	-29.89

1 20,000 , DSC 가 3가 PLGA-PEG 가 , GPC (Mw) 2 : mPEG-PLGA mPEG-PLGA 3g p- 80mg 30Mℓ 가 0.25 , 63mg (pyridine) 가 3 (doxorubicin-HCl, Sigma C hem. Co., U.S.A) 6.75mg (dimethylformamide) 7.5Mℓ , 10mg 24 (triethylamine) 가 , 300Mℓ (: 2). 3 3 , 5 , mPEG-PLGA 가 DMSO (: 2).

[2]

mPEG-PLGA

	(/)	(/)
DOX - PLGA - mPEG750	37.32%	2.2%
DOX - PLGA - mPEG3350	36.52%	2.2%
DOX - PLGA - mPEG8000	34.22%	2.2%

2 , mPEG-PLGA 34 38%(w/w) , 2.2%(w/w) 가 mPEG-PLGA 3 : mPEG-PLGA 3g p- 80mg 30Mℓ 가 (hydrazine, NH₂-NH₂) 2mg 가 , 3

가 mPEG-PLGA (: 3).
 4 : 가 mPEG-PLGA
 3 가 mPEG-PLGA 0.25g 10mg 7.5Ml
 24
 300Ml
 3 , 5
 2 (: 3). (: 3)

[3]

mPEG-PLGA

	(/)	(/)
DOX-PLGA-mPEG750	28.32%	1.7%
DOX-PLGA-mPEG3350	27.11%	1.7%
DOX-PLGA-mPEG8000	26.07%	1.7%

3 , mPEG-PLGA 26 29%(w/w)
 1.7%(w/w)
 5 : 2 4 100 mg 10Ml
 100Ml 3 가 6
 mPEG
 DLS(dynamic light scattering) (: 4).

[4]

mPEG

	(nm)
DOX-PLGA-mPEG750	62.0
DOX-PLGA-mPEG3350	61.48
DOX-PLGA-mPEG8000	66.21

4 , mPEG
 6 :
 5 DOX-PLGA-mPEG8000 1mg/ml
 (pH 6.5) 20ml (dialysis bag, : 10,000) , 60ml
 , 37 16
 480nm (: 4). 4

7 :
 가
 2 (HepG2 cell line, KCLB(
)) (flow cytometry) (: 5
). 5 . 5
 가 (endocytosis) (

transport)

(PEG)

(57)

1.

() 160 200 가 , 2 (PEG) 6 (stannous octoate)
 가 , ; 가 ,
 () (CDI), N,N'- (DSC) p-
 () 가 , 5-
 () ; ,

2.

1
 () (PLA), (PGA), (D,L- -co-) (PLGA), ()
), () , () 1 ()

3.

1
 () (methoxypolyethyleneglycol, mPEG)

4.

1
 ()

5.

6.

1
 () 1:2:2 1:2:6()

7.

8.

1
 ()

9.

() (D,L- -co-) (PLGA) 180 , 2 6 (mPEG) mPEG-PLGA ;
 () mPEG-PLGA , mPEG-PLGA p- p-

() p-

mPEG-PLGA

5

()

가

10.

9

11.

9

12.

9

13.

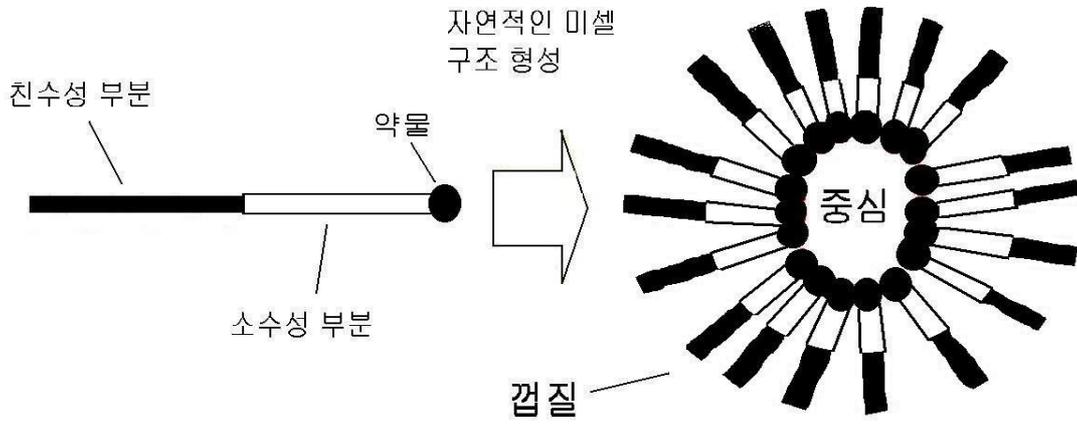
9

14.

9

, 5-

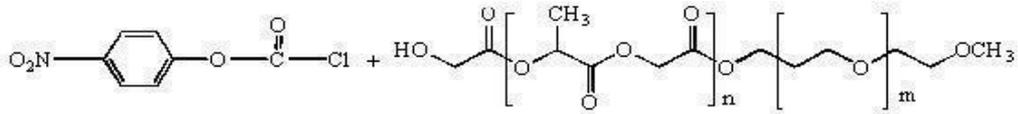
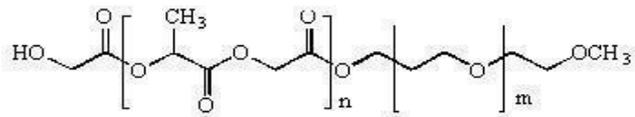
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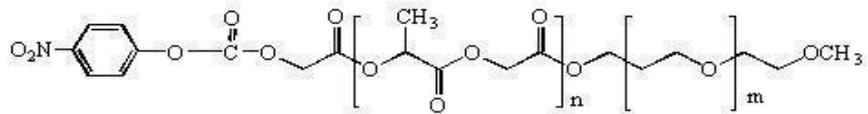
2

PLGA+mPEG

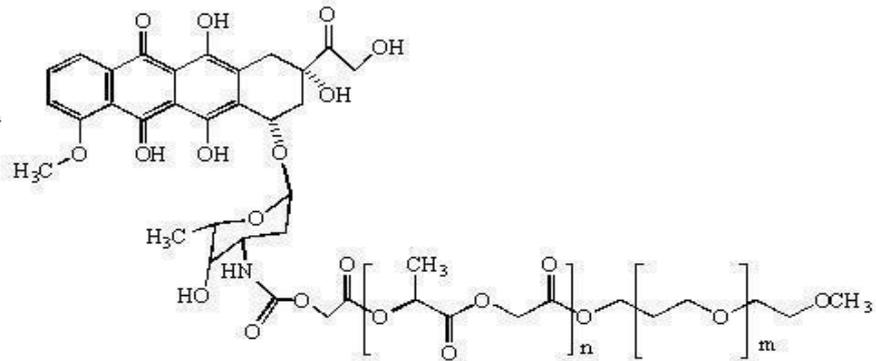
180 ° C
 →
 옥토산주석산염



피리딘
 →
 CH_2Cl_2

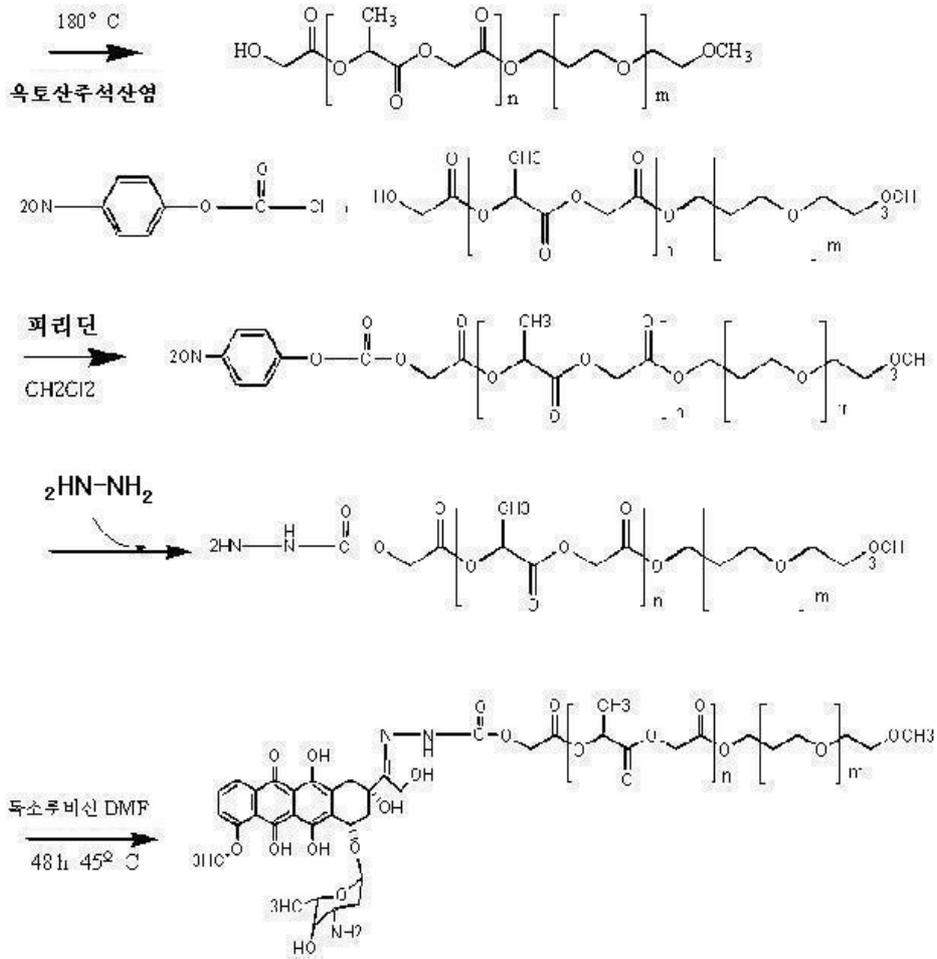


독소루비신
 →
 DMF, TEA

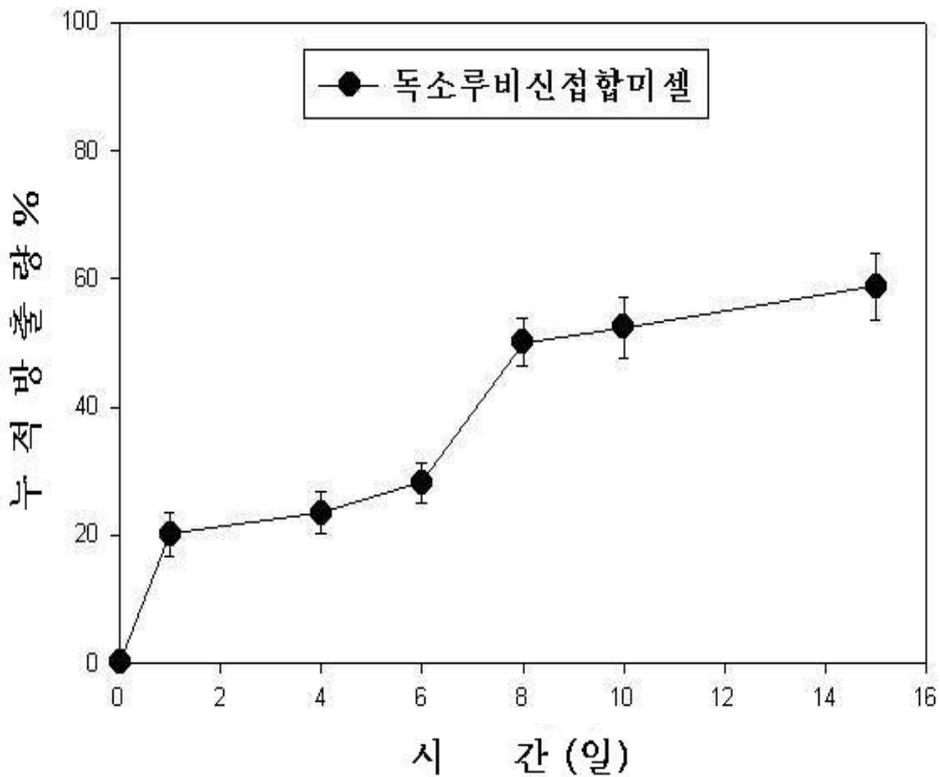


3

PLGA+mPEG



4



5

