

[DRAWINGS]

[FIG. 1]

Category	No.	Item	Composition	P188	PS80	VP (Visual inspection), VP vial#/Total vial#									
						5°C					25°C				
						1M	2M	3M	6M	1M	2M	3M	6M		
1st Pre-stability confirm	1	Phase II formulation (Control 1)	15mM Napi, 5% Sucrose, 50mM NaCl, pH6.9	0.10%	-	0/10	1/10	4/10	8/10	2/10	5/10	9/10	8/8		
	2	Candidate #1		0.10%	0.03%	0/10	0/10	0/10	0/10	0/10	0/10	0/10	1/8		
	3	Phase III formulation (Control 2)	10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 90mM NaCl, pH6.1	0.10%	-	0/10	7/10	8/10	8/10	3/10	8/10	10/10	8/8		
	4	Candidate #2		0.10%	0.03%	0/10	0/10	0/10	0/10	0/10	0/10	1/10	2/8		
New candidate	5	Candidate #3 (New form #1)	10mM Histidine, 55mM Arg, 4.2% Sucrose, 50mM Methionine, pH 6.5	0.10%	-	0/10	5/10	7/10	5/10	3/10	8/10	10/10	8/8		
	6	Candidate #4 (New form #2)		0.10%	0.03%	0/10	0/10	0/10	0/10	0/10	0/10	0/10	2/8		
	7	Candidate #5 (New form #3)	15mM Citrate, 100mM Arg, 30mM NaCl, 50mM Methionine, 1mM EDTA, pH6.5	0.10%	-	0/10	2/10	5/10	6/10	2/10	6/10	9/10	8/8		
	8	Candidate #6 (New form #4)		0.10%	0.03%	0/10	0/10	0/10	0/10	0/10	0/10	2/10	1/8		

[FIG. 2]

Category	No.	Item	Composition	P188	PS80	Sub-visible particle/ MFI (#/mL) Avg. of 2samples											
						5°C						25°C					
						1M		3M		6M		1M		3M		6M	
						(Processed data)	(Processed data)	(Processed data)	(Processed data)	(Processed data)	(Processed data)	(Processed data)	(Processed data)	(Processed data)	(Processed data)	(Processed data)	(Processed data)
						$\geq 10\mu\text{m}$	$\geq 25\mu\text{m}$	$\geq 75\mu\text{m}$	$\geq 10\mu\text{m}$	$\geq 25\mu\text{m}$	$\geq 75\mu\text{m}$	$\geq 10\mu\text{m}$	$\geq 25\mu\text{m}$	$\geq 75\mu\text{m}$	$\geq 10\mu\text{m}$	$\geq 25\mu\text{m}$	$\geq 75\mu\text{m}$
1st Pre-stability confirmation	1	Phase II formulation (Control 1)	15mM Napi, 5% Sucrose, 50mM NaCl, pH6.9	0.10%	-	69	7	0	58	8	0	222	7	0	113	23	0
	2	Candidate #1		0.10%	0.03%	19	4	0	58	19	5	9	0	0	4	0	0
	3	Phase III formulation (Control 2)	10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 90mM NaCl, pH 6.1	0.10%	-	120	12	0	195	15	0	1290	169	0	709	147	7
	4	Candidate #2		0.10%	0.03%	121	5	0	31	2	0	30	0	0	82	28	2
New candidate	5	Candidate #3 (New form #1)	10mM Histidine, 55mM Arg, 4.2% Sucrose, 50mM Methionine, pH 6.5	0.10%	-	168	19	4	102	15	0	810	62	0	429	91	0
	6	Candidate #4 (New form #2)		0.10%	0.03%	13	2	0	58	7	2	5	0	0	16	11	2
	7	Candidate #5 (New form #3)	15mM Citrate, 100mM Arg, 30mM NaCl, 50mM Methionine, 1mM EDTA, pH6.5	0.10%	-	102	12	0	366	38	0	360	11	0	196	34	0
	8	Candidate #6 (New form #4)		0.10%	0.03%	39	5	0	40	7	0	16	0	0	74	14	0

[FIG. 3]

Category	No.	Item	Composition	P188	PS80	SE-UPLC																						
						T=0			5°C, 3M			5°C, 6M			25°C, 1M			25°C, 3M			25°C, 6M							
						HMW %	Main %	LMW %	HMW %	Main %	LMW %	Reduced %	HMW %	Main %	LMW %	Reduced %	HMW %	Main %	LMW %	Reduced %	HMW %	Main %	LMW %	Reduced %				
1st Pre-stability Release-confining	1	Phase II for mulation (Control 1)	15mM Napi, 5% Sucrose, 50mM NaCl, pH6.9	0.10%	-	1.7	95.7	2.5	2.3	93.1	4.6	2.6	3.4	93.9	2.7	1.8	3.8	92.6	3.6	3.1	5.9	86.1	8.0	9.6	9.1	81.0	9.9	14.8
	2	Candidate #1		0.10%	0.03 %	1.8	95.7	2.5	2.3	93.0	4.8	2.7	5.6	91.6	2.8	4.0	3.9	92.6	3.6	3.1	5.7	87.2	7.1	8.5	11.1	79.0	9.8	16.5
	3	Phase III for mulation (Control 2)	10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 90mM NaCl, pH 6.1	0.10%	-	1.4	96.1	2.5	1.6	93.9	4.5	2.2	4.5	92.8	2.7	3.3	2.2	94.9	2.9	1.2	5.3	88.6	6.1	7.6	7.0	87.0	5.4	8.6
	4	Candidate #2		0.10%	0.03 %	1.4	96.0	2.6	1.7	93.4	4.9	2.7	2.9	94.3	2.8	1.8	2.4	94.8	2.8	1.2	4.9	89.1	6.0	6.9	7.7	87.1	5.2	9.0
New candidate	5	Candidate #3 (New form #1)	10mM Histidine, 55mM Arg, 4.2% Sucrose, 50mM Methionine, pH 6.5	0.10%	-	1.6	95.8	2.6	1.7	93.8	4.6	2.1	3.1	94.6	2.4	1.3	2.5	94.6	3.0	1.3	4.3	89.3	6.4	6.6	8.6	85.6	5.7	10.1
	6	Candidate #4 (New form #2)		0.10%	0.03 %	1.5	96.1	2.4	1.8	93.3	4.9	2.7	3.4	94.1	2.6	2.0	2.5	94.5	3.0	1.5	5.7	88.0	6.3	8.1	9.8	84.5	5.7	11.5
	7	Candidate #5 (New form #3)	15mM Citrate, 100mM Arg, 30mM NaCl, 50mM Methionine, 1mM EDTA, pH6.5	0.10%	-	1.5	96.1	2.5	1.5	93.8	4.7	2.2	3.2	94.4	2.4	1.7	2.2	94.6	3.1	1.4	3.9	89.6	6.5	6.5	6.6	86.5	6.9	9.5
	8	Candidate #6 (New form #4)		0.10%	0.03 %	1.4	96.1	2.5	1.5	93.4	5.0	2.7	4.1	93.2	2.7	2.9	2.4	94.3	3.3	1.8	4.2	89.5	6.3	6.7	8.5	84.5	7.3	12.0

[FIG. 4]

Category	No.	Item	Composition	P188	PS80	RP-HPLC																	
						T=0			5°C, 3M			5°C, 6M			25°C, 1M			25°C, 3M			25°C, 6M		
						Pre% n	Post n	Mai n	Pre %	Redu ced%	Post %	Mai n	Pre %	Redu ced%	Post t%	Mai n	Pre %	Redu ced%	Post t%	Mai n	Pre %	Redu ced%	Post n
1st Pre-s tability R e-confir ming	1	Phase II form ulation (Control 1)	15mM Napi, 5% Sucrose, 50mM NaCl, pH6.9	0.10%	-	4.6 0	86. 0	9.5 4	87. 1	8.5 1	-1.1 4.4	87. 8	7.8 8	-1.8 5.6	83. 7	10. 7	2.3 7	14.5 68.1	17. 5	17.9 24.5	58. 9	16.6 27.1	
	2	Candidate #1		0.10%	0.03 %	4.8 9	85. 9	9.3 4	87. 0	8.7 0	-1.1 4.3	88. 2	7.5 2	-2.3 5.4	83. 7	10. 9	2.3 7	14.1 69.6	16. 3	16.3 25.2	58. 6	16.2 27.3	
	3	Phase III form ulation (Contr ol 2)	10mM Histidine, 55mM Arginine, 55mM Glutamic acid,	0.10%	-	4.3 6	86. 6	9.1 4	87. 5	8.3 5	-1.0 4.3	88. 5	7.2 5	-1.9 5.1	85. 8	9.2 8	0.8 8	15.0 70.1	14. 6	16.5 25.9	57. 9	16.2 28.7	
	4	Candidate #2	90mM NaCl, p H6.1	0.10%	0.03 %	4.2 4	86. 4	9.5 4	87. 5	8.3 5	-1.1 4.3	88. 3	7.4 3	-1.9 5.0	85. 7	9.3 7	0.7 7	14.9 69.6	15. 5	16.8 24.4	60. 2	15.4 26.2	
New can didate	5	Candidate #3 (New form # 1)	10mM Histidine, 55mM Arg, 4.2% Sucrose,	0.10%	-	4.3 7	86. 7	9.1 4	87. 9	8.1 9	-1.2 4.3	88. 3	7.5 3	-1.6 5.2	85. 8	9.1 9	0.9 7	14.7 70.6	14. 7	16.1 25.7	61. 2	13.1 25.5	
	6	Candidate #4 (New form # 2)	50mM Methionine, pH 6.5	0.10%	0.03 %	4.2 6	86. 6	9.3 4	87. 5	8.4 5	-0.9 4.2	88. 2	7.6 2	-1.6 5.1	85. 3	9.6 3	1.3 3	15.4 69.7	14. 9	16.9 23.4	62. 6	14.1 24.0	
	7	Candidate #5 (New form # 3)	15mM Citrate, 100mM Arg, 30mM NaCl,	0.10%	-	4.3 4	86. 4	9.3 4	87. 7	8.4 7	-1.2 4.2	88. 5	7.3 5	-2.1 5.1	84. 2	9.6 2	2.2 2	15.9 69.3	14. 9	17.1 24.7	61. 2	14.1 25.2	
	8	Candidate #6 (New form # 4)	50mM Methionine, 1mM EDTA, pH 6.5	0.10%	0.03 %	4.2 7	86. 7	9.1 4	87. 7	8.2 7	-1.0 4.3	88. 4	7.3 4	-1.7 5.6	85. 5	8.9 5	1.2 5	16.1 69.9	14. 1	16.8 26.6	58. 8	14.6 27.9	

[FIG. 5]

2R Type I glass vial/ Flurotec stopper					VP (Visual inspection)			
					T0	25°C 1M	25°C 2M	25°C 3M
No.	Conc/ Vol	Composition	P188	PS80	VP vial#/Total vial#			
1	60mg/mL, 0.8mL/vial	10mM Histidine, 55 mM Arginine, 55m M Glutamic acid, 90 mM NaCl, pH6.1	0.10%	-	0/10	8/10	7/8	6/6
2				0.01%	0/10	0/10	2/8	5/6
3				0.03%	0/10	0/10	0/10	2/6
4				0.05%	0/10	0/10	0/10	1/6
5				0.07%	0/10	0/10	0/10	0/6
6				0.10%	0/10	0/10	0/10	0/6
7				0.15%	0/10	0/10	0/10	1/6
8				0.20%	0/10	0/10	0/10	0/6

[FIG. 6]

2R Type I glass vial/ Flurotec stopper					SVP (MFI) #/mL									
					25°C 1M (Processed)				25°C 2M (Processed)				25°C 3M (Processed)	
No.	Conc/ Vol	Compositi on	P188	PS80	≥ 10µm	≥ 25µm	≥ 75µm	≥ 10µm	≥ 25µm	≥ 75µm	≥ 10µm	≥ 25µm	≥ 10µm	≥ 75µm
1				-	482	78	10	1269	258	16	1583	203	2	2
2				0.01%	65	6	0	100	3	0	383	12	2	2
3				0.03%	50	10	0	49	12	0	19	2	0	0
4				0.05%	54	12	0	51	17	0	21	0	0	0
5				0.07%	36	2	0	103	17	0	18	2	0	0
6				0.10%	73	15	0	49	3	0	129	16	3	3
7				0.15%	58	6	0	89	21	0	21	0	0	0
8				0.20%	69	23	0	22	4	0	51	19	0	0

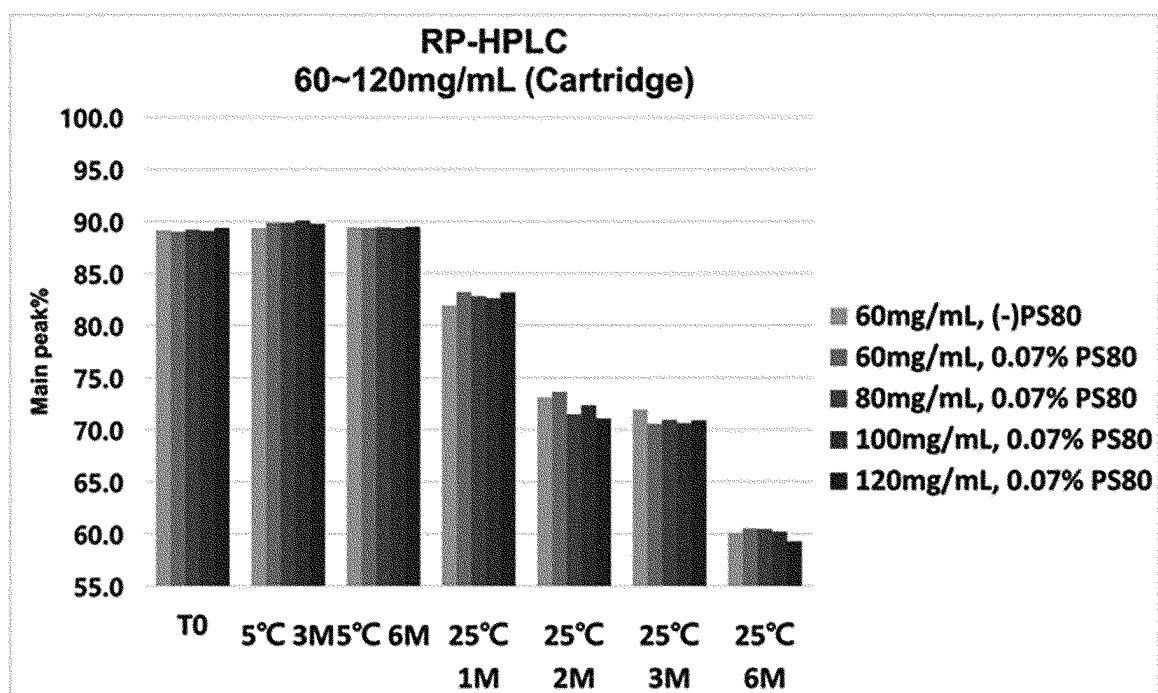
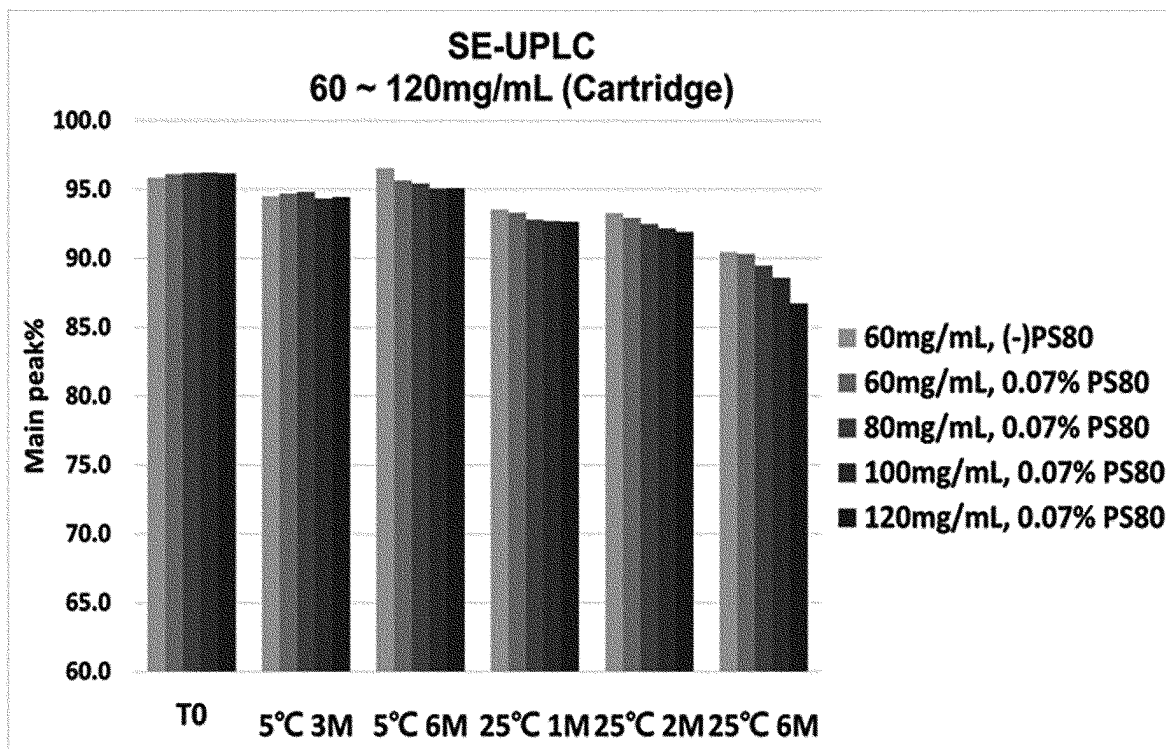
[FIG. 7]

2R Type I glass vial/ Fluoretec stopper					SE-UPLC										RP-HPLC																			
					T=0					5°C 3M					25°C 3M					T=0					5°C 3M					25°C 3M				
					HMW %	Main peak%	LMW %	HMW %	Main peak %	Main peak reduction % (T0(T0))	LMW %	Main peak %	Main peak reduction % (T0(T0))	LMW %	Main peak %	Main peak reduction % (T0(T0))	Pre-peak %	Main peak %	Post-peak %	Pre-peak %	Main peak %	Post-peak %	Main peak reduction % (T0(T0))	Pre-peak %	Main peak %	Post-peak %	Main peak reduction % (T0(T0))	Pre-peak %	Main peak %	Post-peak %	Main peak reduction % (T0(T0))			
No.	Conc/ Vol	Composition	P188	PS80	-	1.3	93.9	4.8	1.7	95.4	2.9	-1.6	5.1	90.4	4.5	3.4	4.6	86.1	9.3	4.0	88.3	7.2	-2.2	17.1	67.8	15.1	18.3							
2				0.01%	1.4	93.8	4.8	2.4	94.5	3.0	-0.7	5.2	90.3	4.5	3.5	4.6	86.2	9.2	3.9	88.2	7.3	-2.0	17.0	67.5	15.5	18.7								
3			10mM Histidine, 55mM Arginine	0.03%	1.4	93.8	4.9	2.2	94.6	3.2	-0.9	5.6	89.5	4.9	4.3	4.7	86.2	9.2	4.0	88.2	7.3	-2.0	17.7	66.5	15.5	19.7								
4	60mg/mL, 0.8 mL/vial	55mM Glutamic acid, 90mM NaCl, pH6.1	0.10%	0.05%	1.4	93.7	4.9	1.9	95.3	2.8	-1.6	6.6	88.8	4.6	4.9	4.7	86.3	9.0	4.0	88.3	7.2	-2.0	17.7	67.7	14.6	18.7								
5				0.07%	1.4	93.4	5.2	2.2	94.8	3.0	-1.4	6.6	88.8	4.6	4.6	4.7	85.9	9.4	4.0	88.3	7.1	-2.4	17.3	67.7	15.0	18.3								
6				0.10%	1.5	93.5	5.0	2.1	95.0	2.8	-1.5	7.7	87.4	4.9	6.1	4.7	86.2	9.2	3.9	88.4	7.1	-2.2	17.7	66.5	16.0	19.6								
7				0.15%	1.4	93.7	4.9	2.1	94.9	2.9	-1.3	8.0	87.6	4.4	6.0	4.7	86.1	9.2	4.0	88.3	7.2	-2.3	17.1	68.0	14.9	18.0								
8				0.20%	1.4	93.6	5.0	4.6	92.5	2.8	1.1	6.0	89.4	4.6	4.1	4.7	85.8	9.5	4.0	88.2	7.2	-2.4	17.3	67.5	15.2	18.4								

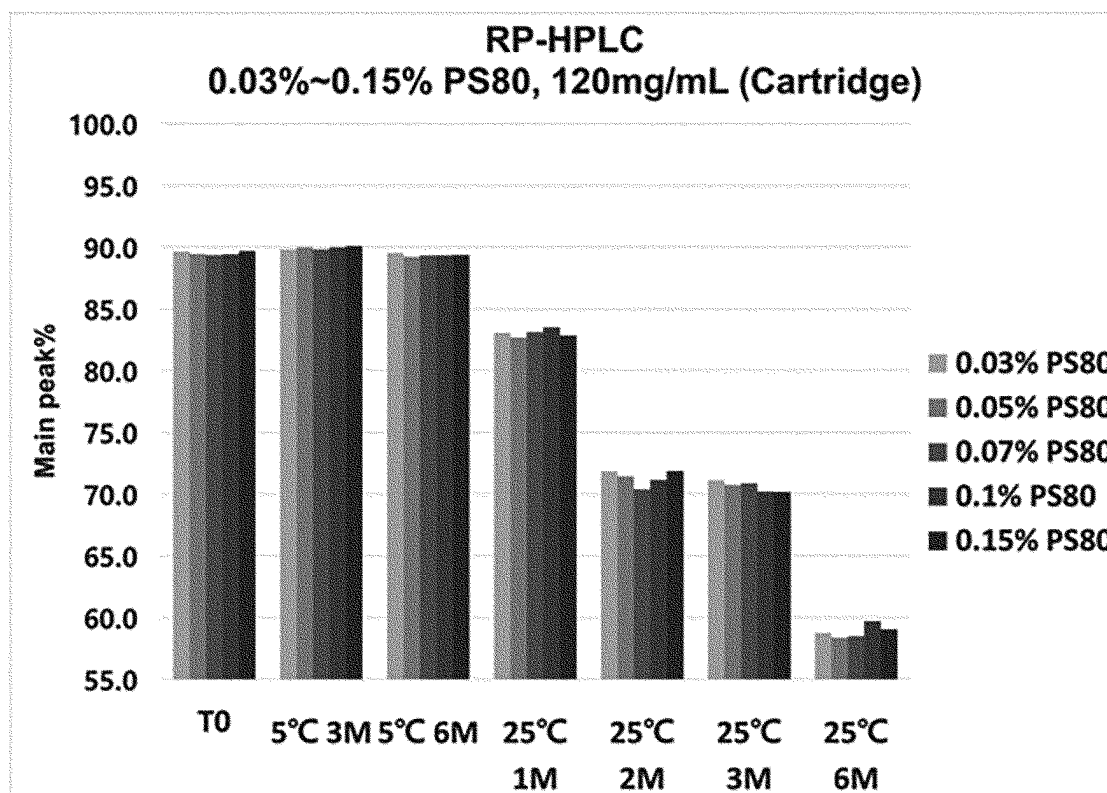
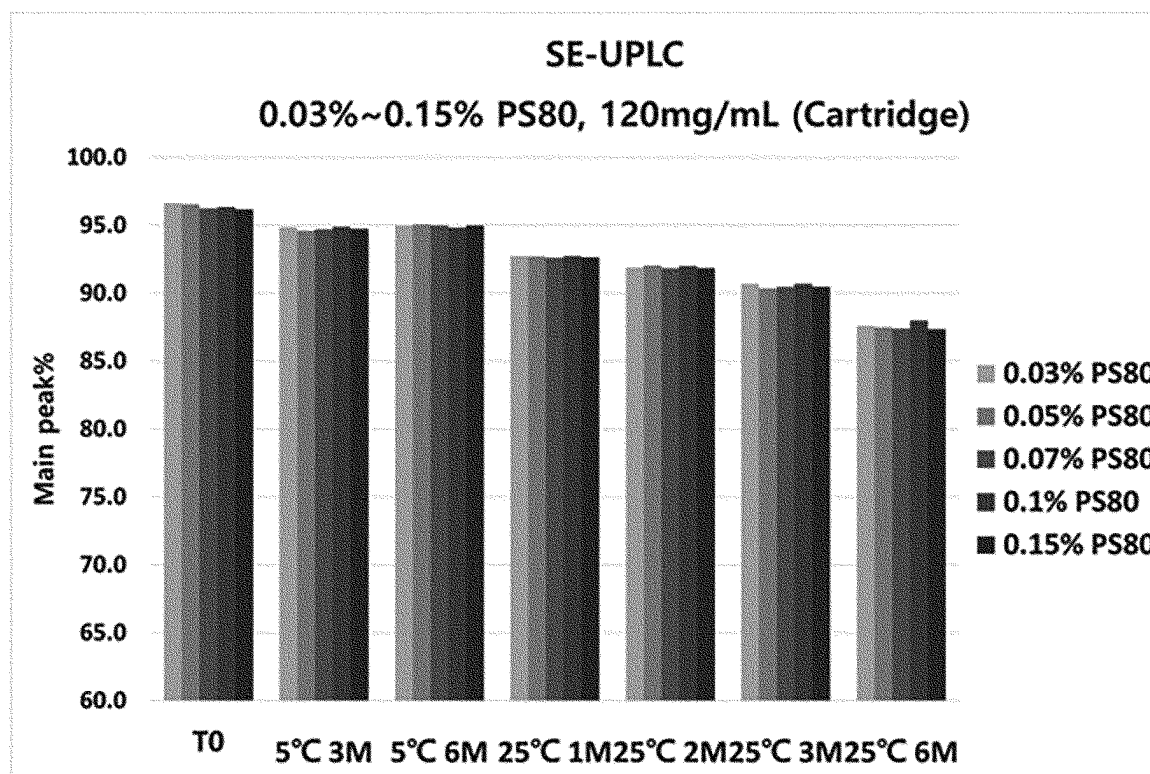
[FIG. 8]

Items	No.	Conc. / Vol / Container	Buffer Co mpositio n	PS80 co nc.	Preservative	Visible particle (VP vial/total vial)									
						cold storage (5°C)			room temperature (25°C)						
						T0	3M	6M	T0	1M	2M	3M	6M		
Control	1	60mg/mL /Cartridge		-	-	0/12	7/13	9/9	0/13	5/13	10/11	7/9	5/7		
Conc.	2	80mg/mL /Cartridge		0.07%	-	0/13	0/13	0/8	0/16	0/16	0/14	0/12	0/9		
	3	100mg/mL /Cartridge		0.07%	-	0/13	0/13	0/9	0/16	0/16	0/14	0/12	0/10		
	4	120mg/mL /Cartridge		0.07%	-	0/13	0/13	0/9	0/16	0/16	0/14	0/12	0/10		
	5	120mg/mL /Cartridge		0.07%		0/13	0/13	0/9	0/16	0/16	1/14	1/12	0/10		
PS80	6	120mg/mL /Cartridge	10mM Hi stidine, 5 mM Argi nine, 55m M Glutam ic acid, 9 0mM Na Cl, pH6.1	0.03%		0/13	0/13	0/10	0/13	3/13	3/11	1/9	1/7		
	7			0.05%	-	0/13	0/13	0/10	0/16	0/16	0/14	0/12	0/10		
	8			0.07%	-	0/13	0/13	0/9	0/16	0/16	0/14	0/12	0/10		
	9			0.10%	-	0/13	0/13	0/10	0/16	0/16	0/13	0/11	0/9		
	10			0.15%		0/13	0/13	0/10	0/16	0/16	0/14	0/12	0/10		
Preserv ative	11 (P1)	60mg/mL / Vial		0.07%	m-cresol (3mg/mL)	0/6	6/6	4/4	2/6	13/13	11/11	9/9	8/8		
	12 (P2)				m-cresol (1mg/mL)	0/6	1/6	0/4	1/6	1/13	0/11	1/9	0/8		
	13 (P3)				phenol (3mg/mL)	0/6	0/6	1/4	0/6	0/13	0/11	0/9	0/8 (+++)		
	14 (P4)				phenol (1mg/mL)	0/6	0/6	0/2	0/6	0/13	0/11	0/9	0/5		
	15 (P5)				Benzyl alcohol (9mg/mL)	0/6	1/6	0/4	0/6	1/13	1/11	1/9	3/7 (++)		
	16 (P6)				Benzyl alcohol (3mg/mL)	0/6	3/6	0/4	1/6	3/13	2/11	1/9	1/7		

[FIG. 9A]



[FIG. 9B]



[FIG. 9C]

