

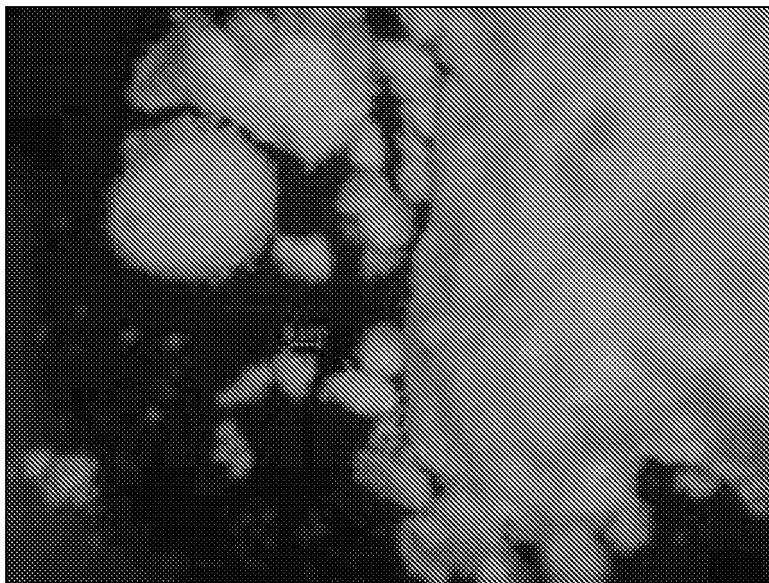


Fig. 1

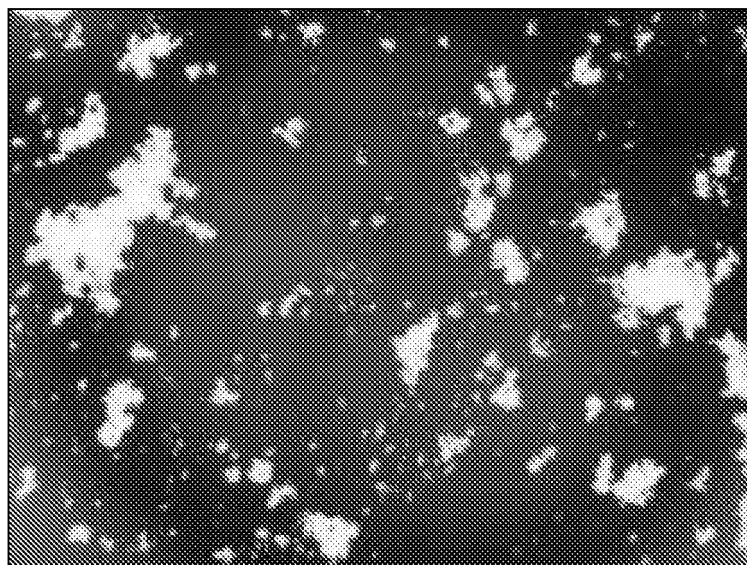


Fig. 2

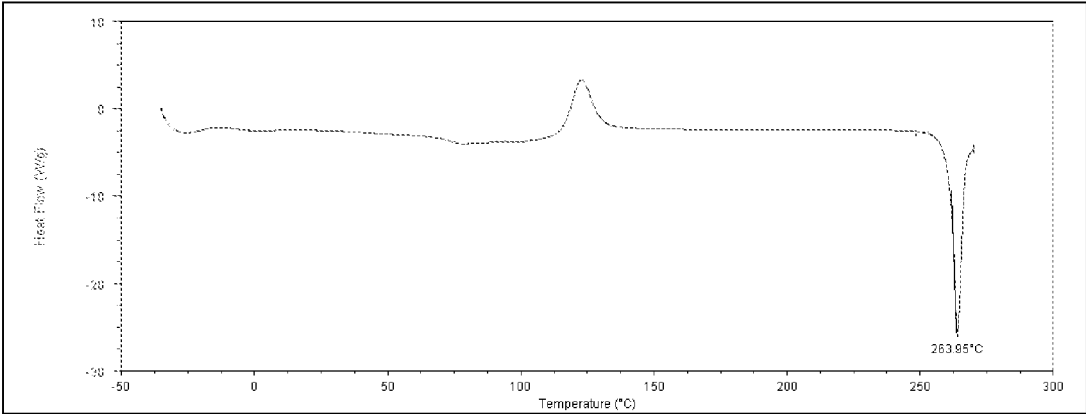


Fig. 3

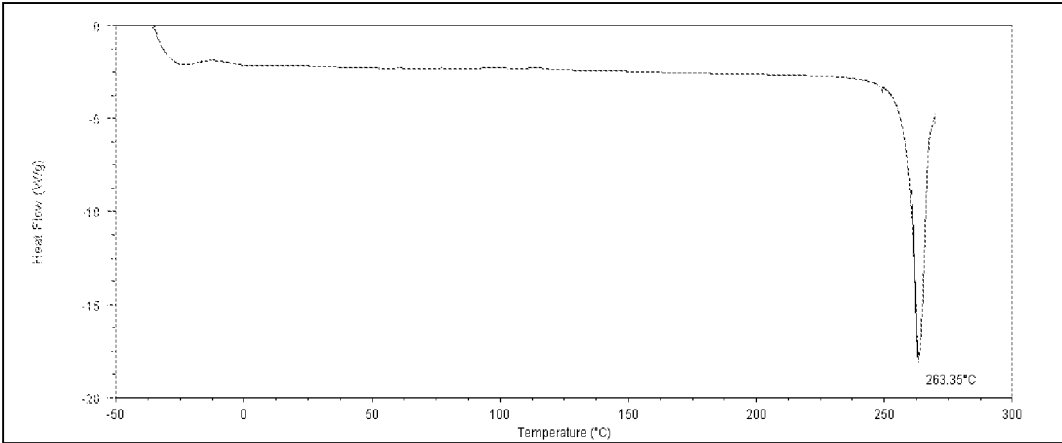


Fig. 4

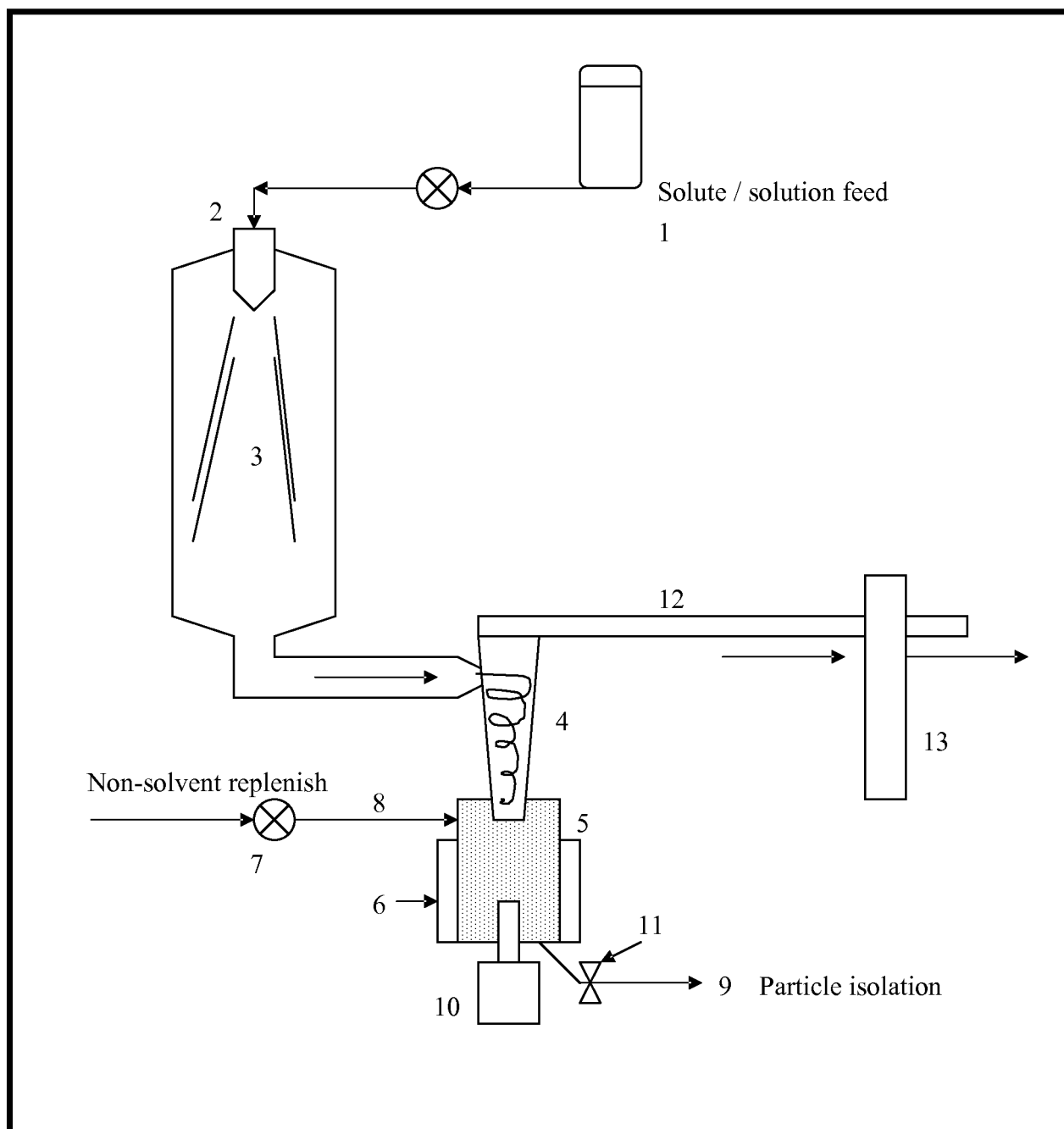


Fig. 5

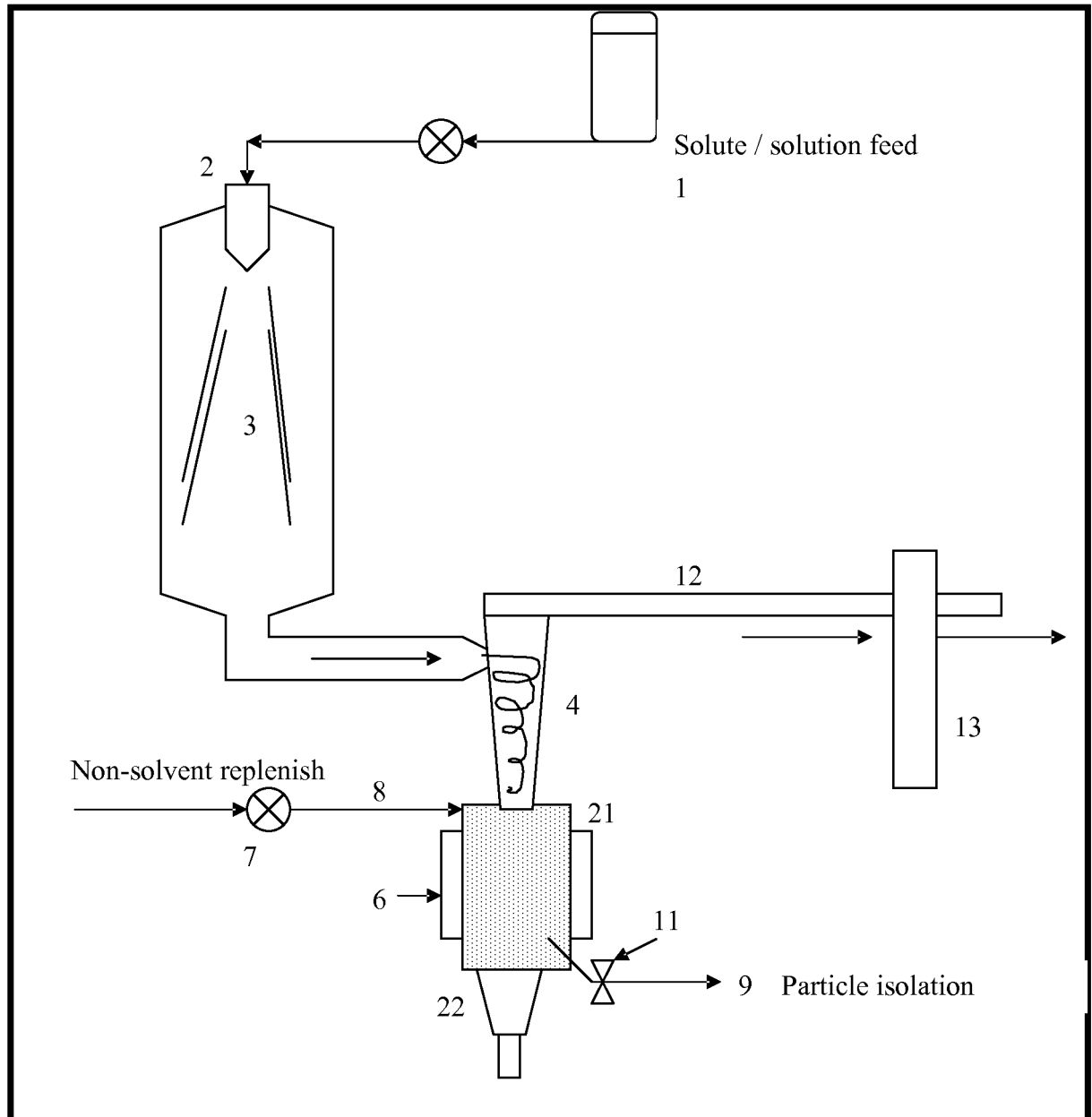


Fig. 6

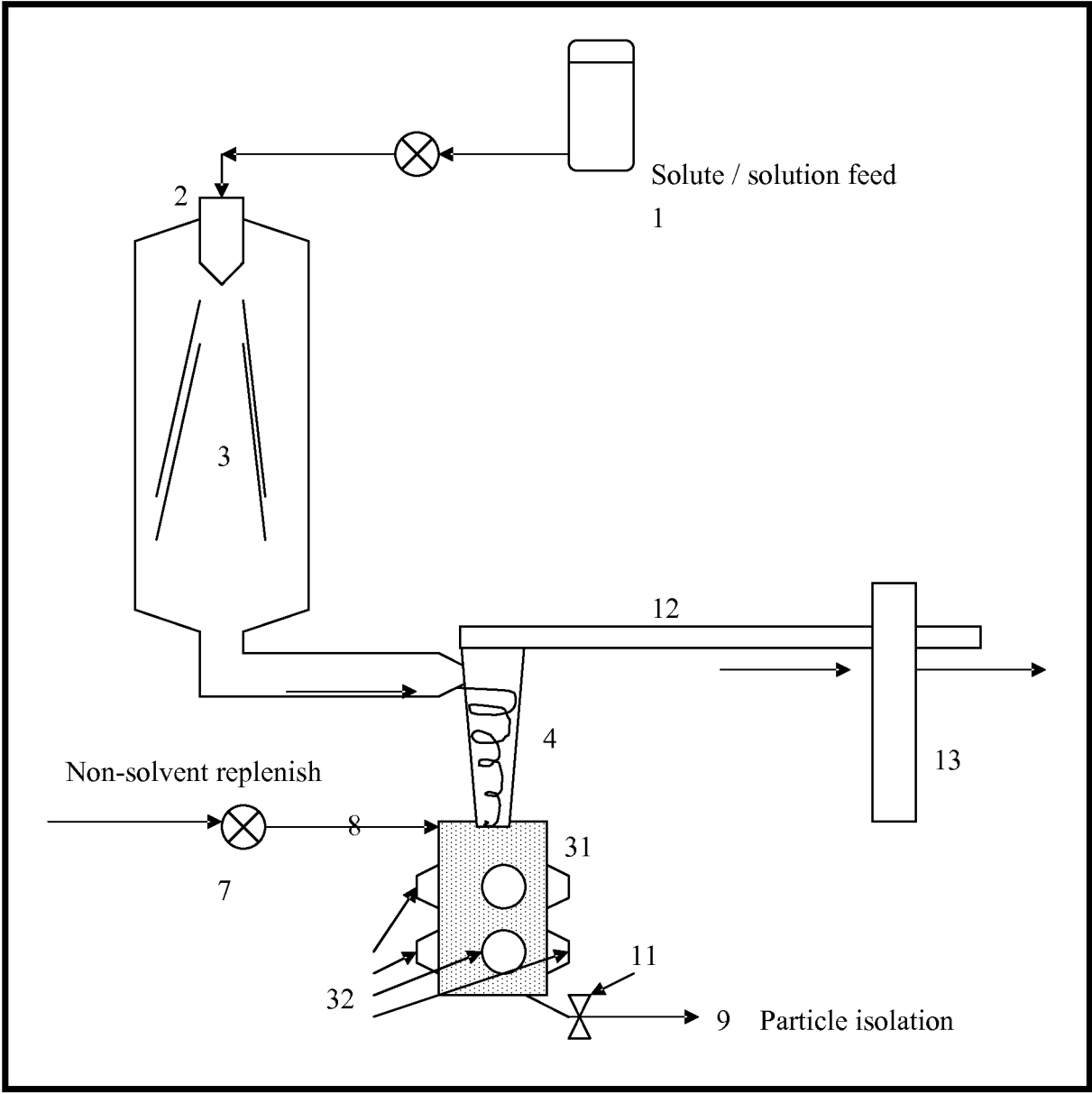


Fig. 7

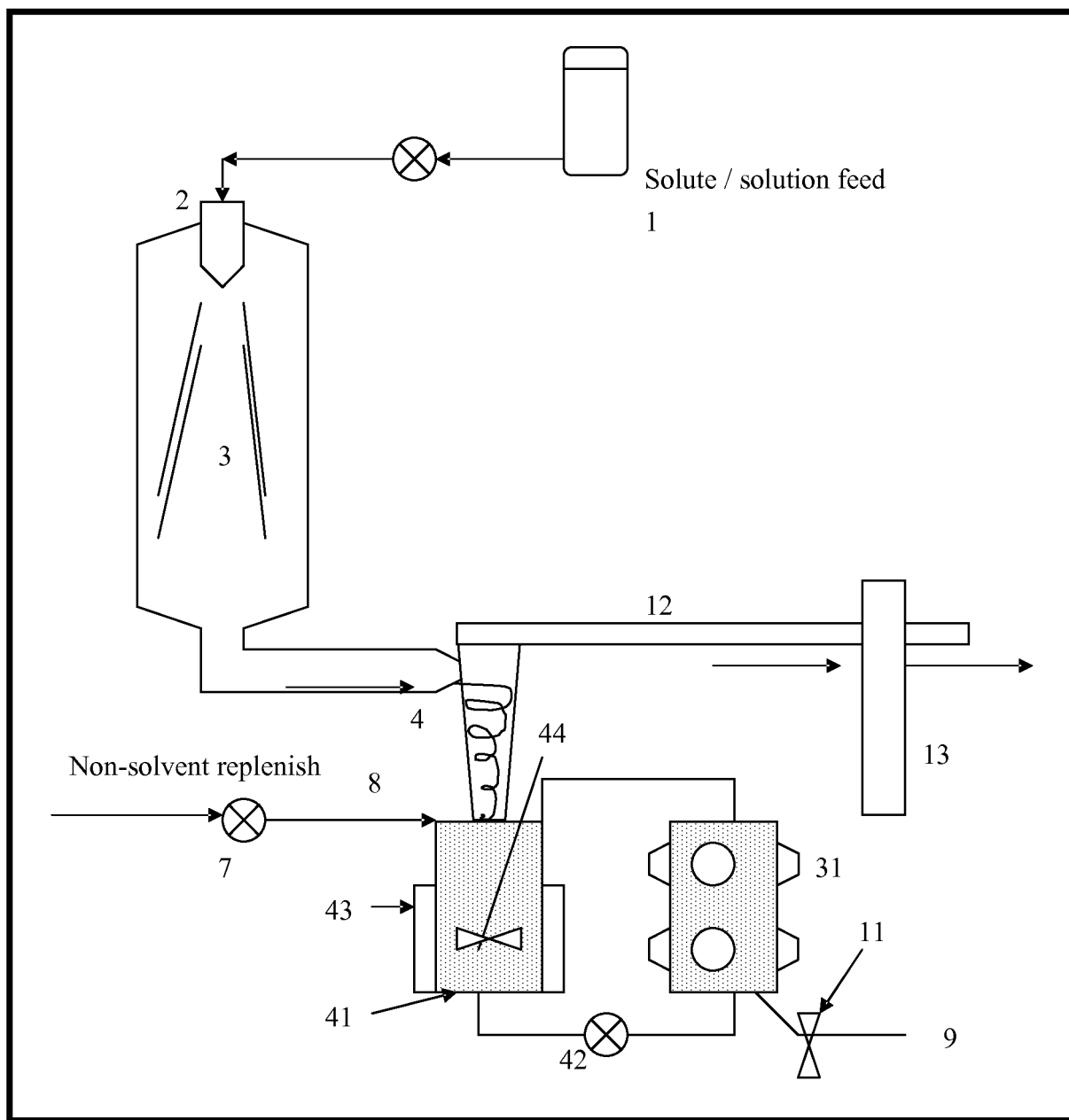


Fig. 8

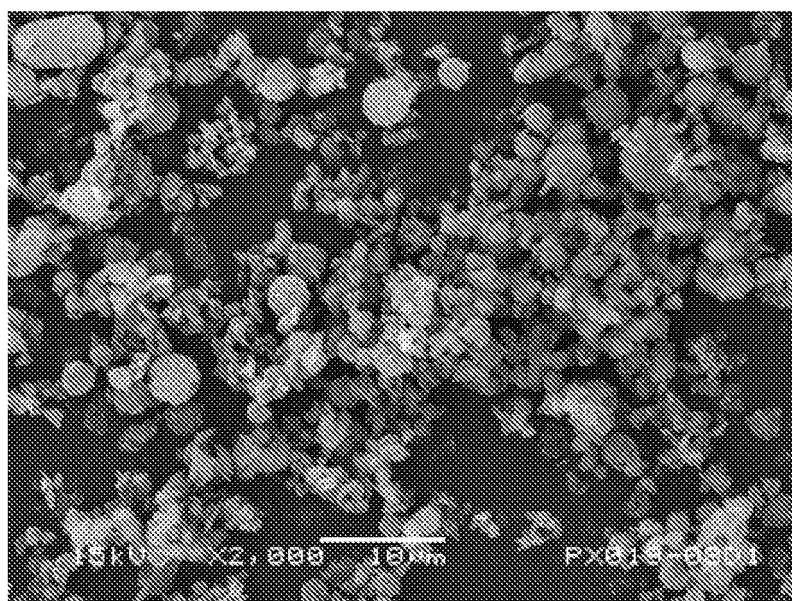


Fig. 9

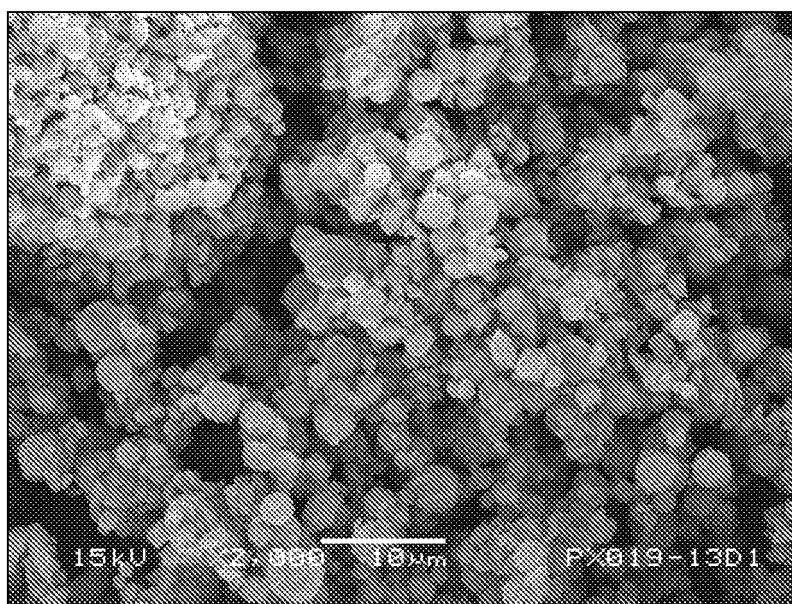


Fig. 10

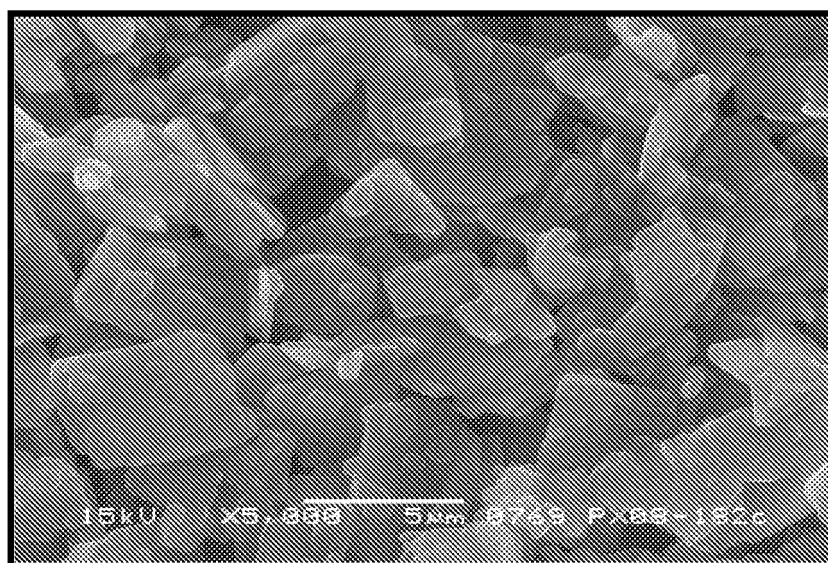


Fig. 11

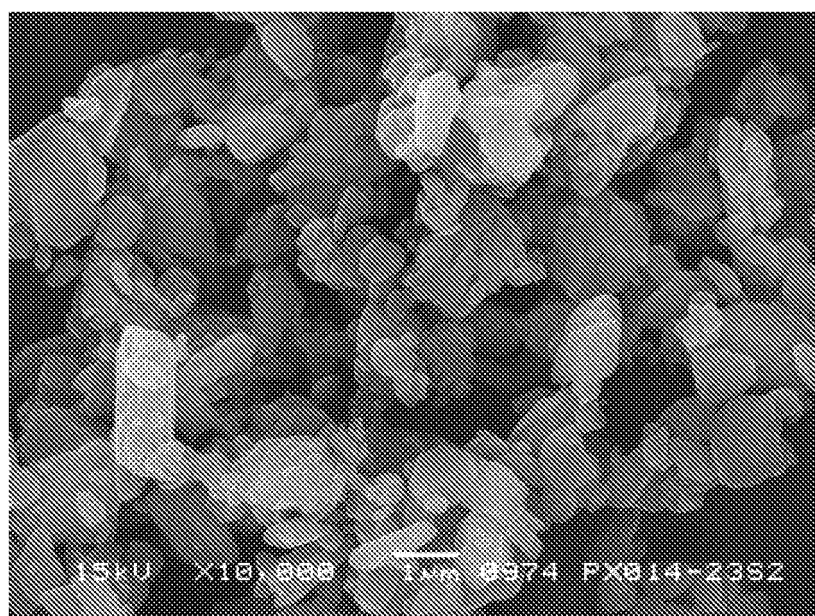


Fig. 12

Results: Aerosolization Efficiency				
	% Emitted Fraction ($\pm$ S.D.)	Fine Particle Dose ($\pm$ μ g)	FPF _{LD} ($\pm$ %)	MMAD ($\pm$ GSD)
Micronized	85.6 (4.2)	4.9 (0.9)	9.7 (0.7)	4.87 $\pm$ 1.97
Sample 2	93.7 (3.8)	7.5 (0.2)	14.9 (0.6)	4.48 $\pm$ 1.90
Sample 3	89.7 (3.7)	7.8 (0.4)	15.6 (0.5)	3.73 $\pm$ 2.17
Sample 4	90.7 (4.2)	2.5 (0.3)	5.1 (0.7)	4.85 $\pm$ 2.08

Fig. 13

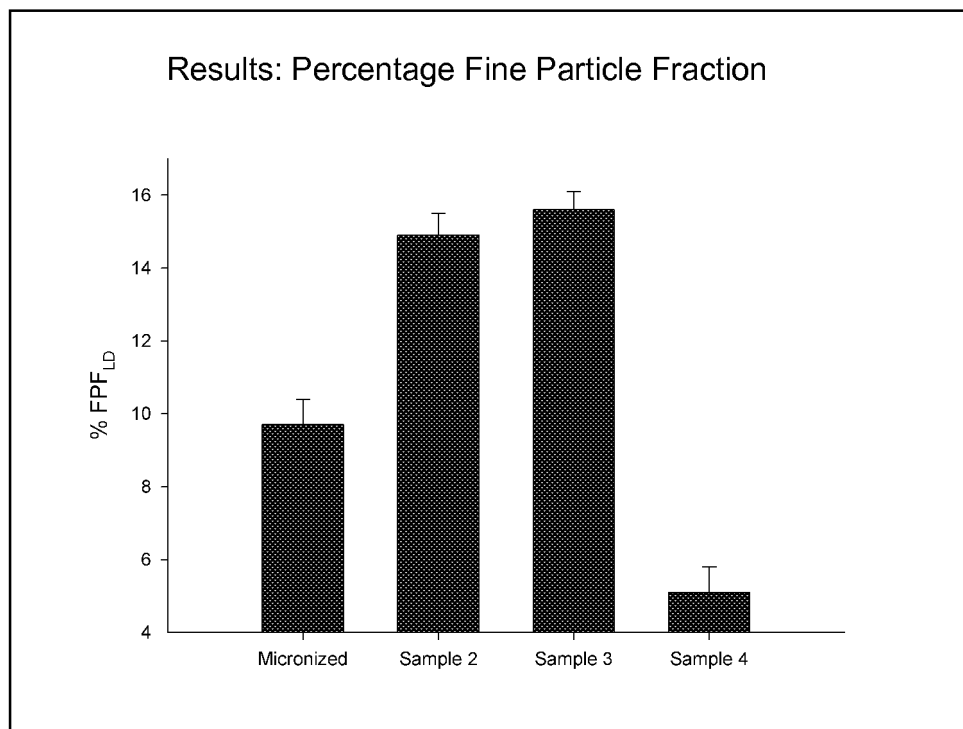
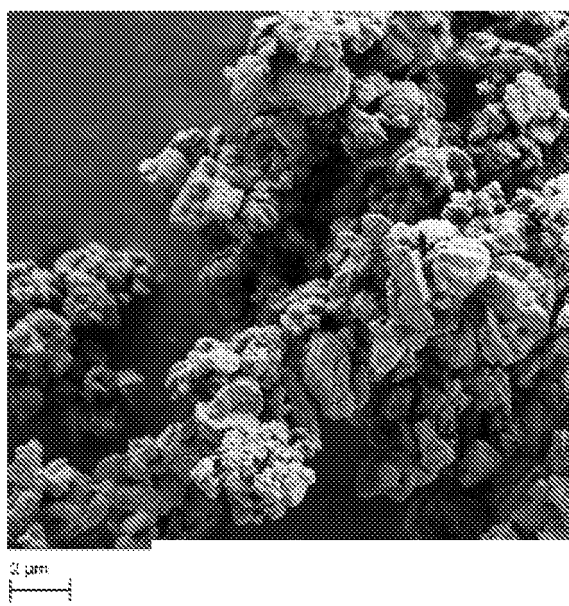


Fig. 14

Results: Aerosolization Efficiency Compared to Flixotide

	% Emitted Fraction ($\pm$ S.D.)	Fine Particle Dose ($\pm$ μ g)	FPF _{LD} ($\pm$ %)	MMAD ($\pm$ GSD)
Flixotide	94.3 (3.4)	6.1 (0.2)	12.1 (0.2)	3.43 $\pm$ 2.13
Sample 2	93.7 (3.8)	7.5 (0.2)	14.9 (0.6)	4.48 $\pm$ 1.90
Sample 3	89.7 (3.7)	7.8 (0.4)	15.6 (0.5)	3.73 $\pm$ 2.17
Sample 4	90.7 (4.2)	2.5 (0.3)	5.1 (0.7)	4.85 $\pm$ 2.08

Fig. 15**Fig. 16**

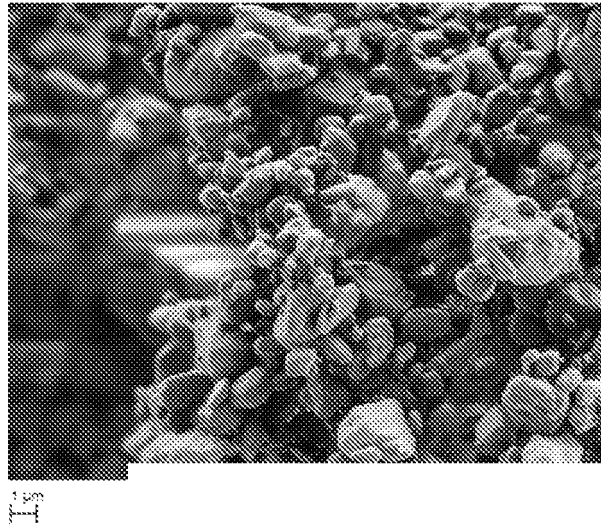


Fig. 17

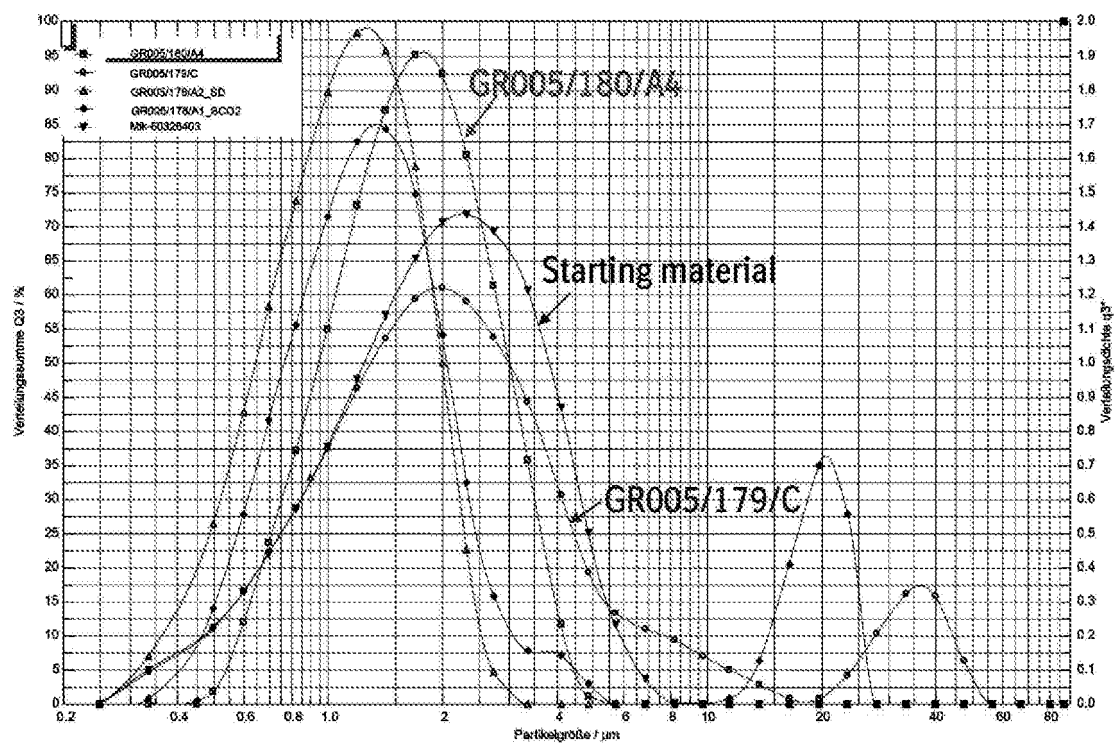


Fig. 18

	Micronised Starting material		GR005/179/C Pre ultrasonic treatment		GR005/180/A4 Post ultrasound	
Formulation	100% (drug only)	25%	100%	25%	100%	25%
Content [%]		24.2		25.06		24.3
RSD [%]		1.7		3.2		1.6
FPF [%]	15.8	21.9	20.3	18.5	25.5	28.6
RSD [%]	20.3	13.2	8.9	11.9	6.6	11.2
FPD [mg]	4.8	1.6	6.1	1.4	7.6	2.1
DD [%]	72.7	84.1	77.6	91.8	68.8	82.9
RSD [%]	16.5	1.2	5.9	2.4	15.7	1.2
RSD Relative Standard Deviation; DD Delivered Dose						

Fig. 19

	Micronised Starting material		GR005/179/C Pre ultrasonic treatment		GR005/180/A4 Post ultrasound	
Formulation	100%	25%	100%	25%	100%	25%
Content [%]		24.2		25.06		24.3
RSD [%]		1.65		3.2		1.64
FPF [%]	3.4	15.1	5.7	15.2	7.4	21.6
RSD [%]	14.7	13.2	26.3	3.9	10.8	3.7
FPD [mg]	1.0	1.1	1.7	1.1	2.3	1.6
DD [%]	93.9	88.0	93.2	91.4	93.8	89.8
RSD [%]	2.9	3.9	3.4	3.0	1.9	3.7
RSD Relative Standard Deviation; DD Delivered Dose						

Fig. 20

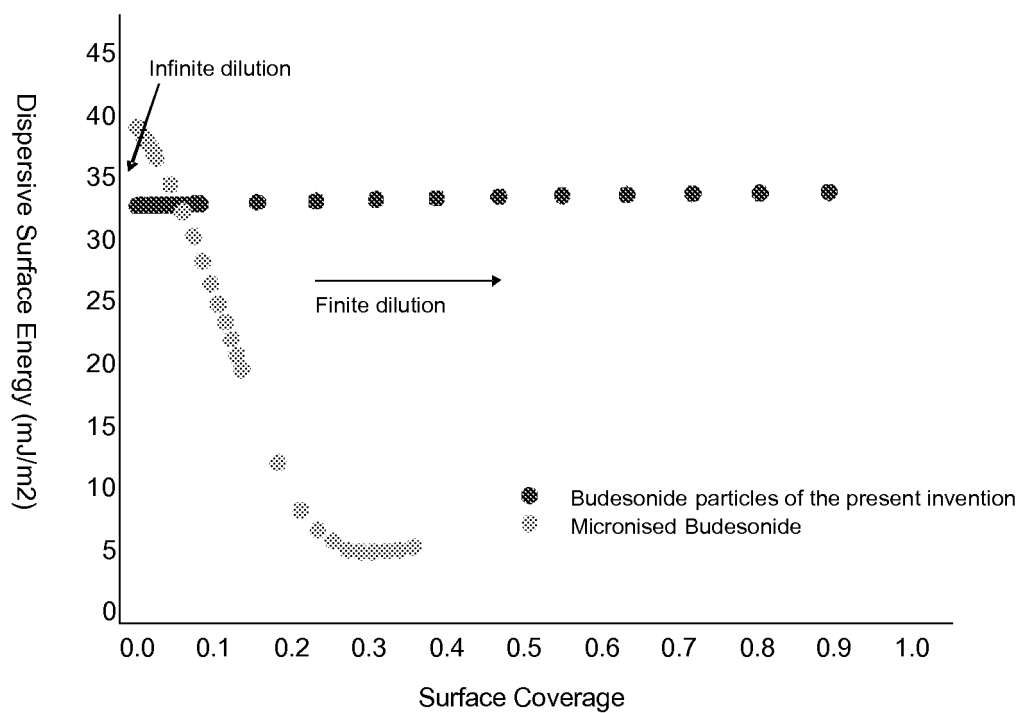


Fig. 21

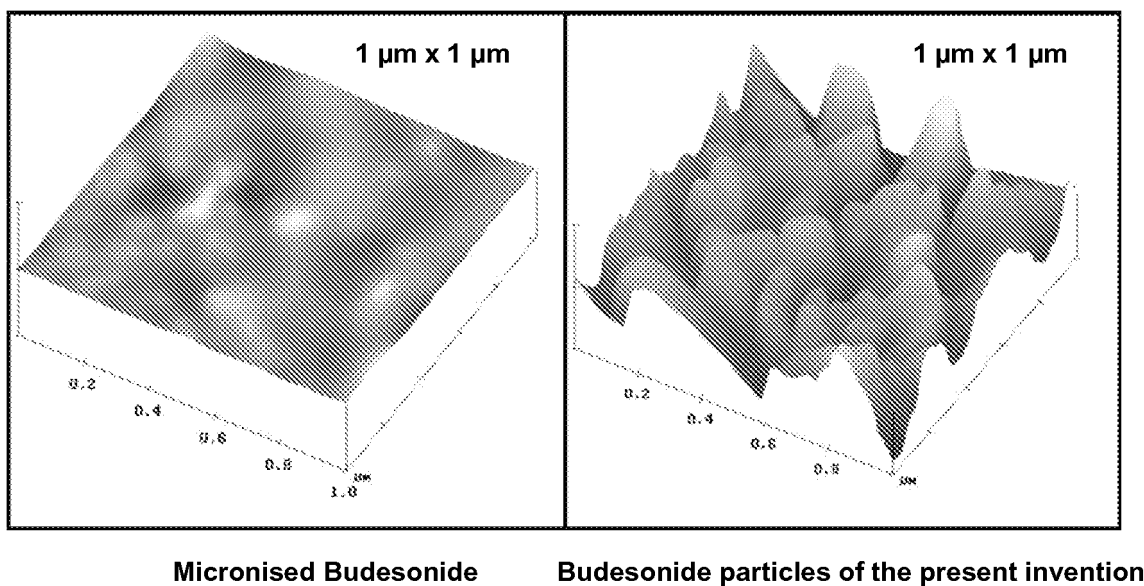


Fig. 22

Results: Aerosolization Efficiency – 3 Months

	FPD ($\pm$ μ g) t = 0	FPF _{LD} ($\pm$ %) t = 0	FPD ($\pm$ μ g) t = 1 m	FPF _{LD} ($\pm$ %) t = 1m	FPD ($\pm$ μ g) t = 3 m	FPF _{LD} ($\pm$ %) t = 3m
Micronized	4.9 (0.9)	9.7 (0.7)	2.5 (0.1)	5.0 (0.2)	1.6 (0.2)	3.2 (0.7)
Sample 2	7.5 (0.2)	14.9 (0.6)	6.9 (1.3)	13.8 (1.8)	5.4 (1.2)	10.7 (1.2)
Sample 3	7.8 (0.4)	15.6 (0.5)	7.3 (0.4)	14.6 (0.6)	7.6 (0.3)	15.2 (1.6)
Sample 4	2.5 (0.3)	5.1 (0.7)	1.8 (0.2)	3.6 (0.3)	1.9 (0.5)	3.9 (0.7)

Fig. 23

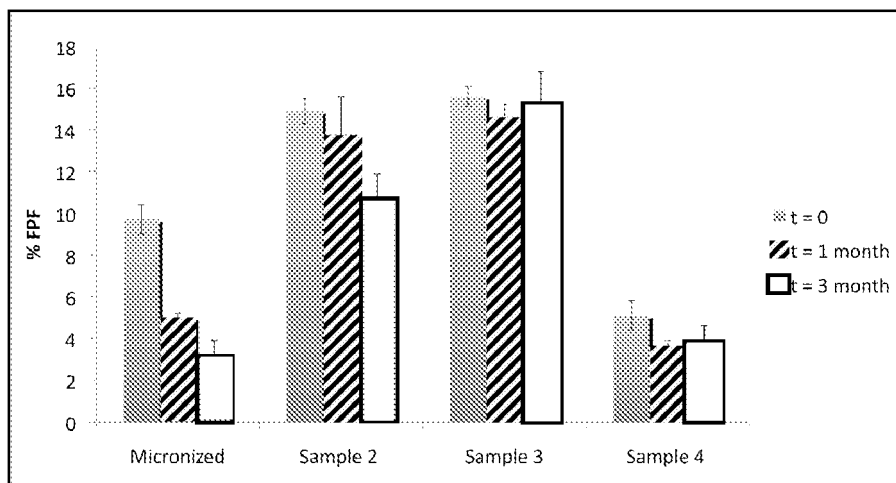


Fig. 24

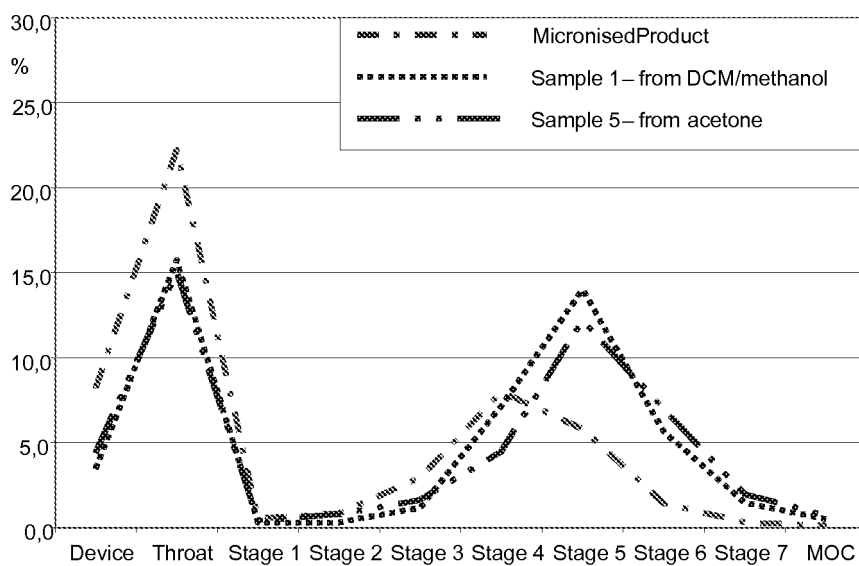


Fig. 25

Results: % Fine Particle Fraction of FP after 1 m storage

			T = 0		T = 1 month	
			FPF [%/LD]	SD	FPF [%/LD]	SD
FP	Cyclohaler	Micronized	13.9	1.2	15.4	0.2
		Sample_2	16.7	1.1	17.5	0.4
		Sample_3	18.9	0.8	17.2	0.8
		Sample_4	17.6	3.1	17.7	1.1
	Rotahaler	Micronized	14.4	2.0	14.4	0.9
		Sample_2	15.5	1.7	17.5	0.6
		Sample_3	18.5	1.1	19.0	0.9
		Sample_4	5.3	0.7	8.2	1.3

Fig. 26

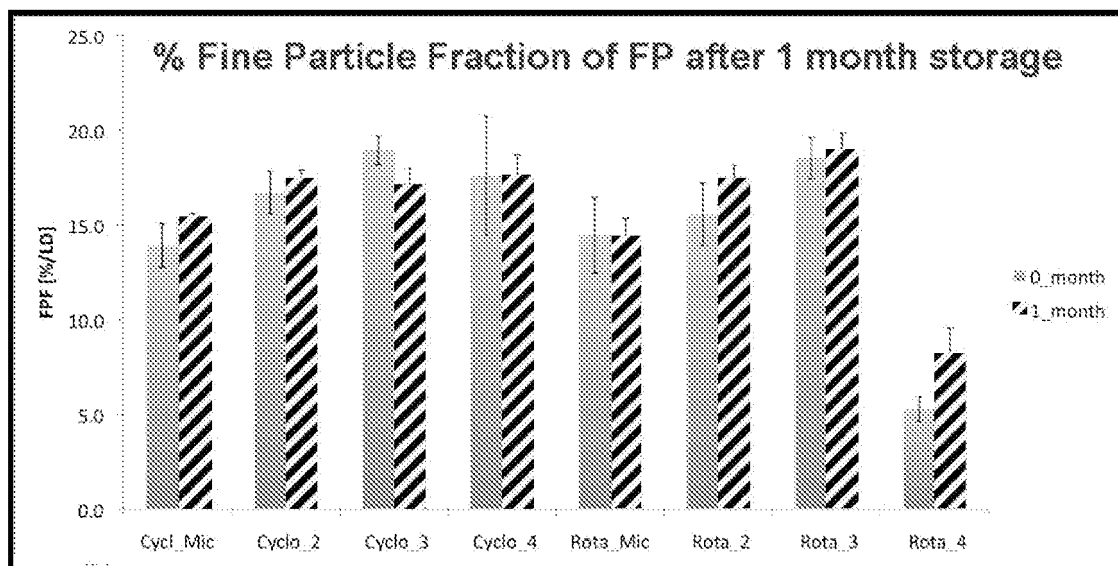


Fig. 27

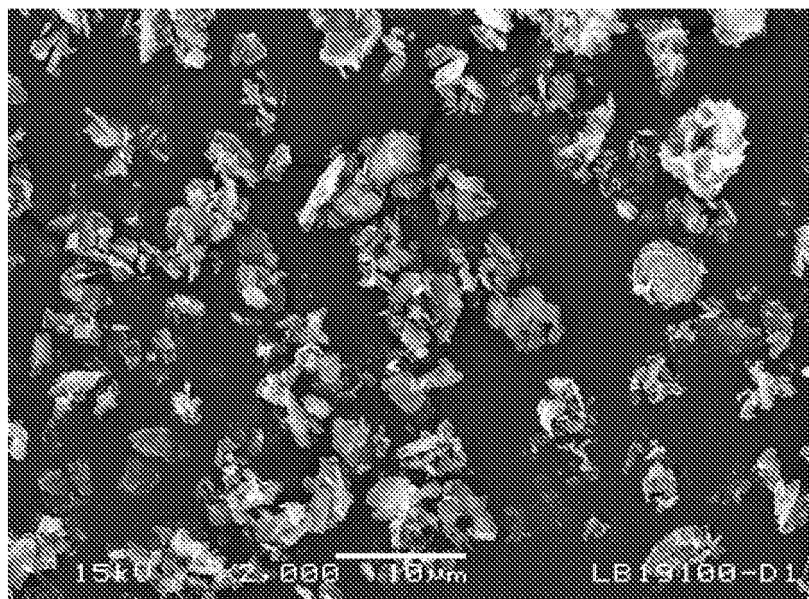


Fig. 28

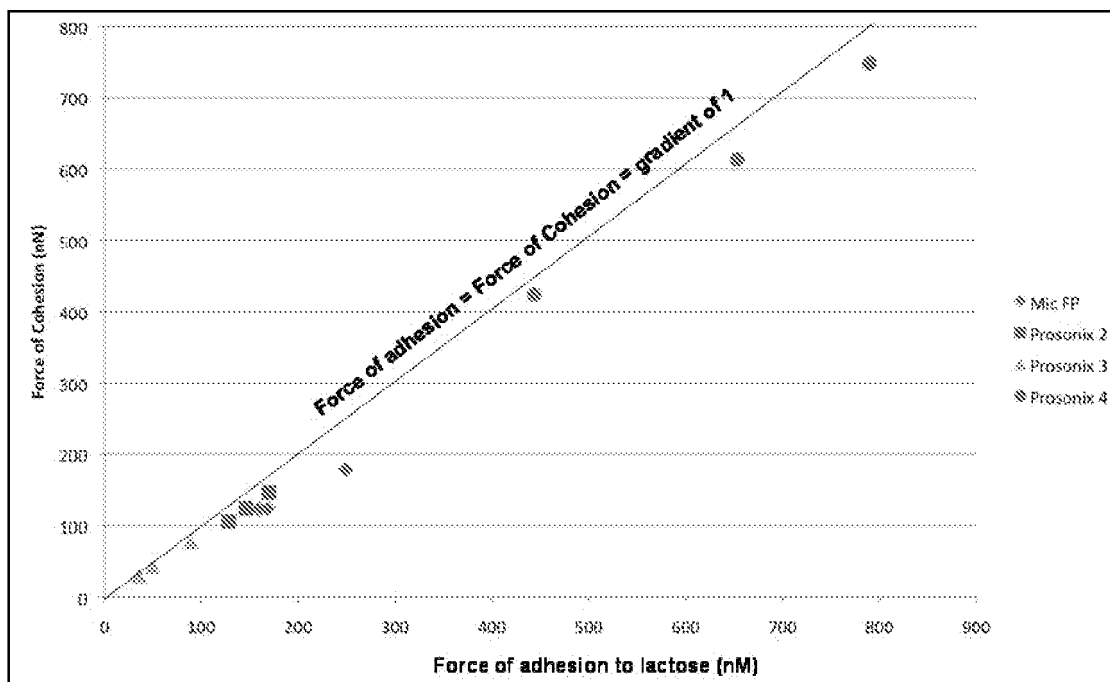


Fig. 29

Example 6: Content Uniformity for 500 (FP) / 25 (SX)		
•The poor content uniformity of the micronized formulation resulted in the formulation not being fired.	% Relative Standard Deviation	
	Micronized	Prosonix 3
FP	8.76	3.43
	% Relative Standard Deviation	
	Micronized	Prosonix 3
SX	15.95	4.55
Example 6: % Fine Particle Fraction of FP and SX for 500 (FP) / 25 (SX)		
	Fine Particle Dose (μ g $\pm$ S.D.)	Fine Particle Fraction of loaded dose (% $\pm$ S.D.)
FP	79.1 (2.6)	15.8 (0.8)
	Fine Particle Dose (μ g $\pm$ S.D.)	Fine Particle Fraction of loaded dose (% $\pm$ S.D.)
SX	11.0 (1.0)	44.0 (2.6)

Fig. 30

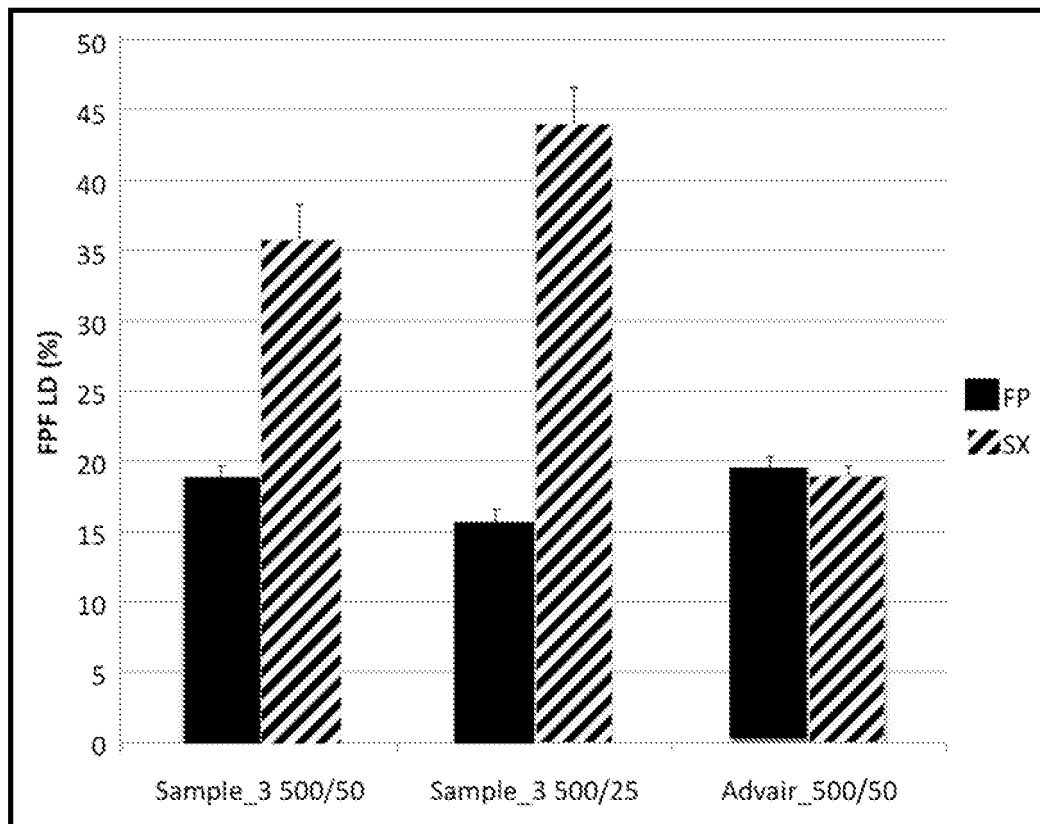


Fig. 31

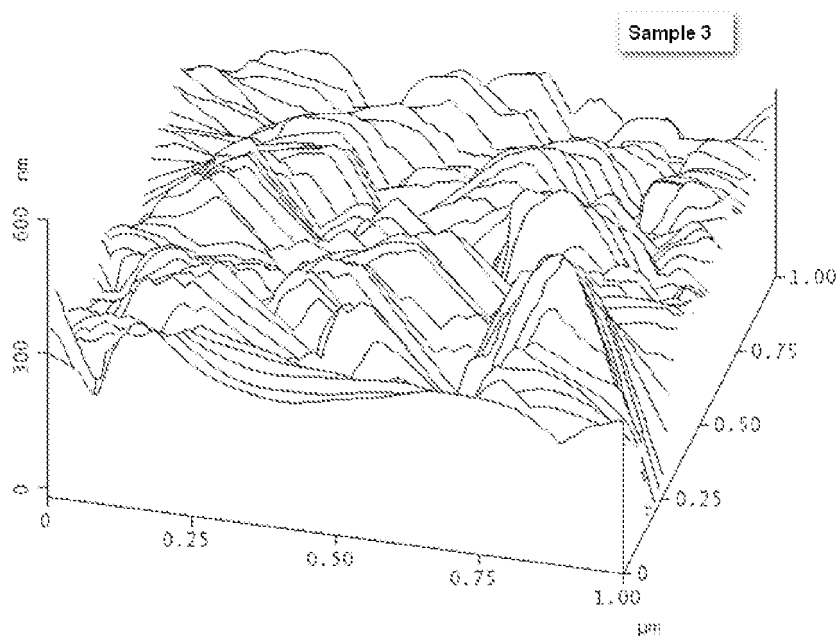
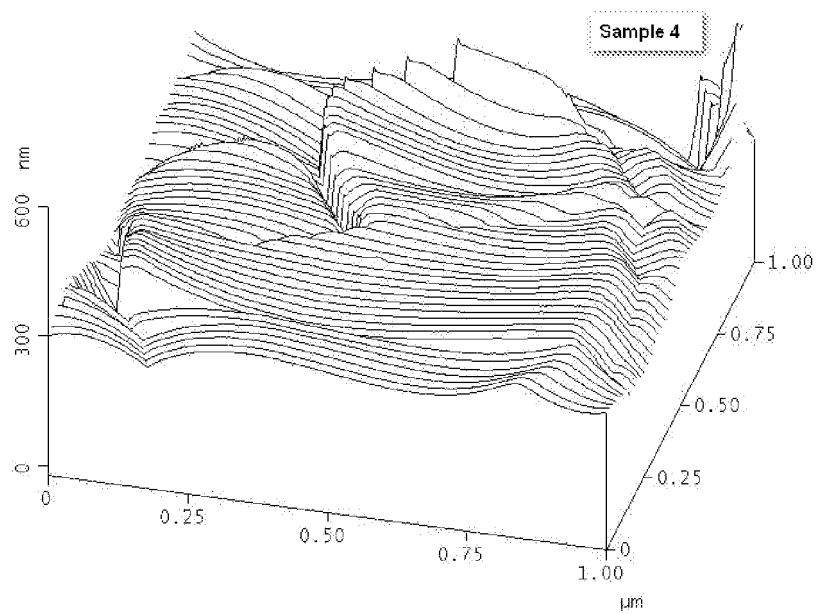


Fig. 32

**Fig. 33**