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Novel Continuous Wet Granulation Using Twin Screw Fractional Lobe Processor

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1. PURPOSE

The desired paradigm shift from batch to continuous scale in pharmaceutical sector requires a reliable continuous granulation process. The objective of the present study was to evaluate the effect of screw element geometries for continuous wet granulation operation using a Twin screw processor. Physical properties of granules and compressed tablets were compared for conventional Bi- lobed geometry (BLP**)** and the Steer patented Fractional lobed geometry (FLP)

2. METHOD

2.1: Formulation

Table 1: Composition for Metformin HCl Granules

Sr. No.	Ingredients	% w/w
1.	Metformin Hydrochloride	95.67
2.	Pregelatinized starch	1.01
3.	Povidone	3.32

2.2 Preparation of Granules:

The entire sequence of feeding, kneading, drying and sizing was accomplished in a single and continuous processing step. The process was carried out for two different screw geometries at their respective optimized processing conditions. Granulation was performed using a STEER Omega 20 mm co-rotating twin screw processor L/D of 60 and Do/Di of 1.71.

Fig. 1: BLP Element Sample

Fig. 2: FLP Element Sample

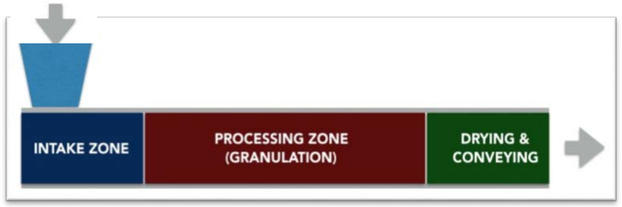

Fig. 3: Continuous Twin Screw Granulation Process

Table 2: Processing Conditions for FLP

Machine	FLP	BLP
Screw Speed (rpm)	800	800
Feed Rate (g/minute)	200	100
Drying zone temperature (°C)	100	100

2.3: Evaluation of Granules:

Granules were Evaluated for LOD, Sieve Analysis, Friability Test, Bulk and Tapped Density.

2.4: Tablets Compression and Evaluation :

The dried granules were lubricated using 0.5% w/w magnesium stearate and 0.2% w/w crospovidone and compressed into tablets and evaluated for - Weight Variation, Hardness, Friability and Disintegration Time.

3. RESULTS

3.1: Particle Size and Shape Analysis:

Table 3: Comparative Particle Size Distribution

Sieve No.	Cumulative % Retained (% w/w)	
	BLP	FLP
# 20	15	9
# 100	66	87
Fines	34	13
Median Diameter	250 microns	380 microns

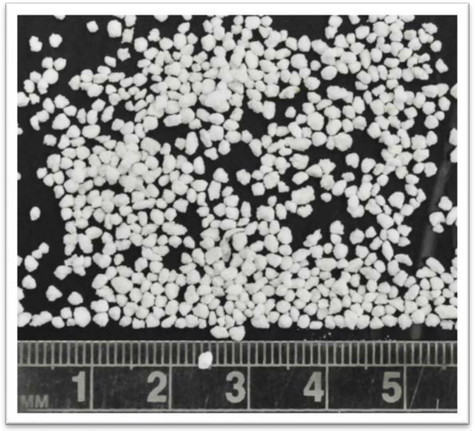

Fig 4: Morphology of FLP Granules

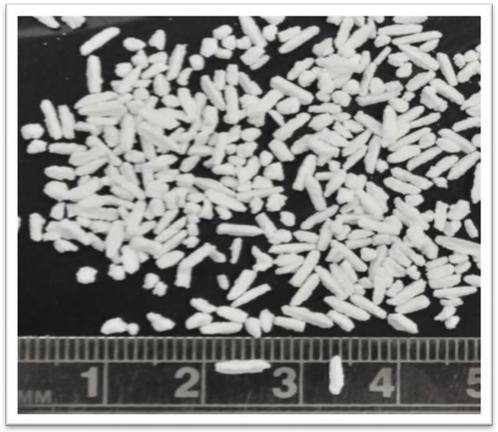

Fig 5: Morphology of BLP Granules

(particles retained on 20 mesh sieve were isolated and photographed)

Table 4: Physical Properties of Granules:

Parameters	BLP Granules	FLP Granules
Particle Diameter after friability (µm)	150	350
Bulk Density (g/cc)	0.342	0.51
Tapped Density (g/cc)	0.502	0.621
Carr's Index	31.70	17.23
Angle of Repose	33	24

Table 5: Physical Properties of Compressed Tablets

Tablet Thickness (mm)	Avg Weight (mg)		Weight Variation (%)		Friability (%)		Hardness (KP)		DT (min)	
	BLP	FLP	BLP	FLP	BLP	FLP	BLP	FLP	BLP	FLP
5.6	520	521	4.72	2.08	0.53	0.17	10- 12	10- 12	5-8	6-8
5.8	526	522	3.71	1.72	0.73	0.18	8-10	8-10	5-8	6-8
6.0	527	525	4.82	1.93	0.88	0.20	6-8	6-8	4-6	5-7
6.2	522	527	3.65	1.78	1.35	0.39	4-6	4-6	4-6	5-7

Results:

Comparing FLP vs BLP, the FLP granules have following properties :

- Better Tensile strength and Friability.
- Higher mean particle diameter with lower fines
- More Symmetrical Morphology
- Better flow and higher compressibility
- Better flow properties hence lower tablet weight variation.
- Tablets with lower friability

4. CONCLUSION

Fractional lobe geometry showed significant improvement in all granule properties as compared to Bi-lobed. The throughput was doubled for Fractional lobe processor as compared to Bi-lobe processor. **STEER*Life's*** experience with this process demonstrates improved ability to produce customized granules measured in terms of both mean and distribution of particle size without involving separate drying and milling steps .

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