

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

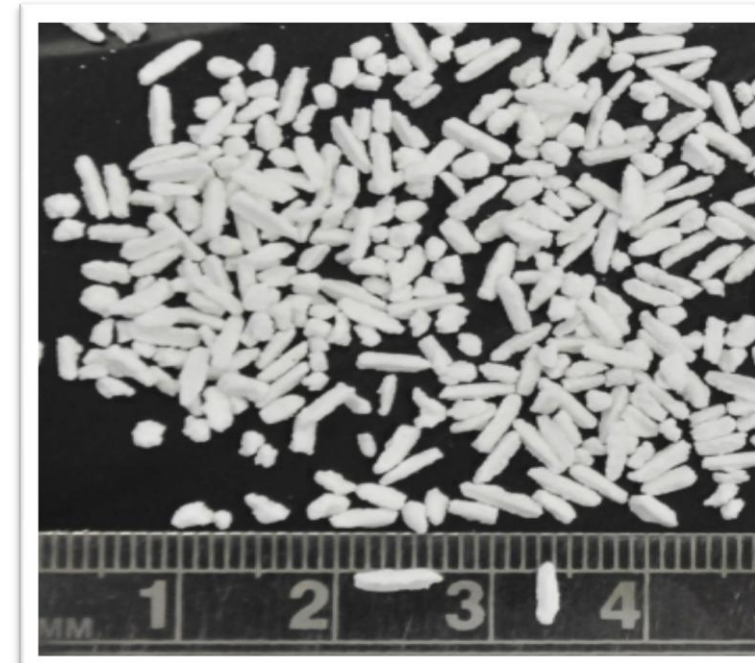
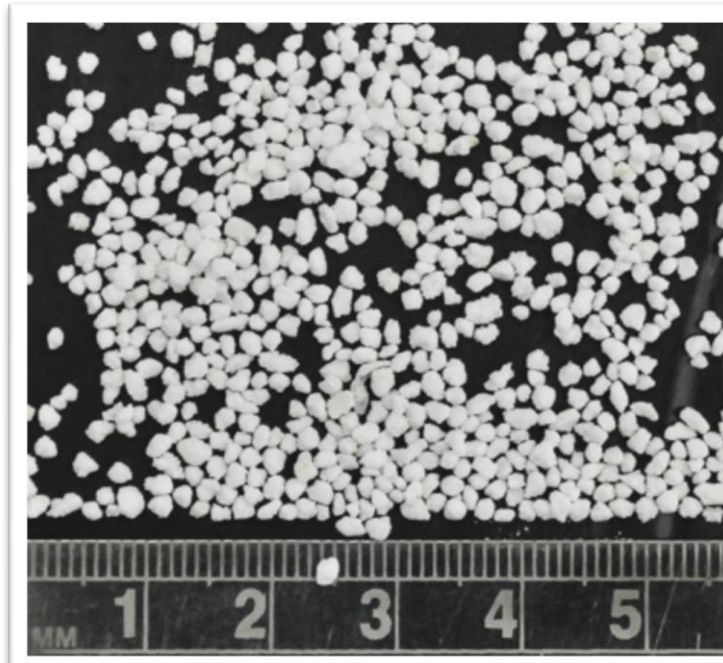


Fig 4: Morphology of FLP Granules Fig 5: Morphology of BLP Granules
(particles retained on 20 mesh sieve were isolated and photographed)

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 had following properties :

- Better Tensile strength and Friability.
- Higher mean particle diameter with lower fines
- More Spherical Morphology across studied feed rates.
- 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. STEERLife's experience with this process demonstrates improved ability to produce customised granules measured in terms of mean distribution of particle size without needing separate drying and milling steps downstream.