

# Fractional Lobe Hot Melt Extrusion Technology: 21<sup>st</sup> Century Smart Compounding for Improving Process Capabilities

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## PURPOSE

To explore the STEER developed **fractional lobe twin screw element (FLE)** geometry for solubility enhancement of antiretroviral drugs using hot melt extrusion process for smart compounding and improving the process capabilities.

## Method

### Composition:

Lopinavir (LPV) and Ritonavir (RTV) were selected as APIs, Copovidone (polymeric matrix), Silicon dioxide and Sorbitan monolaurate (granulating fluid).

### Screw Elements at Melt mixing Zone:

STEER developed *Fractional geometry lobes - (21<sup>st</sup> Century elements)* and Integer lobed (20<sup>th</sup> century elements) elements.

### Extrusion Process:

The granulated mixture of above mentioned composition was processed using 20 mm diameter, 40 L/D Co-rotating Twin screw processor (**Omega 20P, Steer Engineering Pvt. Ltd, Bengaluru, India**) at various screw speed, feed rate, at the barrel temperature of 120°C in the melt mixing zone with vacuum (400 mmHg). Each 537 mg of extrude contains 100 mg Ritonavir and each 1212 mg of extrudate contains 200 mg Lopinavir and 50 mg Ritonavir.

### Tablet Compression:

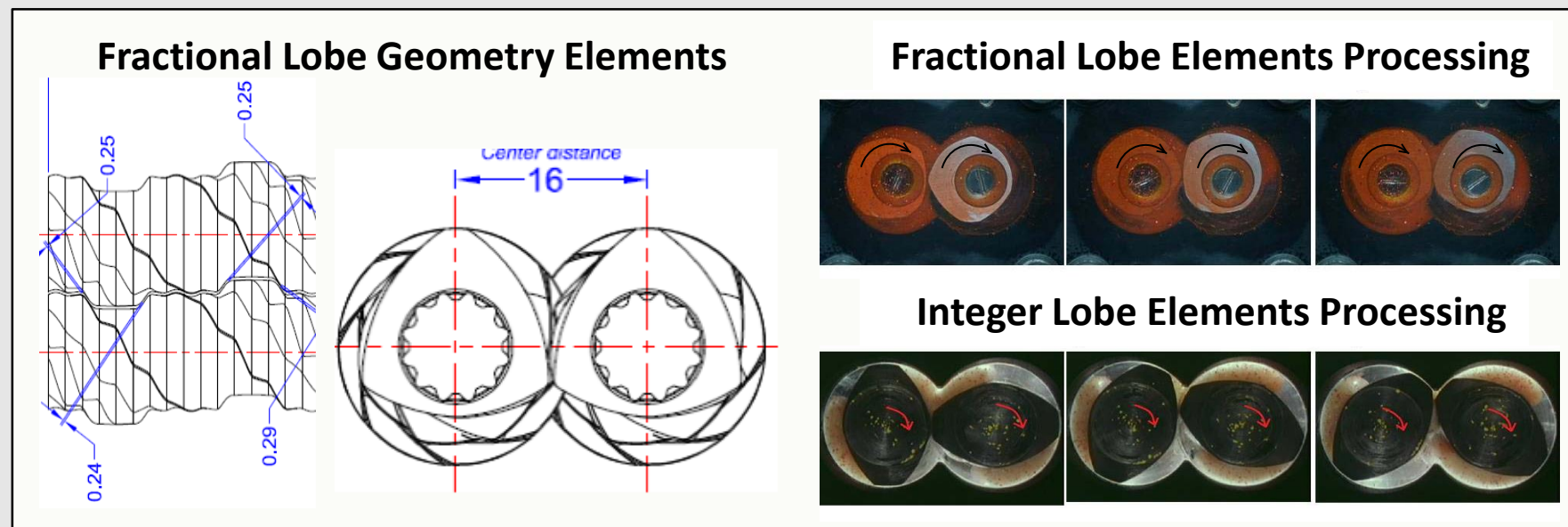
The extrudates were milled and mixed with other tablet ingredients and compressed into tablets.

### Evaluation:

Related substances in the extrudates were performed using HPLC method.

Dissolution of tablets were performed as per USP monograph of approved products.

## RESULTS



### Ritonavir Extrusion process details and Extrudate properties

Process Parameters	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
Screw Speed (rpm)	500	700	700	700	900
Feed rate (kg/hrs)	12	12	16	20	20
Torque (%)	37	66	55	76	58
Total impurities (Limits: NMT 3.5 %)	Tighter than the limits of USP Specifications.				

### Lopinavir & Ritonavir Extrusion process details and Extrudate properties

Process Parameters	Trial 6	Trial 7	Trial 8	Trial 9
Screw Speed (rpm)	300	400	500	700
Feed rate (kg/hrs)	5	5	5	15
Torque (%)	52	36	33	60
Total impurities (Limits: NMT 3.5 %)	Tighter than the limits of USP Specifications.			

### Dissolution of Ritonavir tablets

Time (min)	Avg. Drug Release (%)
15	25
30	41
60	65
120	89

### Extrudes of Ritonavir



## RESULTS

- At all the processing parameters using fractional lobe element resulted in clear transparent extrudates.
- Only one fractional kneading block of length 40 mm in the melt and mixing zone could provide the same results as that of a combination of integer lobe elements of length 50 mm.
- The FLEs had low residence time and torque for the similar process parameters.
- In a 20 mm extruder, using FLE there was enhancement in the throughput to 20 kg/hr.
- The total organic impurities were tighter than the limits of USP Specifications.

## CONCLUSION

- FLE(s) in the melt zone allows processing of the APIs and/or meltable excipient(s) at low torque.
- FLE(s) in the melt zone eliminates shear peaks and ensures a uniform transfer of energy to polymers being processed, giving the capability and the control to work with sensitive materials.
- FLE(s) can be explored for further reducing the residence time of the compounded material in the processor and also increase the throughput.



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