Benchmarking of particle engineering technologies for nasal powder manufacture

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Powder formulations of a drug and mucoadhesive polymer have increased residence time in the nasal cavity and can be manufactured by blending, spray-drying or agglomeration of primary particles into chimeral agglomerates (CA). While spray-drying allows particle size control and generation of amorphous solid dispersions (ASD), blending is simpler and CA should allow faster dissolution after breakup into smaller particles. Our research hypothesis is whether spray-dried microparticles (SDM) have significant advantages over blends and CA for a poorly soluble drug (piroxicam).

ASD screening was performed by differential scanning calorimetry and the solvent shift method. SDM and CA primary particles were prepared by spray-drying, CA by sieve shaker, and corresponding blends by Turbula. Formulations were characterized regarding particle size distribution (PSD), morphology, solid state and water content. *In vitro* performance was assessed by emitted dose, aerodynamic profile, dissolution (paddle-over-disk) and real-time PSD monitoring (RTPM) in simulated nasal fluid.

Formulations with 20% drug load and PVP/VA or HPMC E3 were selected. CA presented the lowest (~50%) and most variable (standard deviation >30%) emitted doses. All formulations presented a very high fraction potentially retained in the nasal cavity (<95%). Dissolution testing revealed poor performance of blends and HPMC CA, possibly due to the crystalline content (confirmed by XRPD), and higher performance for SDM and PVPVA CA. RTPM showed prolonged deagglomeration times for PVPVA CA.

SDM provided advantages over CA and blends, which presented challenges on emitted dose and dissolution performance. Spray-drying generates particles with more predictable performance and highly suitable profile for nasal delivery.