

Rapid and Lossless Screening of Hot-melt Extruded Formulations

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Introduction

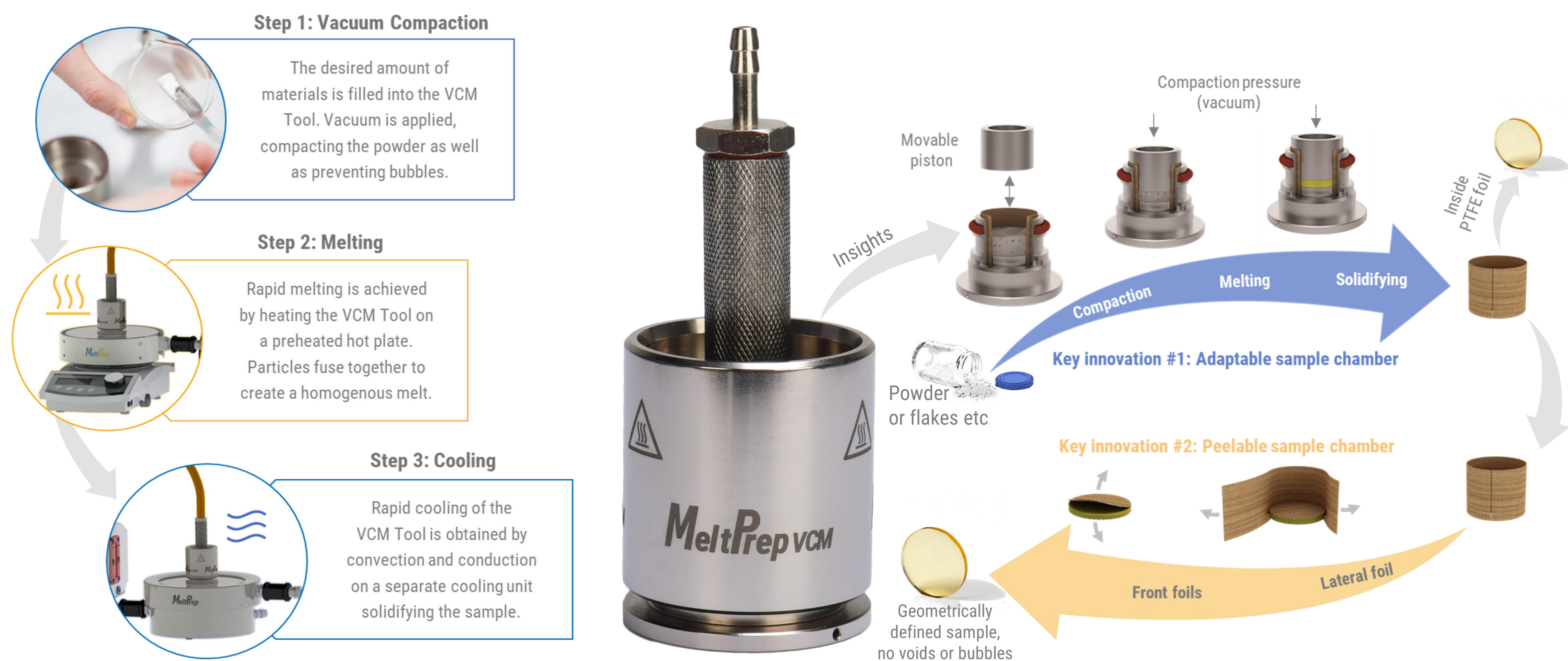
Hot-melt extrusion is well established in the plastics industry and is applied in pharmaceutical application for more than 30 years. Pharmaceutical formulations are often more complex as each formulation is unique in terms of compositions of active pharmaceutical ingredients, carrier and additives compared to plastics applications. First screening approaches to find suitable formulations are typically pursued by solvent casting at very low amounts (mg scale) and a wide range of different combinations of carrier materials, active pharmaceutical ingredients and additives are evaluated. However residual solvents and the different nature of processing can lead to

different results compared to fusion based methods. To a large extent, fusion based methods are later applied for the production of large quantities of the drug formulations (metric to ton scale). Thus, the screening results from solvent casting are typically used as a decision basis to narrow the choice of suitable formulations. A following fusion based screening is typically performed with miniaturized extruders (5 g scale per formulation). This approach is involved with unavoidable losses and tremendous cleaning requirements for each trial, which makes it slow and expensive.

Vacuum Compression Molding (VCM)

VCM is a novel fusion based method. It mimics extrusion by melting a homogeneous powder in an evacuated and adaptable sample chamber. The chamber is formed by disposable PTFE foils. Prototype tablets with defined

geometries are obtained within minutes and without tedious cleaning. Separation foils form the sample chamber and are simply replaced when the formulation is changed. Sample quantity can be as low as 10 mg per sample.



Applications

Prototype tablets can be used for solid-state characterization, stability testing or dissolution testing to identify the most promising formulation. In general, the results correlate well with results produced by hot melt extrusion. The big advantage is, that the sample geometry is precisely defined and performance parameters e.g. dissolution rate can be related to defined surface areas for different samples. This facilitates a geometry independent investigation of crucial key parameters for amorphous solid dispersions (ASDs), such as intrinsic dissolution rate. Once suitable formulations are identified for the next stage, e.g. extrusion with pilot scale equipment (e.g. 18 mm - kg scale), the homogeneous VCM samples can be used to characterize material properties relevant for processing development. Material data such as viscosity curves is rarely available in

literature for specific combinations of APIs, carriers and other additives. In many cases, process development is carried out based on operator's experience. However, reliable material data can accelerate and rationalize process development and reduce material and time consumption for optimization. One use case is the measurement of rheological data such as viscosity curves, which are hardly accessible without VCM sample preparation. Once they are determined, required processing temperatures can be estimated rationally, even before the processing equipment has been started for the first time. This is of particular importance when complex processes are developed, e.g. processes for dosage forms with complex structures such as co-extrudates or injection molded tablets.

Conclusions

It can be concluded that the VCM process is a straight forward, multi-purpose and rapid approach to produce prototypes of thermoplastic materials. The implementation of VCM in the formulation development can lead to a lean formulation and process design in which less material and

time is required to achieve development goals based on material understanding. It reduces the material amount for fusion based screening from 5 grams down to comparable low amounts as used in solvent casting applications.