Development of an Investigation Protocol to Assess the Processability of Pharmaceutical Polymeric Materials by a Micromolding Press

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Purpose

The successful use of injection molding (IM) and micromolding (µIM) for the development of drug products is related to an in-depth knowledge of the thermal and rheological characteristics of pharmaceutical polymers and to the evaluation of their processability through experimental or modeling approaches. In this work, an investigation protocol to assess the moldability of the material through tests performed on a simple disk-shaped specimen (screening item) was developed. Ethylcellulose (EC), which is broadly employed in the formulation of prolonged delivery systems, was selected as a model pharma polymer.

Methods

EC and EC blends plasticized with 10, 20 and 25% of triethyl citrate, TEC (ECTEC10, ECTEC20 and ECTEC25, respectively), were processed by a bench-top hydraulic µIM press (BabyPlast 6/10P; Cronoplast S.L.) equipped with a disk-shaped mold (Ø 30mm) provided with a central gate and allowing to control the cavity thickness in the 200-1000µm range. Digital photographs of the disks were taken (4128x3096 pixels resolution) and analyzed by ImageJ. Aspect ratio (AR=Rmax/Rmin) and effective radius (Reff=(Rmax+Rmin)/2) were calculated using the major axis (2Rmax) and minor axis (2Rmin) of the best fitting ellipses.

Results

The need for a plasticizer to enable EC processing below its decomposition temperature (≈180°C), i.e. in the 170-175°C range, was assessed by air shot trials and rheometry tests. Preliminary µIM processes were carried out in order to select the cavity thickness to get both complete and incomplete fillings, the melt shot-size needed for filling, and the injection rate. The maintenance pressure was kept constant at the lowest setting conditions (10bar, 0.0s). Several injection processes were then performed at different injection pressures (10-100bar, 10bar increments) and fixed fill time (1.0s). In the case of incomplete disks, the fill time was also increased up to 2.5s (0.5s increments). Based on this protocol the melt progression into the mold was evaluated with different ECTEC blends. As the AR of both complete and incomplete disks was always very close to 1, the screening specimens were considered circular and Reff was assumed as a suitable parameter for comparing them. By rising the injection pressure within the 400µm thick mold, different rates of melt progression for the different polymeric blends were observed, leading to the formation of disks with radius increasing up to the theoretical one (Image 1). The same injection pressure was required for ECTEC20 and ECTEC25 blends to give complete disks, while a higher pressure was needed for ECTEC10. Moreover, by extending the injection time, the radius of incomplete disks also increased though to a lesser extent (Image 2).

Conclusion

An investigation protocol for the evaluation of pharma polymers processability by IM was proposed, which allowed to assess the effect of plasticization on EC processing. A simplified fluid dynamic model is under development to describe the process and estimate the relative effects of polymer properties and processing parameters on the progression of ECTEC blends into the mold.

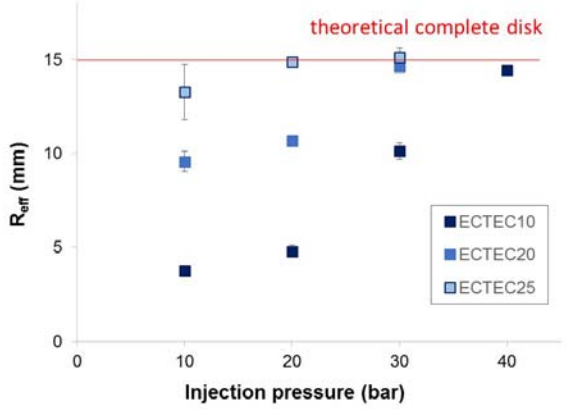

Image 1: effective radius of disks based on different ECTEC blends as a function of injection pressure.

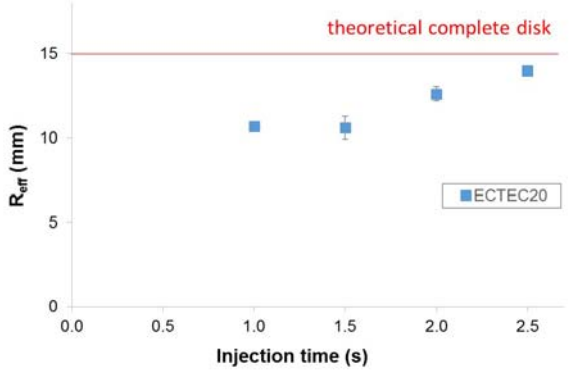

Image 2: effective radius of disks based on ECTEC20, obtained at 20 bar of injection pressure, as a function of injection time.