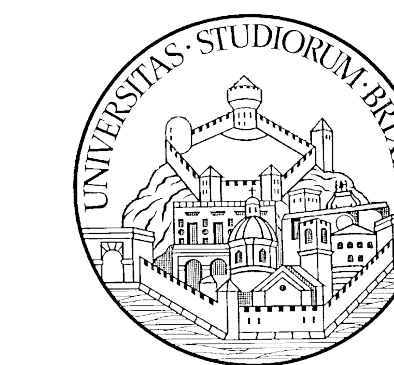


# Development of an investigation protocol to assess the processability of pharmaceutical polymeric materials by a micromolding press

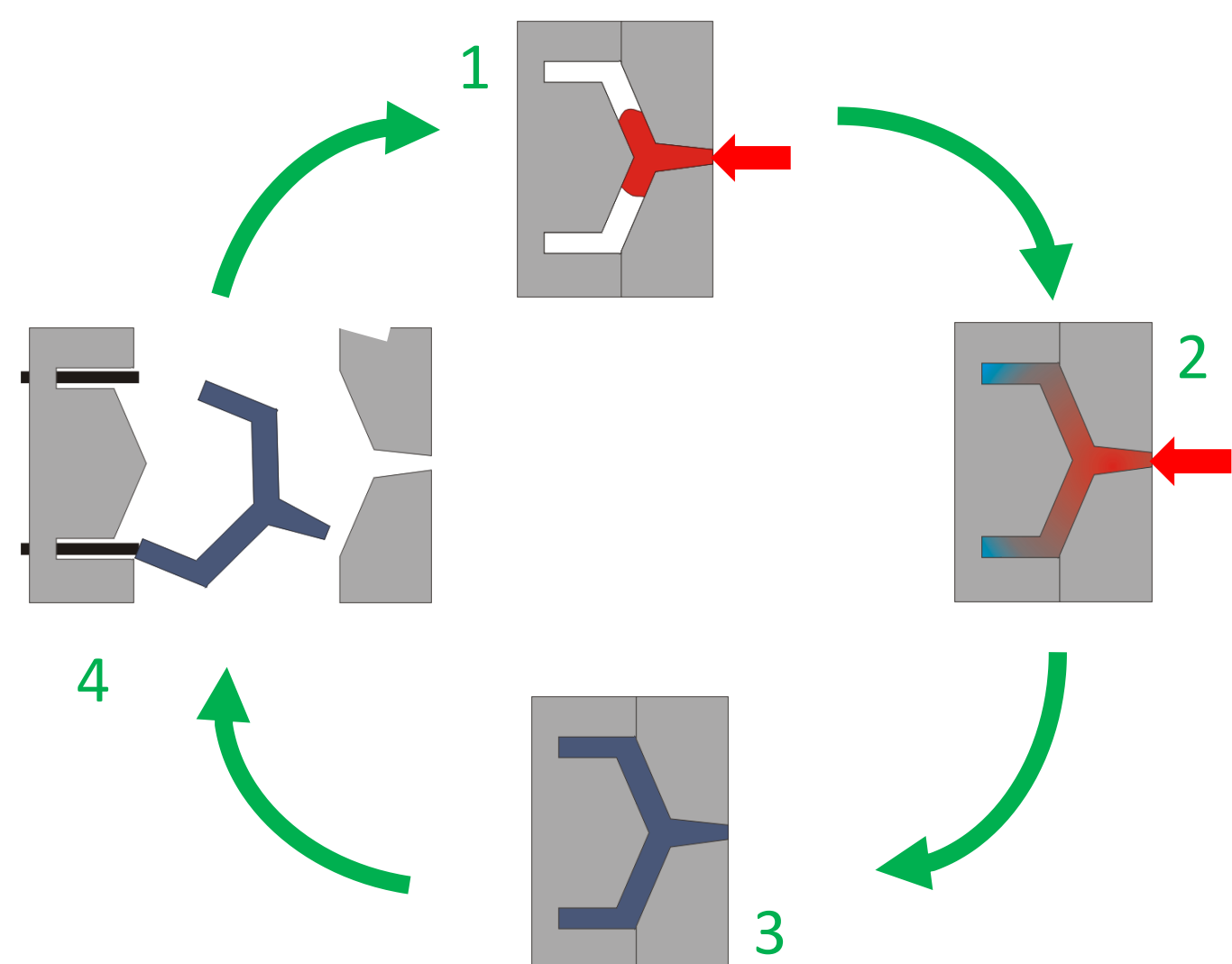
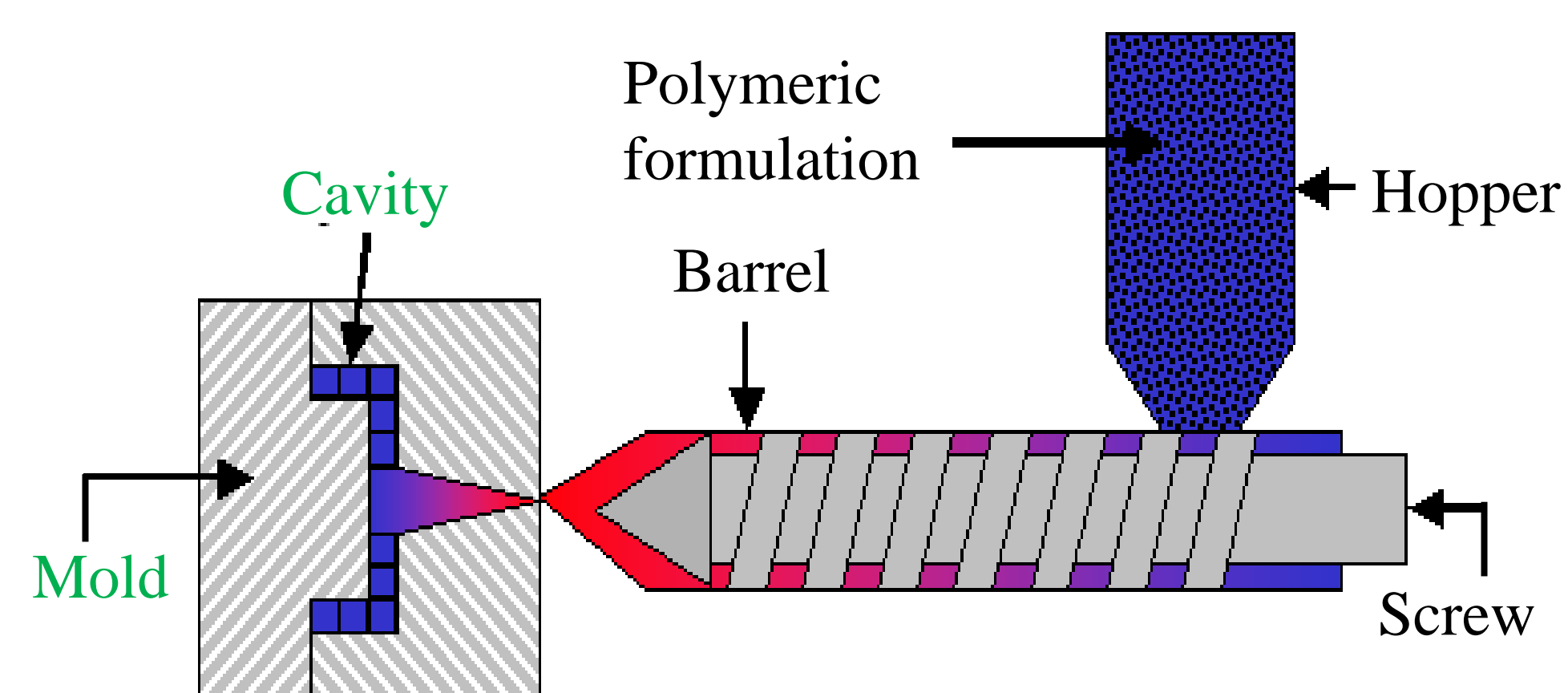
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## PURPOSE

The successful use of injection molding (IM) and micromolding ( $\mu$ IM) for the development of drug products is linked to the knowledge of the thermal and rheological characteristics of pharma-grade polymers and to the evaluation of their processability through experimental or modeling approaches. Ethylcellulose (EC), which is broadly employed in the formulation of prolonged delivery systems, was selected as a model pharma polymer.



The development of an investigation protocol to assess the moldability of the material through tests performed on a simple disk-shaped specimen (screening item) has been undertaken.

## MATERIALS AND METHODS

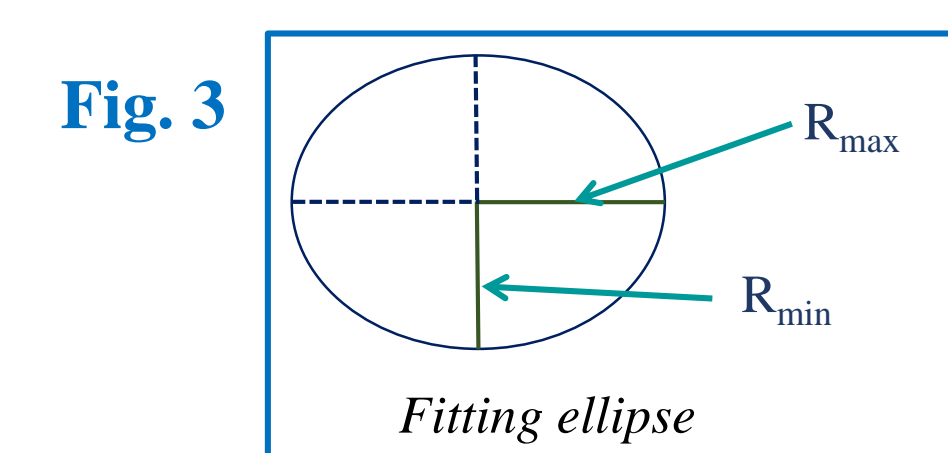
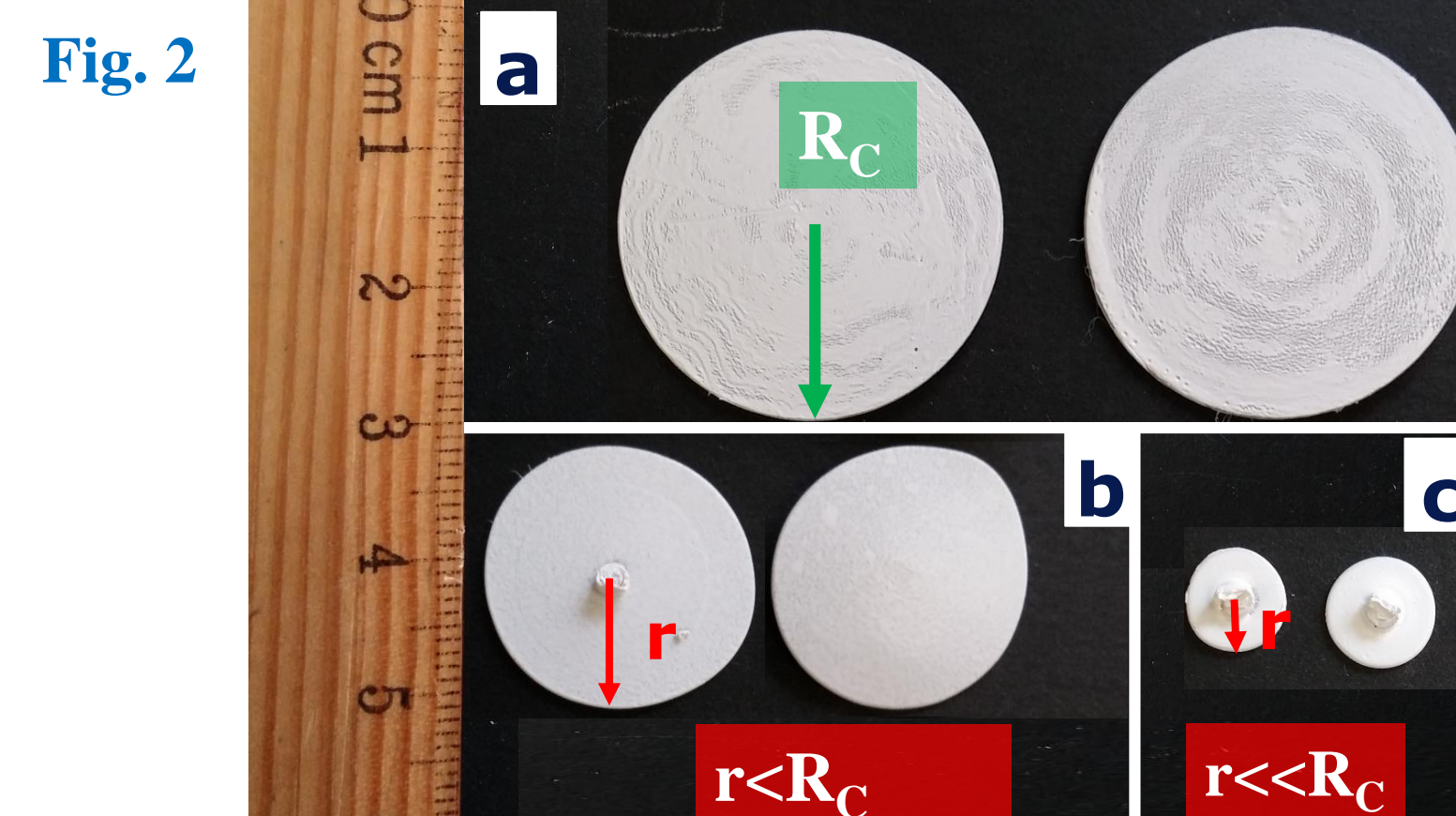
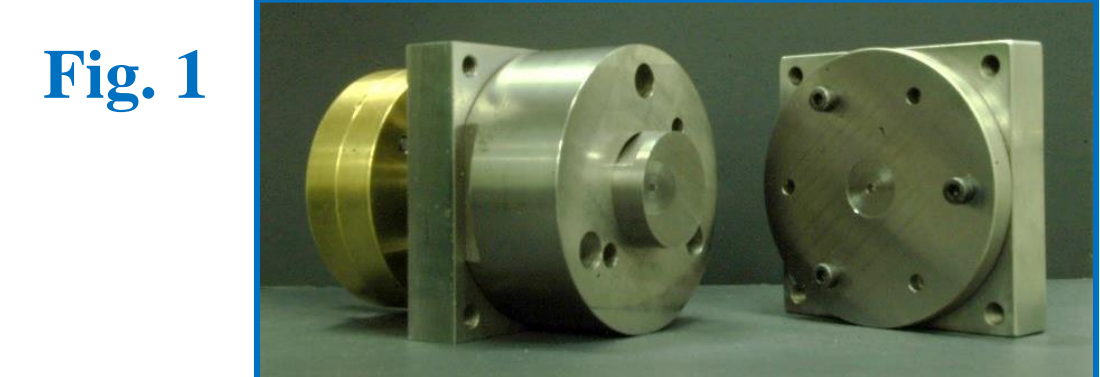
**EC**: neat ethylcellulose (Ethocel<sup>TM</sup> Std. 100 premium; Dow, US-MI);

**ECTEC10**, **ECTEC20**, **ECTEC25**: blends of EC with triethyl citrate, TEC (Aldrich, DE), 10, 20, 25% by weight, respectively;

- **Assessment of viscosity**: **EC** and **ECTEC** blends were analyzed with capillary rheometer Rheologic 5000 (Ceast-Instron, IT);
- **Assessment of moldability**: - **ECTEC** blends were processed by a bench-top hydraulic  $\mu$ IM press (BabyPlast 6/10P; Cronoplast S.L., ES) equipped with a disk-shaped mold ( $\varnothing$  30 mm) (Fig. 1) provided with a central gate and allowing to control the cavity thickness (200, 400, 600, 1000  $\mu$ m); - digital photographs of both complete (Fig. 2, a) and incomplete (Fig. 2, b and c) disks were taken (4128x3096 pixels resolution) and analyzed by ImageJ. Aspect ratio (AR) and effective radius ( $R_{eff}$ ) were calculated using the major ( $2 \cdot R_{max}$ ) and minor ( $2 \cdot R_{min}$ ) axis of the best fitting ellipses (Fig. 3):

$$AR = R_{max}/R_{min}$$

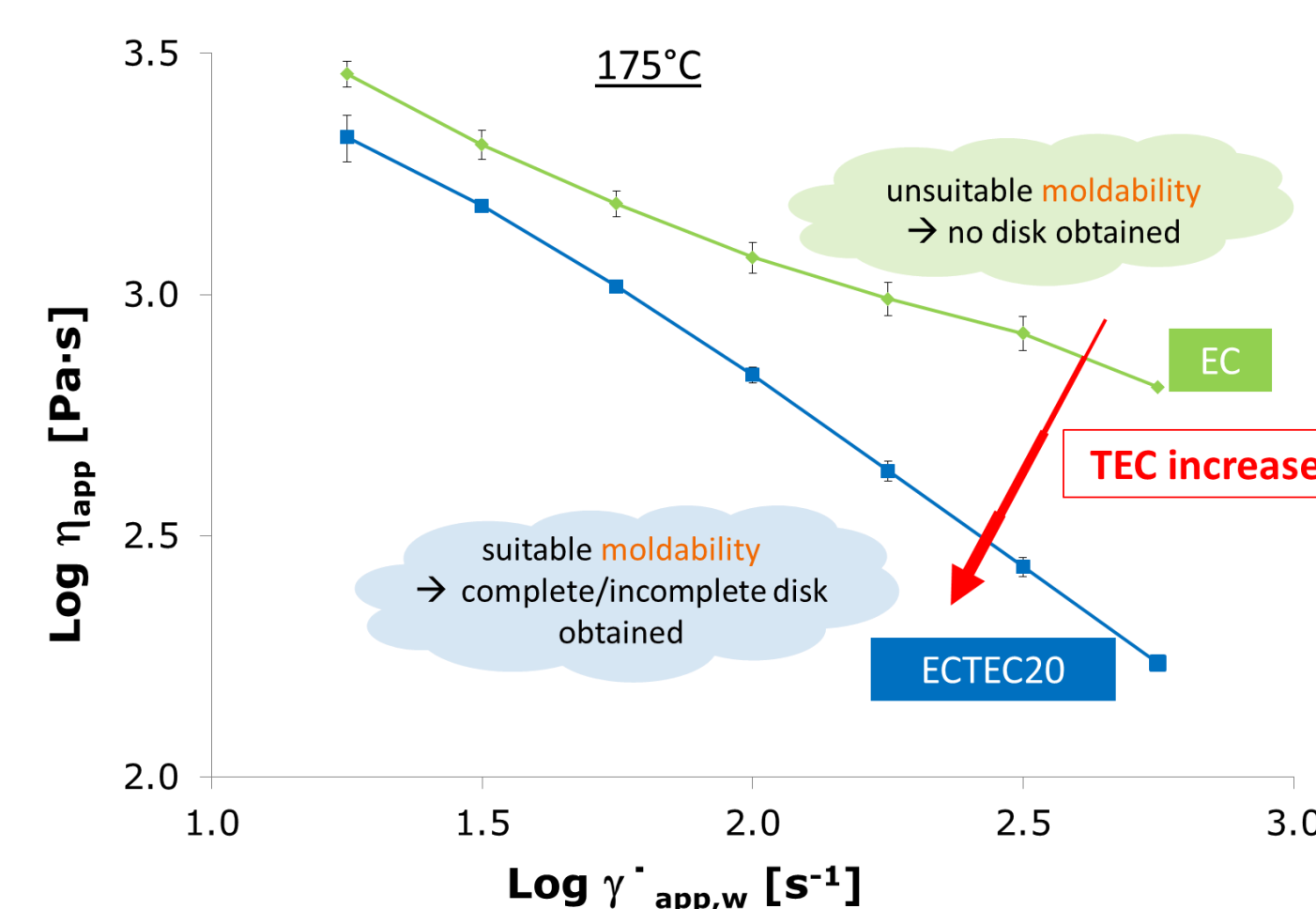
$$R_{eff} = (R_{max} + R_{min})/2$$



## RESULTS

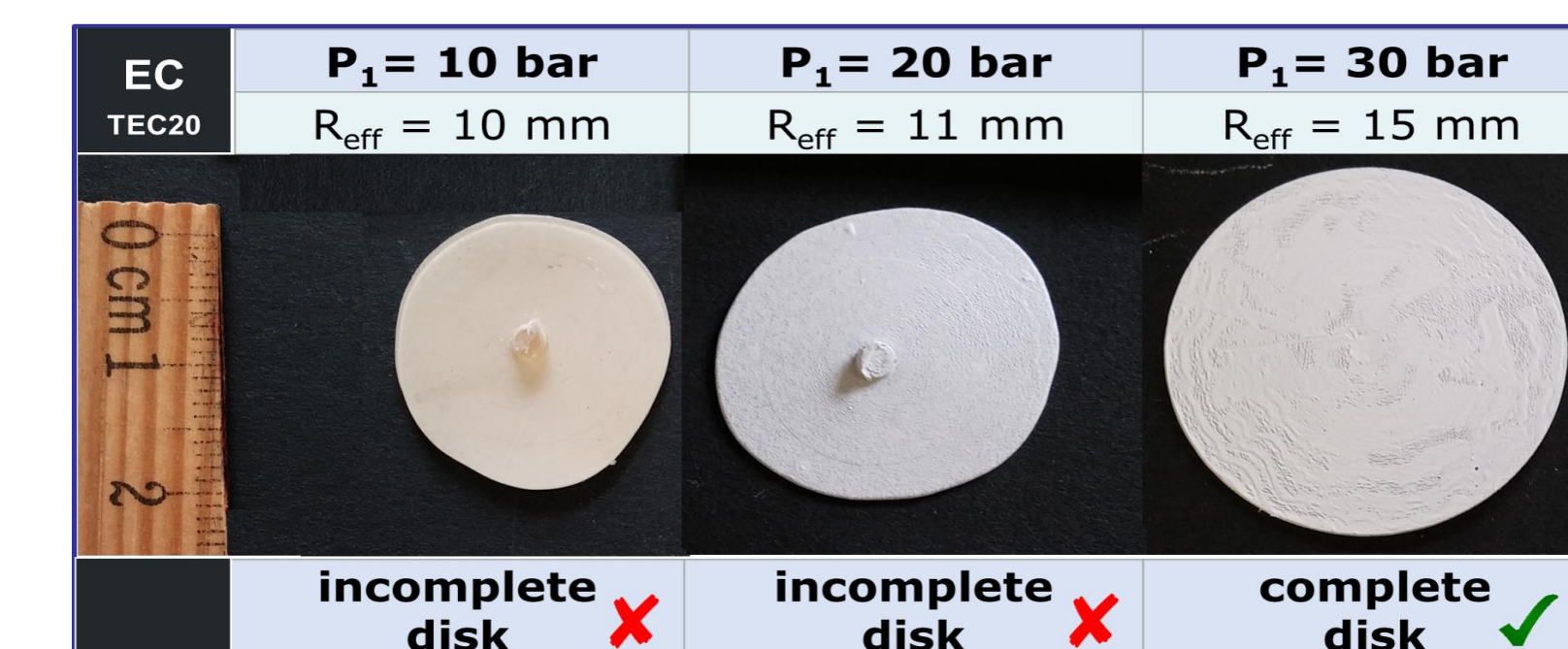
### 1. Rheological studies

The need for a plasticizer (TEC) to enable EC processing below its decomposition temperature ( $\approx 180^\circ\text{C}$ ) was assessed by capillary rheometry tests.

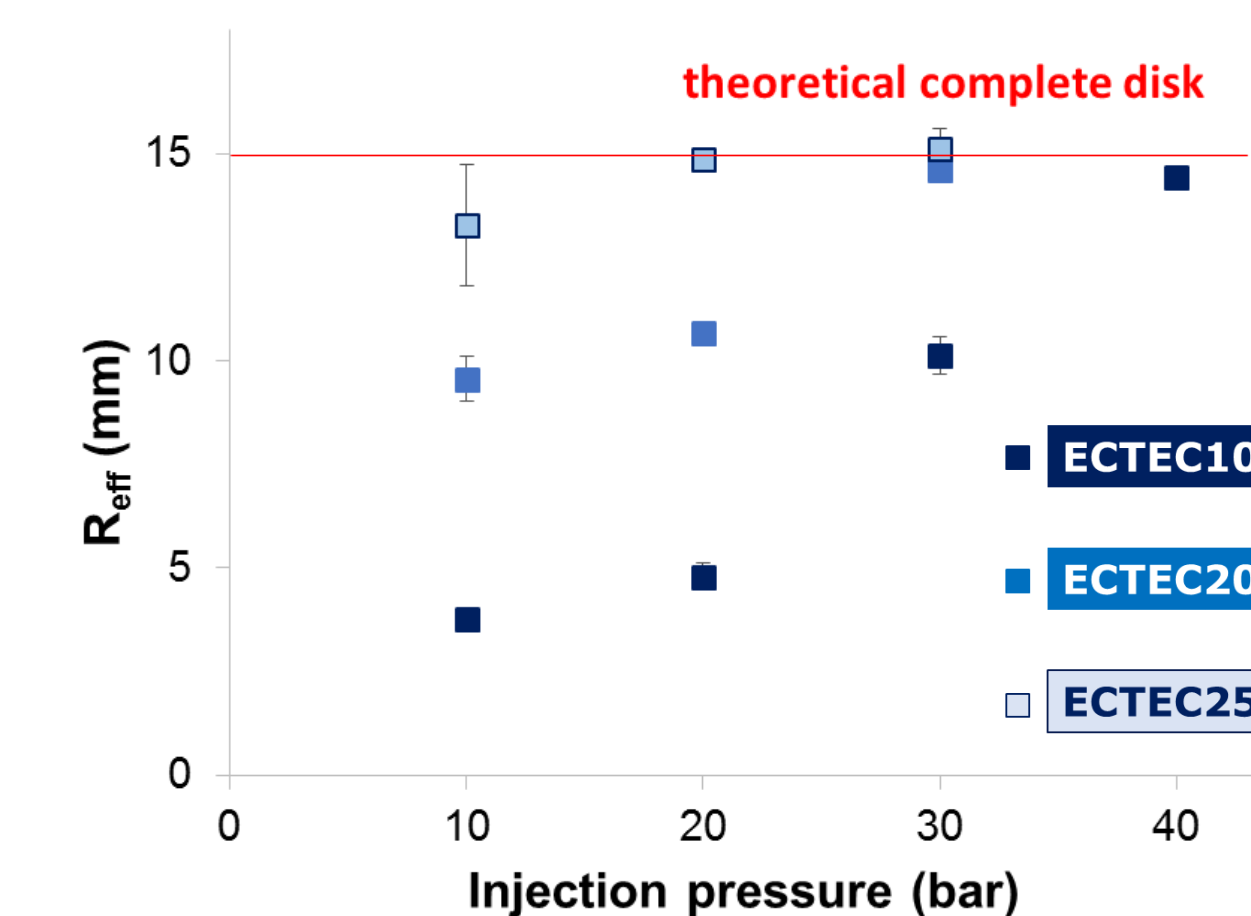


### 2. Short shots

Injection tests were performed at different injection pressures  $P_1$  (10-100 bar, 10 bar increments) and fixed fill time (1.0 s) obtaining both complete (✓) and incomplete (✗) disks. In the case of incomplete disks, the fill time was also increased up to 2.5 s (0.5 s increments).



#### 2.1 Disk shape evaluation

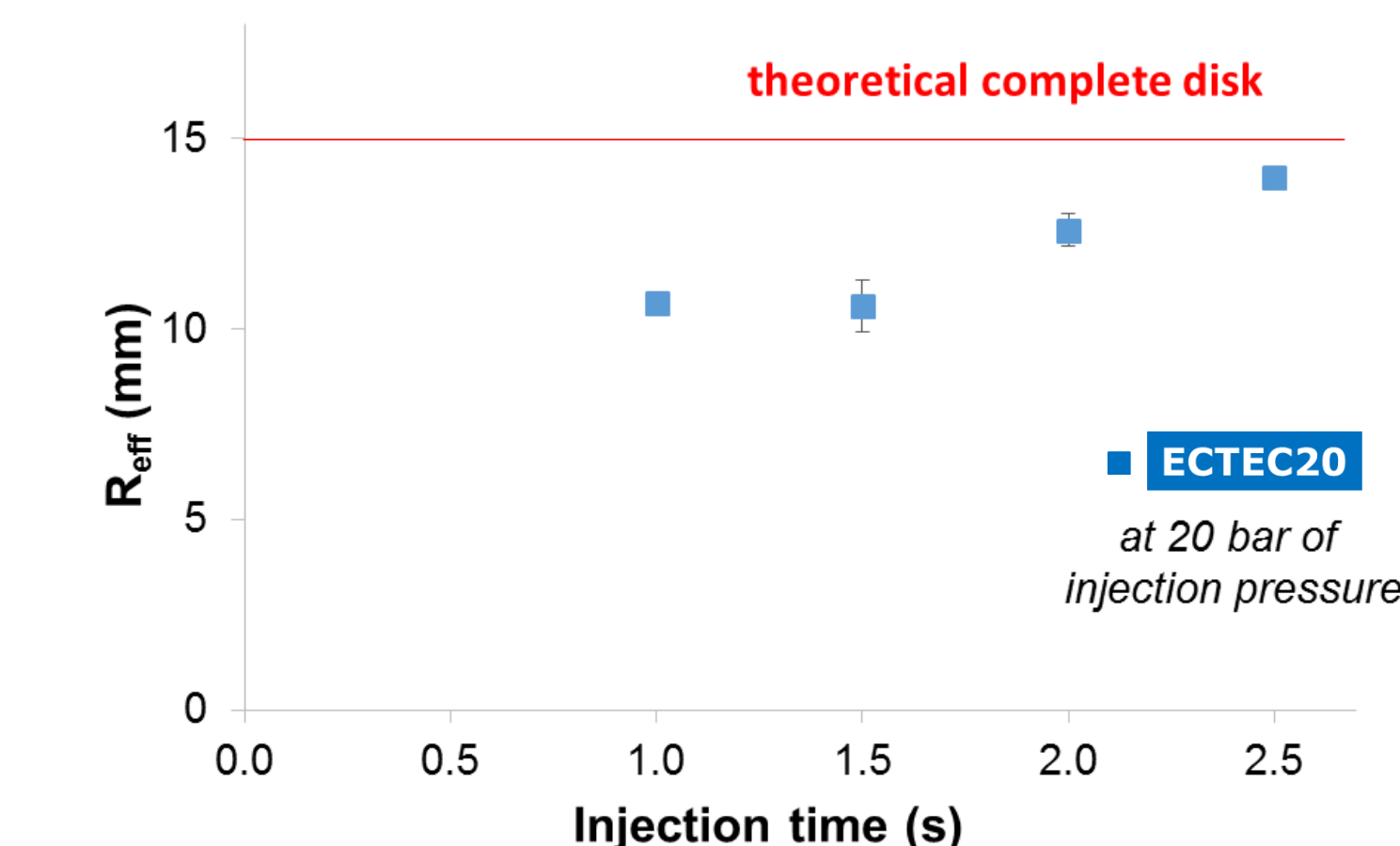


By rising the injection pressure, different rates of melt progression for the different polymeric blends were observed, leading to the formation of disks with radius increasing up to the theoretical one.

The same injection pressure was required for **ECTEC20** and **ECTEC25** blends to give complete disks, while a higher pressure was needed for **ECTEC10**.

#### 2.2 Melt progression evaluation

By extending the injection time, the radius of incomplete disks also increased though to a lesser extent.



## CONCLUSIONS

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.