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APPLICATION OF FUSED DEPOSITION MODELING IN THE CUSTOMIZATION OF PHARMACEUTICAL DOSAGE FORMS CONTAINING TIMAPIPRANT

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Abstract

The interest in 3D printing has recently increased in the pharmaceutical field, being fused deposition modeling (FDM) among the most promising technologies, likely due to its ability to customize dosage forms, create simple and complex geometries and produce small batches with low equipment costs[1]. After evaluating feasibility of FDM in the manufacturing of immediate release (IR) dosage forms containing Timapiprant (TMP), an active molecule potentially useful in oral treatment of eosinophilic asthma proposed by Chiesi Farmaceutici S.p.A., the present work investigates the possibility of customizing the product from different points of view. First, suitable thermoplastic pharmaceutical-grade polymeric carriers, in principle capable to promote the prompt release of TMP were selected. Indeed, TMP is poorly soluble and its formulation in IR products would be particularly challenging, especially using hot-processing techniques that are well-known to provide high-density specimens characterized by slow penetration of fluids[2]. In-house-extruded (Haake™ MiniLabII) filaments were used as feeding material for the printer (Kloner3D 240® Twin). Form preliminary trials, the formulation based on poly(vinyl alcohol) was identified as the best compromise between *i)* achievable TMP load, which ranged from 5% to 40% w/w, *ii)* processability by FDM, especially in terms of number of samples produced without process interruptions setting different infill percentages (*i.e.* 100, 50 and 30%), *iii)* overall quality of the printed specimens in terms of weight and TMP content reproducibility, *iv)* prompt dissolution performance (USP apparatus II, Distek), *v)* possibility to add soluble fillers. The infill percentage turned out one of the most important printing parameters for controlling the porosity of molded products (measured by helium pycnometer, Pycnomatic ATC) and speeding up sample dissolution. After a thorough evaluation of the solid-state of TMP after processing (*via* X-ray and differential scanning calorimetry, which confirmed the stability of the formulation and the crystallinity of the TMP, prototypes containing a fixed amount of TMP (50mg) were successfully printed with attractive design from both patient-compliance and business marketing perspectives. They also resulted compliant with the set of dissolution specifications (≥ 80% of TMP dissolved within 30 min). Overall, the data collected strengthened the idea that FDM could be successfully applied to the manufacturing of dosage forms to be orally administered, which could be personalized in terms of shape, composition and performance. Overall, such aspects make this technique particularly interesting also for possible industrial implementation in the next future.

References

1. A. Melocchi, et al., Int. J. Pharm., *592*, 119901, **2021**
2. F. Casati, et al., Int. J. Mol. Sci., *21(6),* 1917, **2020**