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Preparation of medicines by three-dimensional printing and personalization of therapy in compounding pharmacies: a case study

3D printing (3DP) is an innovative approach to manufacturing personalized medicines. The incorporation of 3DP in the pharmaceutical compounding landscape is expected to promote flexibility, efficiency, safety, and quality [1] of existing medicines.

This work aims to identify the most relevant requirements impacting the use of Fused Deposition Modelling (FDM) to compound medicines. This should be achieved by identifying the main challenges that a pharmacist faces prior to defining the strategies to be considered for the successful implementation of this 3DP technology in the daily practice of compounding pharmacies. For this purpose, a case study where paroxetine (PRX), an antidepressant drug needing regular dose readjustments and pharmaceutical intervention for therapy compliance, is presented. The work was conducted in a research pharmaceutical laboratory, mimicking the dedicated manipulation areas present in community pharmacies.

PRX-loaded tablets were printed using FDM. The polymer-based filaments required to feed the printer were previously prepared by Hot-Melt Extrusion (HME), from powder mixtures of raw materials (PRX, hydroxypropylcellulose and other adjuvants, such as dicalcium dihydrate phosphate, magnesium stearate and triethylcitrate) [2]. In this work, the coupling of HME-FDM manufacturing process for the production of PRX tablets has proven to be expedite, provided that the optimal mechanical and thermal properties of the filaments were ensured. It has been also demonstrated that the storage of filaments under controlled environmental conditions was critical for the successful printing of tablets. In fact, filaments kept in a controlled atmosphere (desiccator) were printable, while those stored in higher humidity conditions failed to successfully feed the 3DP printer's gears and die. Post-treatment drying of the filaments (e.g. microwave, oven) was also explored in this work. While the removal of water was slow under a dried atmosphere (desiccator), it was speeded up when active drying methods were considered. Microwave-mediated drying seems to have been the method that brought the greatest benefit since it streamlined the 3DP process with an increase in the dissolution rate of PRX. Noteworthy is that microwave drying must be carried out under well-controlled instrumental conditions, considering the larger variability of results, by comparison to oven drying. Furthermore, complementary studies involving drugs and polymers with different physicochemical properties will enable the construction of models that will speed up the design and manufacture of new medicines supporting the compounding pharmacies in implementing this manufacturing process.

Overall, prior production of the filaments with adequate properties for printing may be a limiting step for using FDM in compounding at the point of care. As an alternative, filaments may be

manufactured in a facility that would centralize their manufacture, and supplied as intermediate materials to community pharmacies, which are expected to be able to convert different combinations of filaments into personalized medicines, based on individual prescriptions, to fulfil the patient's needs. This approach, not only presents irrefutable benefits for the patient's health, minimizing waste of medicines, but also repositions and strengthens the role of the pharmacy and the pharmacist in health care provision to the population.

References:

1. Melnyk, L.A.; Oyewumi, M.O. Integration of 3D printing technology in pharmaceutical compounding: Progress, prospects, and challenges. Annals of 3D Printed Medicine 100035, 4 (2021).
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