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Study on 3D Printed Innovative Modified Release Formulation

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1. Introduction

The interest toward modified release (MR) is growing considering the formulation of personalized medicine. Osmotic Release Oral System (OROS) is a type of the MR formulations. Osmotic drug delivery systems appeared in the second half of the 20th century. In 1980, the first two products operating as osmotic systems were launched. The creation of the so-called "push- pull" type tablet was a big step towards their spread.(1, 2)

OROS formulations have numerous benefits. Their release is controlled and prolonged, so more balanced blood levels can be provided compared to conventional release tablets, and they cause less side effects. The dissolution of the active ingredient from the osmotic tablets is independent of pH and gastrointestinal motility. Beside these formulations need lower administration frequency than conventional tablets, they have a more favorable dosing profile, thereby the patient compliance can be increased. (2, 3)

A traditional OROS tablet can contain two or three layers. One of these contains osmogene, and a large amount of swellable polymer, that swells on contact with water, and push out the active agent from the upper layer through the orifice which is designed on the semipermeabile coating. (4)

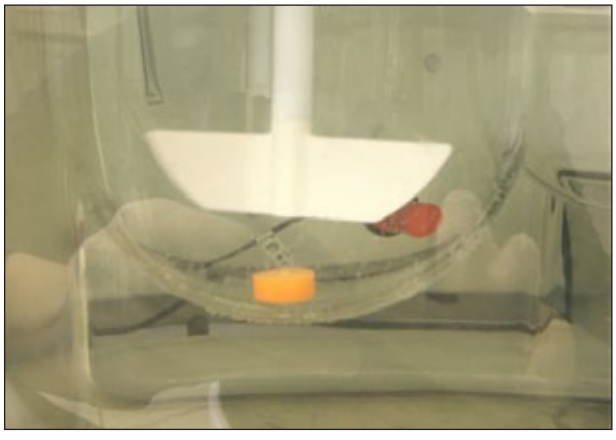

Figure 1 *During the dissolution test*

The objective of our study was to create a novel formulation by combining two new and innovative areas of the pharmaceutical industry: osmotic tablets and 3D printing. My goal was to make bilayer, and single layer tablets by compression, and then to design a 3-dimensional frame and then built it around the tablet using PLA polymer, and after this procedure only the "push" layer had to be coated. (5, 6)

2. Materials and methods

The tablets were compressed with Fette Exacta excentric tablet machine (flat press tool, diameter: 12 mm). Control tests have been performed on the formulations including mass (Kern ABT 320-4M), the height, the diameter, and the strength uniformity of the tablets (TBH 200 Erweka instrument GmbH, Germany). In case of this innovative composition, it was sufficient to create a semipermeable or permeable coating on the lower surface of the swelling layer using vertical lamination, spraying and solvent evaporation films.

The 3- dimensional frame was designed with Autodesk® Fusion 360 (USA) and the objects were sliced with Ultimaker Cura 3.6 (Netherlands). After the designing step a Fused Deposition Modelling (FDM) printer equipped with 0,4 mm aluminium nozzle was used to print the objects. From the huge variety of applicable filaments polylactic acid (PLA) was used due to its water insolubility, so the osmotic controlled drug release could be secured.

The dissolution profile of the model drug was examined in different pH media (1.2; 4.5; 6.8) (Hanson SR8 Plus).

3. Results

Swelling tests have been executed with the "push" layer and with the application of image analysis it was experienced that the swelling layer have doubled its size during the process.

As a result of this study, the structure of the microfabricated carriers were optimized, and tablets were met the regulations of the control tests of the dosage form.

According to the biorelevant dissolution studies, the tablets surrounded by a 3-dimensional skeleton were released the active ingredient over a prolonged period of time. During the dissolution tests it became clear that using either a semipermeable or a permeable coating the initial first-order kinetics of the dissolution, after six hours, turns into zero order kinetics. The drug release was significantly influenced by the number of orifices designed on the 3-dimensional frame.

4. Conclusions

Regarding these results, advances in this territory can be achived so innovative osmotic tablets can be reasonable options for personalized medication in public healthcare. The additive manufacturing such as 3- dimensional printing provides the opportunities to overcome the disadvantages of current formulations, while retaining the beneficial properties, which we can see in the dissolution studies.

Figure 2 The final formulation

References

1. *Ghosh; T, Ghosh A. Drug Delivery Through Osmotic Systems- An Overview. Journal of Applied Pharmaceutical Science. 2011;01(02):38-49.*
2. *Malaterre V, Ogorka J, Loggia N, Gurny R. Oral osmotically driven systems: 30 years of development and clinical use. European Journal of Pharmaceutics and Biopharmaceutics. 2009;73(3):311-23.*
3. *Gupta; BP, Thakur; N, Jain; NP, Banweer; J, Jain; S. Osmotically Controlled Drug Delivery System with Associated Drugs. Journal of Pharmacy & Pharmaceutical Sciences. 2010;13(3):571-88.*
4. *Keraliya RA, Patel C, Patel P, Keraliya V, Soni TG, Patel RC, et al. Osmotic drug delivery system as a part of modified release dosage form. ISRN pharmaceutics. 2012;2012:528079.*
5. *Norman J, Madurawe RD, Moore CMV, Khan MA, Khairuzzaman A. A new chapter in pharmaceutical manufacturing: 3D-printed drug products. Advanced Drug Delivery Reviews. 2017;108:39-50.*
6. *Gioumouxouzis CI, Tzimtzimis E, Katsamenis OL, Dourou A, Markopoulou C, Bouropoulos N, et al. Fabrication of an osmotic 3D printed solid dosage form for controlled release of active pharmaceutical ingredients. European Journal of Pharmaceutical Sciences. 2020;143:105176.*