British Journal of Pharmacy

https://doi.org/10.5920/bjpharm.1153

British Journal of Pharmacy

www.bjpharm.hud.ac.uk

Proceedings of the 13th APS International PharmSci 2022

Formulation of an implantable device from mini tablets-in-PCL cylinders for sustained delivery of a hydrophobic drug

Camila J. Picco[a], Peter E. McKenna[a], Ryan F. Donnelly[a], Eneko Larrañeta[a]*

[a]School of Pharmacy, Queen's University Belfast, Belfast, UK

ARTICLE INFO

Received: 18/07/2022
Accepted: 25/07/2022
Published: 04/11/2022

*Corresponding author.
Tel.: +4428 90972360
E-mail: e.larraneta@qub.ac.uk

KEYWORDS: Implants; 3D printing; drug delivery; tablets.

SUMMARY

Implantable drug delivery systems are presented as a potential alternative to current treatments of chronic conditions. The aim of this work was to formulate a subcutaneous implantable device made with prefabricated poly(caprolactone) (PCL) cylinders, loaded with olanzapine (OLZ) as a model drug and cyclodextrin in a mass ratio of 1:1. The final formulation was characterized using optical microscopy, infrared spectroscopy, thermal analysis, and X-ray diffraction. The proposed device was successfully fabricated and demonstrated ability to control drug release for 60 days. With continued development, these novel implants could be an alternative to currently available treatments for schizophrenia.

INTRODUCTION

Implantable drug delivery systems offer an alternative to conventional dosage forms for the treatment of chronic conditions (i.e., schizophrenia, HIV, or Parkinson's disease among many others) (Langer, 1990). These conditions normally require continuous and repeated oral drug administration, which can often lead to a pill fatigue, followed by non-adherence to treatment and finally treatment discontinuation (Gendelman et al., 2019). Implantable systems may improve treatment efficacy and patient adherence, which, in turn, would prove beneficial for the quality of life of individuals receiving treatment. (Rajgor et al., 2011). This type of drug delivery system has been widely investigated for medical applications, with multiple fabrication techniques such as hot melt extrusion, 3D printing and solvent casting used to great effect (A. S. Stewart et al., 2018). The objective of the present work was to formulate subcutaneous implantable devices composed of drug-containing directly compressed pellets encased within a rate-controlling poly(caprolactone) (PCL) membrane (Figure 1). Olanzapine (OLZ) was selected as a model drug because it is indicated for conditions such as schizophrenia, mania and bi-polar disorder, all of which are chronic in nature. The resulting implants were characterized using optical microscopy, infrared spectroscopy, thermal analysis and X-ray diffraction. Additionally, a 60-day study investigating the release of OLZ was also performed

MATERIALS AND METHODS

Formulation of mini tablets: An OLZ: Hydroxypropyl-β-cyclodextrin (HP-β-CD) mass ratio 1:1 was evaluated. A powered blend of OLZ and HP-β-CD was uniformly mixed and compressed using hydraulic press at 0.5 tonnes to produce mini tablets (diameter = 2.9 mm, 5mm length). ***Formulation of tubular membranes*:** 1.2 g of PCL (50 kDa), 1.8 g of PCL (550 Da) and 30 mL of dichloromethane were mixed to form a solution that was subsequently casted on a spinning metal rod (75 rpm). Three consecutive castings were added to the metal rod, allowing 4 min of drying in between castings. ***Device fabrication*:** 6 mini tablets loaded into each PCL tube and tube ends were closed using heat. The resultant

https://doi.org/10.5920/bjpharm.1153

implant measured 4 cm in length and 3 mm in diameter. ***OLZ release study***: Implants were placed in 100 mL of PBS (pH: 7.4) at 37°C with 0.05%w/v sodium azide to prevent bacterial growth, and agitated at 40 rpm at 37˚C in an incubator. 1 mL samples were taken at specific time points during over the course of 60 days and quantified using RP-HPLC.

RESULTS AND DISCUSSION

Mini tablets and tubular PCL membranes were successfully prepared. Figure 1 depicts the individual components of the formulated implants, with Figure 1d presenting an image of the final device.

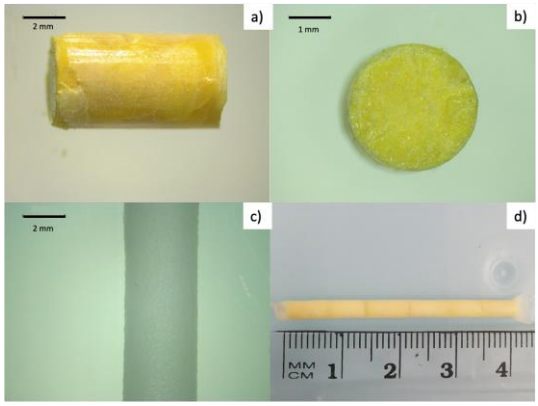

Fig. 1. *a-b) tablet of OLZ-cyclodextrin, c) PCL tube and d) final device.*

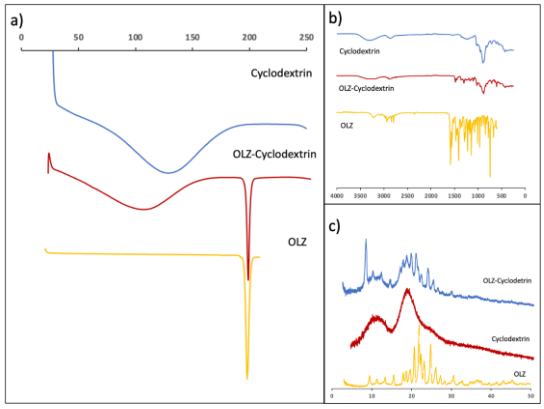

Fig. 2. *a) DSC, b) FT-IR and c) PXRD – Powdered X-Ray Diffraction of OLZ powder, Cyclodextrin powder and a physical mixture of OLZ and cyclodextrin.*

DSC analysis of the physical mixture of compressed pellets show the peaks obtained for both OLZ and cyclodextrin (Figure 2a). Characteristic crystalline peaks of OLZ were observed in FT-IR and the PXRD f pure OLZ and minitablets containing OLZ (Figure 2, b and c) indicating that the drug remains crystalline when formulated into a tablet with HP-β-CD.

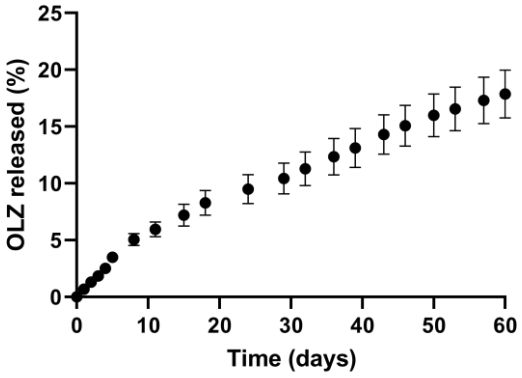

Fig. 3. *Percentage of OLZ released for 60 days.*

The implants demonstrated linear drug release between day 10 and day 60 (Figure 3). The amount of drug released after this time was ca. 17.86 ± 2.11%. *In vitro* release studies indicated that implants containing 50% (w/w) of OLZ were capable of providing drug release for at least 60 days releasing almost 20% of the total amount of the drug.

CONCLUSIONS

An implantable device was obtained using biocompatible materials, and the coating applied demonstrated the ability to control drug release over 60 days. The formulated device holds potential as an alternative to current treatments for schizophrenia. Furthermore, this approach may be suitable for use in the treatment of other chronic conditions.

REFERENCES

Langer R. (1990). New methods of drug delivery. Science 249:1527–33.

Gendelman HE, et al. (2019). The promise of long- acting antiretroviral therapies: from need to manufacture. Trends Microbiol 27:593–606.

Stewart AS, et al. (2018). Implantable polymeric drug delivery devices: classification, manufacture, materials, and clinical applications. Polymers 10:1379.

Rajgor N, Bhaskar V, Patel M. (2011). Implantable drug delivery systems: an overview. Syst Rev Pharm 2:9