British Journal of Pharmacy

https://doi.org/10.5920/bjpharm.1410

British Journal of Pharmacy

www.bjpharm.hud.ac.uk

Proceedings of the 14th APS International PharmSci 2023

3D printed flexible design for personalized drug release

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ARTICLE INFO

Received: 31/07/2023
Revised: 05/08/2023
Accepted: 08/08/2023
Published: 30/12/2023

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KEYWORDS: 3D printing, FDM, personalized medication, theophylline, control released.

SUMMARY

Three-dimensional printing is becoming more appealing to pharmaceutical research in recent years, especially after the approval of Spritam® by the FDA. However, its role in personalized medication is still hindered by quality control barriers among other development barriers. In this work, a novel design is suggested to offer a middle ground to solve regulatory barriers. This design was printed into four units that can be attached through hinges like a jigsaw puzzle. This work will showcase the capability of this design to control the release of the model drug theophylline. Two formulations were prepared one immediate release using PVP 40K and one sustained release using Eudragit EPO. Using the principles of surface response method, the experiment was designed where three variables - drug load, infill density and number of immediate release units- were adjusted to study their effect on theophylline release in the dissolution test. Both the drug load and number of units had a significant effect on both the level and the shape of the drug release curve in 24 hours dissolution study.

INTRODUCTION

The current paradigm is the administration of the same drug to different patients at the same dose and frequency -one size fits all-. However, recent advancements in the field of pharmacogenomics revealed how this paradigm is wrong and can lead to under medication or overdose (Vaz & Kumar), which will lead to ineffective treatment and side effects, respectively. In addition to improving efficacy and safety, personalized medication can improve patient compliance and decrease the cost of treatment.

Three-dimensional printing (3DP) is an inclusive term for all additive manufacturing techniques, where a solid model is constructed layer by layer. These techniques can be divided according to the type of ink into extrusion printing, powder solidification and liquid solidification (Kalaskar & Serra). Fused deposition modelling (FDM), which is an extrusion-based 3DP technique, is the most studied technique due to its low operation cost and ease of use (Dumpa et al.). Many researchers have demonstrated the ability of FDM to control drug release through controlling; formulation (Goyanes et al., 2015), drug load (Li et al., 2017), infill density (Kempin et al., 2018)and other design factors.

Therefore, the aim of this work was to investigate the possibility of using the design flexibility that comes with FDM to print a novel polypill that can be personalized to meet patient needs.

MATERIALS AND METHODS

Theophylline anhydrous, Triethyl citrate, talc and Polyvinylpyrrolidone 40,000 M.W (PVP 40K) were purchased from Sigma-Aldrich Co. Ltd. (Dorset, UK). Eudragit RL PO was supplied by Evonik Industries AG (Darmstadt, Germany). Scotch blue painter's tape 50 mm was obtained from 3 M (Bracknell, UK).

Thereafter, the model drug theophylline was formulated (extruded and printed) using two different polymers Eudragit RLPO and PVP 40K to

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produce sustained(SR) and immediate release(IR) units of a four-units tablet (the Flexible-pill), respectively. Then, the effect of three independent variables, which are the drug load, infill density and the number of immediately release units, was studied using Box–Behnken design.

The dissolution test was performed for 24 hours in HCl and drug release was measured using HPLC-DAD at 273 wavelength. the profiles were analysed and compared using modified-principal component analysis (M-PCA)(Wang et al., 2016).

RESULTS AND DISCUSSION

In this work, the fifteen dissolution runs (n=3) resulted in different release curves. Using the method of M-PCA to compare the level and the shape of the curve the experimental design revealed that both drug load and number of IR units had a significant effect on both the level and the shape of the release curve. Table 1. However, the infill density had no significant effect, Fig 1.

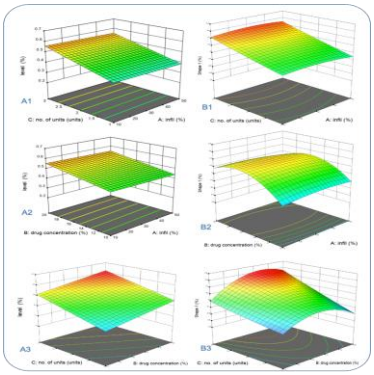

Fig. 1. *A. Effect of the variables on the level B. Effect of the variables on the shape, 1. No. units Vs infill, 2. API conc. Vs infill and 3. No. of IR units Vs API conc.*

Table 1. *The prediction equation for the level and shape of dissolution with the p-value for each term.*

	Intercept	Infill (A)	Conc. (B)	No. Units (C)	B^2
Level	0.48552	0.00276	0.05341	0.08276	
P-values [a]		0.9077	0.0427	0.0046	
Shape 1	0.29143	-0.01290	0.15281	0.30045	0.34071
p-values [a]		0.809	0.0297	0.002	**0.0061**

[a] p-value lower than 0.05 is considered significant

CONCLUSIONS

The Flexible-pill design can be a great step toward personalized medication by using flexible-pill units in pharmacy settings to meet patient needs. This work shows the capability of this design to control drug release and dose.

REFERENCES

Dumpa, N., Butreddy, A., Wang, H., Komanduri, N., Bandari, S., & Repka, M. A. (2021). 3D printing in personalized drug delivery: An overview of hot-melt extrusion-based fused deposition modeling. *International Journal of Pharmaceutics*, 120501.

Goyanes, A., Martinez, P. R., Buanz, A., Basit, A. W., & Gaisford, S. (2015). Effect of geometry on drug release from 3D printed tablets. *International journal of pharmaceutics*, *494*(2), 657-663.

Kalaskar, D. M., & Serra, T. (2017). *3D Printing in Medicine*. Elsevier Science & Technology.

Kempin, W., Domsta, V., Grathoff, G., Brecht, I., Semmling, B., Tillmann, S., . . . Seidlitz, A. (2018). Immediate release 3D-printed tablets produced via fused deposition modeling of a thermo-sensitive drug. *Pharmaceutical research*, *35*(6), 1-12.

Li, Q., Wen, H., Jia, D., Guan, X., Pan, H., Yang, Y., . . . Pan, W. (2017). Preparation and investigation of controlled-release glipizide novel oral device with three-dimensional printing. *International Journal of Pharmaceutics*, *525*(1), 5-11. https://doi.org/https://doi.org/10.1016/j.ijpharm.2017.03.066

Pesce, A. J., Rashkin, M., & Kotagal, U. (1998). Standards of laboratory practice: theophylline and caffeine monitoring. *Clinical chemistry*, *44*(5), 1124-1128.

Vaz, V. M., & Kumar, L. (2021). 3D printing as a promising tool in personalized medicine. *Aaps Pharmscitech*, *22*, 1-20.

Wang, Y., Snee, R. D., Keyvan, G., & Muzzio, F. J. (2016). Statistical comparison of dissolution profiles. *Drug Development and Industrial Pharmacy*, *42*(5), 796-807.