P-05

Biocompatibility and Dissolution Profile of FDM 3D Printed PETG Tablets

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Keywords: *3D printing, FDM, diclofenac sodium, MTT assay, dissolution test*

1. Introduction

Individualized dose is one of the most emerging problems in the pharmaceutical sciences that can be solved with personalized medication. For the manufacturing of personalized medications we can use 3D printing which promise to manufacture complex, personalized products through a low-cost manufacturing process on-demand. [1] 3D printing is an umbrella term referring to different techniques but for our experiments we used FDM (fused deposition modeling) technique because it is an off-patent, widespread and inexpensive technology.[2] Polyethylene terephthalate glycol (PETG) removes the hazing effect during heating and prevents the undesirable crystallization effect that causes standard PET to become brittle during the FDM printing this is we we choose this polymer for 3D printing. [3]

2. Materials and methods

3D printing

Samples with different diameter (16, 19 and 22 mm) and with different infill percentage (0, 5, 10 and 15%) was printed with Prusa i3 MK2 FDM printer by Mariann Zichar and Ildikó Papp. Batches of ten pill was printed and each was containing 30 mg of diclofenac sodium salt as a model active pharmaceutical ingredient (API).

Mtt cell viability assay

our research group developed a long term MTT assay which means that the samples are immersed in medium for 4, 8 and 12 days and the MTT assay is performed on these days to determine if any kind of xenobiotic is dissolved from the samples.

Dissolution test

The dissolution test was carried out using USP Type I Erweka DT 800 dissolution apparatus with an auto sampling system. Dissolution medium of 900 ml of phosphate buffer at pH 7.4 was used at 37°c.

3. Results

3D printing

Our research group developed an easy method to fill the samples with API so we printed separately

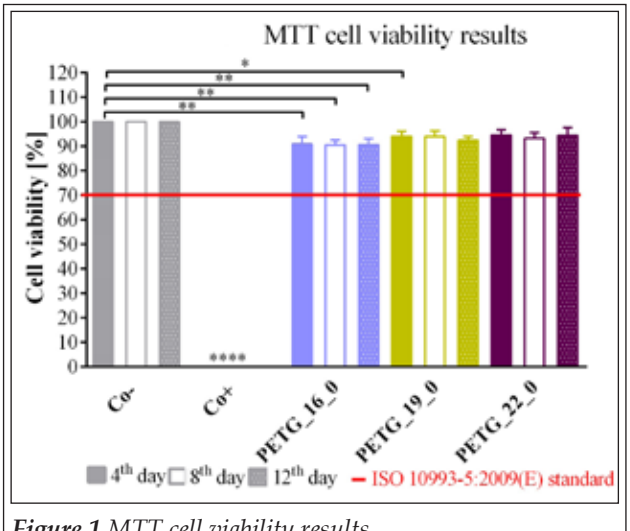

Figure 1 *MTT cell viability results*

 DOI: 10.33892/aph.2021.91.171-172

a cover (labelled with brown) that was placed on the top of the API containing lower part through the 3D printing. This way we can avoid the problems caused by ventilation and the high printing temperature. PETG was printed at 250°C, bed temperature was 90°C, the layer thickness is 200 µm.

Mtt cell viability

a prolonged cell viability test was performed in our work to gain information about the cytocompatibility of our 3D printed samples. The samples were incubated in the cell culture medium for four, eight, and twelve days, and the monolayer formed by Caco-2 cells were treated with this medium. The results are expressed as the percentage of negative or untreated control (Co−). (***Figure 1***) As a positive control (Co+) Triton-X 100 (10% *w/v*) solubilizing agent was used.

We compared cytotoxic values and found that none of the examined samples decreased significantly the cell viability results compared to the untreated control Based on the ISO 10993-5:2009(E) standard, if the relative cell viability is higher than 70% in comparison with the control group (100%), the materials can be considered non-cytotoxic.

Dissolution test

in ***Figure 2*** the dissolved API amount [%] is plotted against the time [h] in case of the PETG samples. Samples was measured at USP type I apparatus with auto sampling systems at 5, 15, 30 and 45 minutes, 1, 2, 4, 6, 8, 12, 14, 16, 18, 20 and 24 hours. In case if we compare the diameter we cannot see a significant difference because 16 mm sample has the lowest and 19 mm sample the fastest dissolution. If we compare the samples with different infill percentage even though PETG_16_0 has the lowest final API dissolution (around 60%) we can see that in case of 5, 10 and 15% the dissolution is less and less. With the increase of the infill percentage we decreased the dissolved API amount. We cannot see a significant difference on the dissolution profile caused by the diameter or the infill percentage.

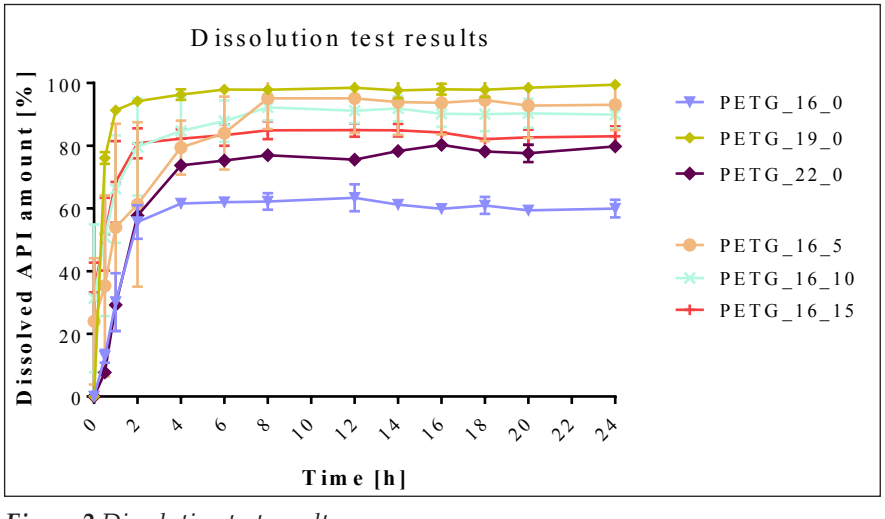

Figure 2 *Dissolution test results*

4. Conclusions

To conclude, we have successfully printed samples from PETG polymer with modified FDM technology so we can put the API directly into the drug dosage form. The printed PETG contain 30 mg diclofenac sodium salt. All samples can be considered to non-cytotoxic based on the ISO standard but cytotoxicity data alone is not necessarily predictive of *in-vivo* tissues. However, the *in vivo* compatibility data can be estimated. The diameter and infill percentage does not show a significant effect on the dissolution profile so our has to extended to other diameter and infill percentage and other polymers.

5. Acknowledgements

The research was financed by the Higher Education Institutional Excellence Program (NK-FIH-1150-6/2019) of the Ministry of Innovation and Technology in Hungary, within the framework of the Therapeutic purposes thematic program of the University of Debrecen. The project was supported by the EFOP-3.6.1-16-2016-00022. The project is co-financed by the European Union and the European Social Fund. The project was supported by the Gedeon Richter's Talentum Foundation (1103 Budapest, Gyömrői út 19-21 Hungary).

References

1. *Chia, H. N., Recent advances in 3D printing of biomaterials, J. Biol. Eng. 9: 1–14 (2015)*
2. *Tagami, T., 3D Printing Factors Important for the Fabrication of Polyvinylalcohol Filament-Based Tablets, Biol. Pharm. Bull. 40: 357–364 (2017)*
3. *Durgashyam, K., Experimental investigation on mechanical properties of PETG material processed by fused deposition modeling method, Mater. Today Proc. 18: 2052–2059 (2019)*