Stereolithographic 3D printing (SLA 3DP) of pharmaceutical tablets

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Abstract: We evaluated the applicability of SLA 3DP in making pharmaceutical tablets. Adding alizarin dye in the printing polymers improved print resolution through minimizing light scattering. 3DP tablets were evaluated for weight deviation, uniformity in drug content and dissolution profiles. 3DP tablets were determined to be uniform in weight and drug content based on European Pharmacopoeia criteria. Tablets with different sizes and shapes were printed with consistency. A lower PEGDA to PEG ratio, addition of xylitol as disintegrant and change in tablet design to improve the surface area-to-volume ratio, were explored to improve rate of drug release from 3DP tablets.

I. Introduction

3D printing (3DP) has been increasingly applied to manufacture products of customized design and sizes. Initially started off as a tool for rapid prototyping, 3DP has been developed toward replacing some of the conventional manufacturing processes due to its versatility in customization (1).

One notable development would be the use of powder-bed printing to make SPRITAM© (Levetiracetam) tablets; the first 3DP drug approved by FDA. 3DP provides the possibility of fabricating tablets using different raw materials, designs and methods not found in tablet compression processes (2). 3DP is a potential approach to make personalized medicines with specific doses tailored to a patient’s profile and disease condition.

II. Material and methods

II.I. Formulation of photopolymer mixtures

To 14 ml of PEG300, 150 mg of xylitol powder was added and mixed using magnetic stirring. Mixture was heated to around 50 °C so as to dissolve the xylitol powder in PEG 300. Mixture was then cooled rapidly in cold water bath to obtain a homogenous mixture of xylitol in PEG300.

6 ml of PEGDA was then added into the mixture, followed by 200 mg of DPPO. The mixture was mixed thoroughly until a homogenous mixture was formed. 5 g of ibuprofen followed by 30 mg of Alizarin dye was added and stirred thoroughly until a homogenous mixture was formed.

II.II. Printing of the photopolymers

The photopolymer mixture was added into the resin tank specified for Form 1+ printer. Tablet was designed using Autodesk fusion 360 © and Autodesk PrintStudio © before being imported into the Preform © software using the stl* file format. The following print settings in Preform © were

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selected: Form 1+, tough resin and print resolution of 0.05 mm. Tablets were printed without support structures to minimize print error, shorten print duration and reduce material wastage. Tablets printed on the support base were carefully removed from the support base and blotted dry.

III. Results and discussion

Twenty tablets were printed each time due to limited space on the platform. Form 1+ took around 52 minutes to print twenty donut-shaped tablets of 60 layers, which is less efficient than a tablet press. Print duration and resolution depends on the number of layers and the thickness of each layer printed. Average dimensions of printed tablets were determined to be 8.4 mm diameter × 2.6 mm height with a central hole of 2.3 mm diameter for donut-shaped tablets and 8.7 mm diameter × 2.0 mm height with two holes of 1.5 mm diameter and mouth-alike curvature of 1.5 mm in depth for smiley-shaped tablets.

Print resolution was affected by changes in the proportion of PEGDA, PEG300, DPPO and alizarin in the formulation. Decreasing the proportion of PEGDA, PEG300, DPPO and alizarin in the formulation. Decreasing the proportion of PEGDA would decrease the hardness of the tablet. Printed tablets would be too soft to handle and print resolution would be poorer at a low PEGDA to PEG300 ratio. However lower PEGDA to PEG300 ratio would improve drug release, thus a suitable ratio was selected to achieve adequate print resolution and desired dissolution rate.

Change in the amount of DPPO can affect print resolution. Decreasing or increasing the concentration of DPPO was observed to produce prints of poorer resolution. Some tablets did not form at high and low concentration of DPPO used in the formulation.

The addition of dye, such as Alizarin, to the formulation improved print resolution significantly. Previous prints were poor in resolution and failed on numerous occasions. Alizarin dye could have focused the laser onto the printed area and minimized light deflection onto other area, thereby improved print resolution. However, increase in the concentration of dye was observed to produce poor prints, possibly due to poorer absorbance of light by the printed area.

Weight of 20 printed tablets printed in a single batch (PEGDA/PEG300: 3/7, 0.8% w/v DPPO, 0.12% w/v alizarin, 0.6% w/v xylitol) met the Ph. Eur standards for uniformity in the weight of tablets as out of 20 randomly selected printed tablets, at least 18 tablets were within 7.5% deviation in weight and not more than 2 tablets exceeded 15% deviation in weight. The average weight and standard deviation of the printed tablets were 139.8 and 4.9 mg respectively.

Percentage recovery of ibuprofen in individual tablets determined after extraction with 50% v/v ACN in water was found within 95 to 102 % from the nominal concentration of ibuprofen in photopolymer mixture, thus ibuprofen in the photopolymer mixture was observed to be loaded fully into the printed tablets.

In a comparative study of dissolution profiles in PBS, pH 7.4±0.2, drug release was observed to be significantly faster in smiley-shaped tablets with 1.2% w/v xylitol, as compared to donut-shaped tablets without xylitol. f1 and f2 were calculated to be 20.61 (>15) and 53.98 respectively; p < 0.05 at 95% confidence when using ANOVA. Drug release was observed to be faster when xylitol was added and the tablet design was changed to increase its surface area to volume ratio.

IV. Conclusions

SLA printed tablets were uniform in weight and drug content. Tablets of different sizes and shapes were printed with consistency. Even though drug release remained slow after several modifications to the formulation were made, the flexibility to print medicines of customized doses and designs would be useful in personalized treatment.

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REFERENCES