SYSTEMATIC EVALUATION OF PHOTOPOLYMER FORMULATIONS FOR STEREOLIGHOGRAPHY 3D PRINTING OF SOLID ORAL DOSAGE FORMS

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Background: Among the most novel technologies emerging in the pharmaceutical field, 3D printing has proved to be a frontrunner technique to manufacture solid oral dosage forms targeting personalised treatments. 3D printing offers a flexible platform to produce medicines directly at the point of care; drug dosage, release profile and tablet geometry can be tailored on the needs of individual patients with the aim to optimize therapeutic outcomes. Stereolithography (SLA) 3D printing, a vat photopolymerization technique already used to fabricate controlled release tablets and polypills, is an attractive technique yet suffering from limitations related to the lack of biocompatible photopolymer formulations that could be used. Therefore, in this work we selected a pool of photopolymers and liquid fillers to prepare 156 formulations to be screened, with the view to identify ideal candidates for future drug loading studies.

Methods: A total of 156 photopolymer formulations were prepared by mixing different ratios of reactive mono/oligomers (polyethylene glycol diacrylate -PEGDA- MW 250, 575 and 700, N-vinyl-pyrrolidone), photoinitiator (diphenyl 2,4,6-trimethyl benzoyl phosphine oxide) and liquid fillers (polyethylene glycol 300, propylene glycol, glycerol). Photoinitiator was added at a concentration of 1%, 0.5%, 0.1% and 0.05% (w/w); liquid fillers were added at a concentration of 12.5%, 25% and 50% (w/w). Formulations were loaded in a modified Form 2 3D printer and cylindrical tablets (12 mm diameter – 4 mm height) were printed at a resolution of 25, 50 and 100 µm. Printability outcomes were evaluated according to an arbitrary scale assigning a Printability Score (PS) from 1 to 6, with 5 being the target value.

Results: Out of the initial 156 formulations tested, 60 were identified as reaching a PS=5 or showing a defined rim when printing a cylindrical tablet at least at one resolution (positive formulations, n=60). Out of these 60 formulations, 35 were identified as reaching a PS=5 and showing a defined rim when printing a cylindrical tablet at least at one resolution, while 5 formulations were identified as ideal candidates because providing the best results at every printing resolution (optimal formulations, n=40). The effect of PEGDA molecular weight was investigated; PEGDA 250 was present in 43.4% and 47.5% of the positive and optimal formulations, respectively. However, PEGDA 700 showed the highest ratio (80%) between optimal and positive formulations, proving to be highly performing when used. The impact of the liquid fillers' concentration was also studied, and the best results were observed at a concentration of 12.5% w/w. Finally, the relation between photoinitiator's concentration and printing resolution used was investigated; according to the results, the most effective photoinitiator concentration was 0.05% w/w used for printing at a resolution of 100 µm. As a result of printing at 100 µm, the number of layers is reduced up to 4 times, with a significant impact on production time.

Conclusions: 5 formulations out of 156 were identified as suitable candidates to be drug loaded and 3D printed as controlled release dosage forms. The investigation of different liquid fillers provides information on which species and which concentration could be used to tune the release profiles in SLA 3D printed tablets. Finally, the use of low concentration of photoinitiator at lower printing resolution is recommended. This not only would result in better printability outcomes but could also have significant implications in reducing toxicity concerns and formulation costs. Furthermore, printing at a lower resolution will decrease the number of layers needed thus speeding up manufacture time.