Inkjet Printing Oral Dosage Forms

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Abstract – **The current study aims to establish an innovative method of effectively solubilising Biopharmaceutical Classification System Class II drugs using inkjet printing. Dosage forms have been produced using an Optomec AJ200 3D Inkjet printer. Printing with an appropriate polymer seems to result in an amorphous product, which will hopefully have a greater overall solubility.**

INTRODUCTION

Oral drug delivery is currently the preferred method of administration, however, the problem of poor solubility means many drugs are not ideally suited to this [1]. Although a number of methods to increase solubility already exist, there is a need for less damaging methods of production which are more flexible to the needs of the patient (Fig. 1). With a view to reducing the risk of degradation and negative polymorphic changes, the potentially damaging steps of granulation, drying and compression will be replaced with the innovative formulation technique of inkjet printing. Inkjet printing has the capasity to produce highly precise dosing in a continuous manner. This is highly advantageous as the exact location of the drug within the dosage form may be able to be known to the micrometre and thus release may prove more efficient and predictable than some conventional methods of dosage form production.

Fig. 1: Changes to the conventional oral dosage form production pathway

MATERIALS AND METHODS

Dosage forms were produced using an Optomec AJ200 3D Inkjet printer (Fig. 2). This particular printer has never been used in the field of pharmaceutical manufacture previously [2-3]. Dosage forms were manufactured by combining the poorly soluble drug with a solubilising polymer as premixed inks. Deposition was achieved through pneumatic atomisation and dosage forms were produced based on AutoCAD drawings. Initial analysis was carried out by Raman spectroscopy, standard microscopy, scanning electron microscopy (SEM) and powder x-ray diffraction (pXRD).

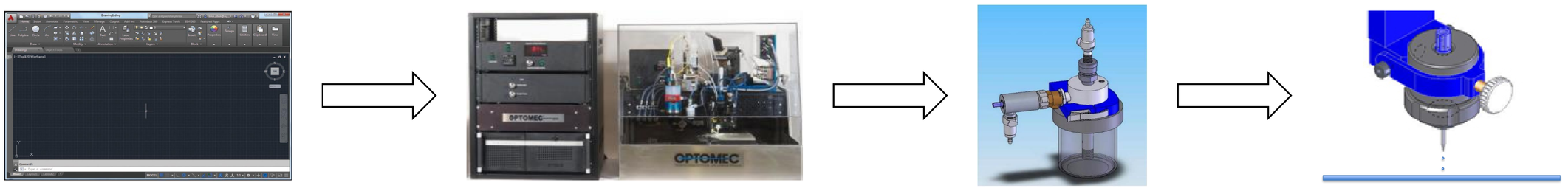

Fig. 2: Inkjet printing using an Optomec AJ200 Inkjet Printer. Images obtained from Optomec Ltd. [3]

RESULTS AND DISCUSSION

pXRD shows the printed drug alone to be fairly crystalline. However, on printing the drug as a premixed formulation with a polymer the crystallinity is reduced, resulting in a fully amorphous product on application of a 1:3 API:polymer content or higher (Fig. 3).

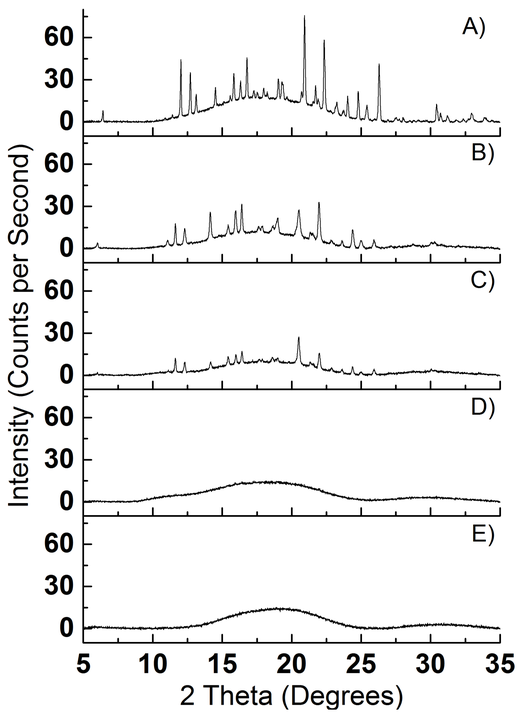

Fig. 3: pXRD of the API printed alone (A)) and with polymer in B) 1:1, C) 1:2, D) 1:3 and E) 1:4 ratios

Raman suggests the major interactions involved in this change are associated with the carbon-carbon double bonds, the aromatic rings or the methyl groups, as represented by a smoothing of the 1500-1650 cm^{-1} and 3050-3100 cm^{-1} regions in the spectra (Fig. 4).

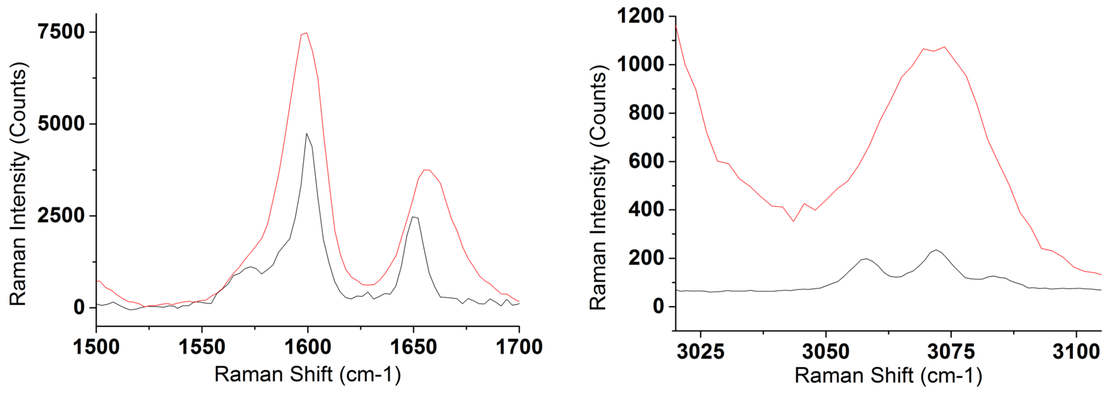

Fig. 4: Raman spectroscopy of the 1500-1650 cm^{-1} (left) and 3050-3100 cm^{-1} (right) regions of the drug as its crystalline powder form (black) and as part of a solid dispersion (red)

The microscopy images demonstrate the loss of crystallinity as the shiny planes of drug seen in the drug alone deposition are replaced by smaller particles (Fig. 5). However the scale was not sufficient to fully determine the nature of the surface as the mass of material deposited by this technique is very low. As such SEM was carried out.

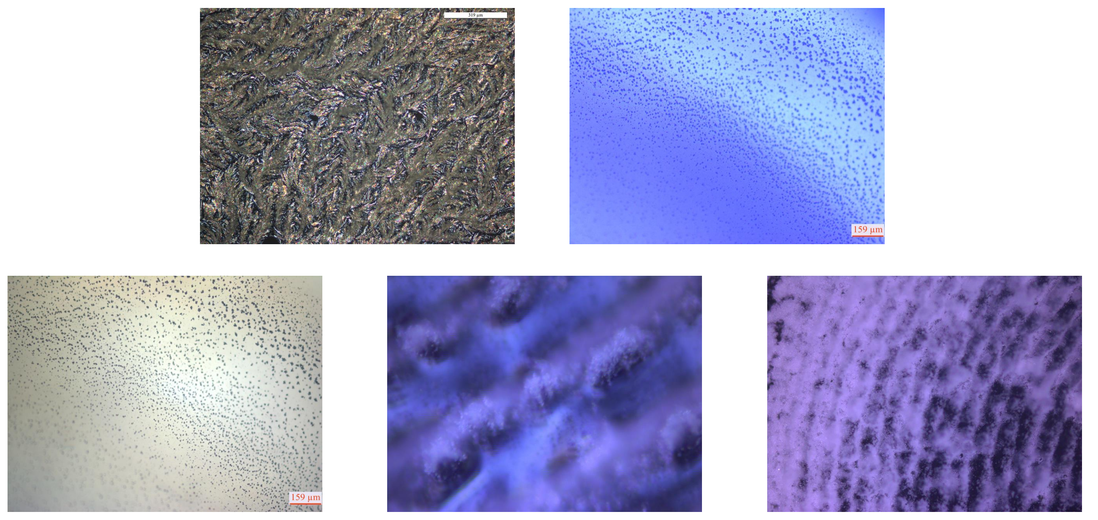

Fig. 5: Microscopy images of API and polymer formulations printed taken at x50 magnification. Top (left to right): Drug alone and premixed in an API:polymer 1:1 ratio. Bottom (left to right): premixed formulations in API:polymer 1:2, 1:3 and 1:4 ratios

The SEM images show a reduction in the plate-like crystalline structures of the drug with increasing polymer content (Fig. 6).

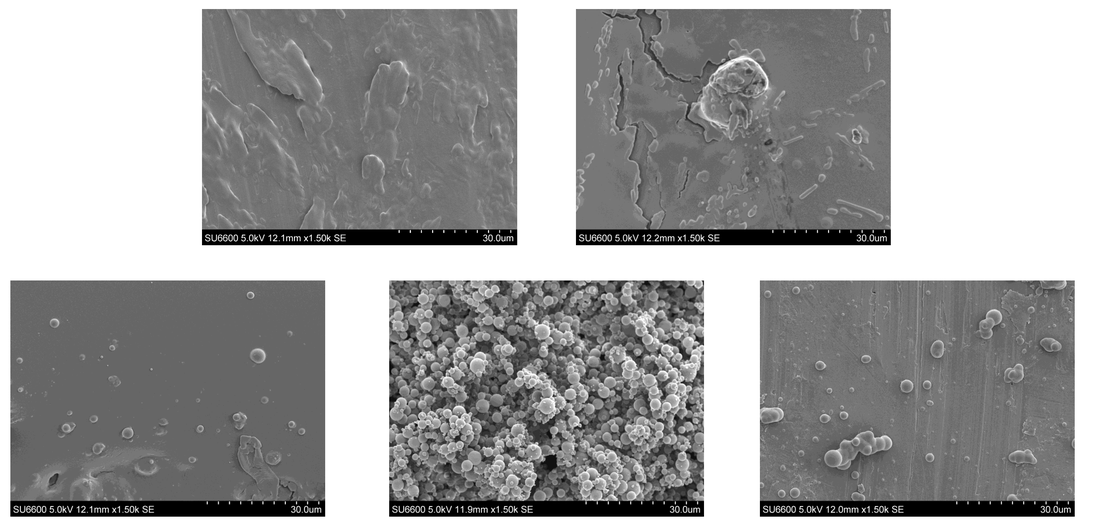

Fig. 6: SEM images of API and polymer formulations printed taken at x1500 magnification. Top (left to right): Drug alone and premixed in an API:polymer 1:1 ratio. Bottom (left to right): premixed formulations in API:polymer 1:2, 1:3 and 1:4 ratios

CONCLUSIONS

Inkjet printing drug alone seems to result in crystalline material but on addition of polymer the crystallinity is reduced. This reduction in crystallinity increases with increasing polymer content, eventually resulting in a fully amorphous product, which may suggest solid dispersion formation. It is hoped this phase change will increase the overall solubility of the drug and thus improve overall performance.

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