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Micro-photogrammetry as a tool for characterization of the dissolution behaviour of pharmaceutical dosage forms

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SUMMARY

The aim of this project is to develop an innovative analytical technique for the 3D chemical mapping of pharmaceutical dosage forms, via simultaneous topographic characterisation and dissolution analysis of solid drug delivery systems. The developed apparatus was optimised using the results obtained from the application of micro-photogrammetry to the analysis of commercial solid drug delivery systems. Results of the application of the developed method on the dissolution of a sugar-coated tablet sample are here presented.

INTRODUCTION

Characterisation of the surface of a product is often essential to better understand its performance. Micro-scale properties, such as topography and component distribution, are known to greatly influence macro-scale properties of formulations such as dissolution (Belu, 2008). Here we propose an approach for dissolution analysis and volume characterisation that is based on 3D modelling of the sample as it is dissolved.

MATERIALS AND METHODS

Dissolution of Ibuprofen sugar coated tablets (Bristol Laboratories) was realised in seven discontinuous steps, the analysis was conducted in triplicate. The sample was located in a container where half of the tablet was exposed to phosphate buffer (10 mM) at pH 2.1 for 50 seconds. After solvent exposure, the dissolution medium was removed manually and analysed by HPLC.

HPLC methods were elaborated and validated for the quantification of sucrose and ibuprofen. Sucrose was detected using an HPLC Agilent 1100 series equipped with refractive index detector, while ibuprofen was quantified with an HPLC Agilent 1100 series with UV detector.

After each solvent exposure, the sample was dried using cold air without removing it from the dissolution cell then, an annulus for the 3D elaboration with three reference posts was placed around the sample.

3D modelling of a dissolved object requires the collection of several images of the sample obtained from different locations and observation angles (Westoby, 2012). A digital microscope (Super eyes B008) was kept in place at different angles by a camera support developed for the specifications of the

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photogrammetry method tailored to the dimension and properties of the samples analysed. A stepper motor, on which the sample is mounted, provides the rotation of the sample at a velocity selected and controlled by dedicated software.

RESULTS AND DISCUSSION

The HPLC analysis of the tablet content from the recovered dissolution medium revealed that the outer sugar layer was dissolved by the fourth analysis step. Once the sugar coating was dissolved (step 4) the ibuprofen release increased with quasi-linear trend (Table 1).

Table 1. *Dissolution profile of Ibuprofen and Sucrose quantified by HPLC (n=3).*

Steps	Sucrose (mg) Mean ± SD	Ibuprofen (mg) Mean ± SD
Step 1	0.73 ± 0.2	0.2 ± 0.08
Step 2	1.68 ± 0.3	0.3 ± 0.17
Step 3	3.63 ± 0.4	0.4 ± 0.39
Step 4	5.16 ± 0.4	0.4 ± 10.56
Step 5	0 ± 0	0 ± 54.95
Step 6	0 ± 0	0 ± 86.11
Step 7	0 ± 0	0 ± 119.62

From the 3D models presented in Table 2, modification of the sample morphology induced by the dissolution process is observed. Results confirmed what was obtained by HPLC analysis. From the fourth dissolution step, with exposure of the formulation underlying the sugar layer, the sample morphology changed significantly with a visible reduction of the sample size.

3D models were used to quantify the volume of the tablet during dissolution analysis (Figure 1). Volume quantification confirmed what was revealed by visual inspection of 3D models. From the first to the fourth dissolution step (where the outer sugar coating was dissolved) 38 mm3 of the tablet volume was displaced. After exposure of the inner tablet components from the fourth to the final dissolution step 130 mm3 of the tablet was removed, that is more than half of the initial sample volume.

Small volume displacement of the initial four steps of the dissolution analysis suggests that dissolution was mainly driven by diffusion. Whereas, from the fourth step onwards, because of the elevated volume displacement, drug release was mainly controlled by progressive surface erosion

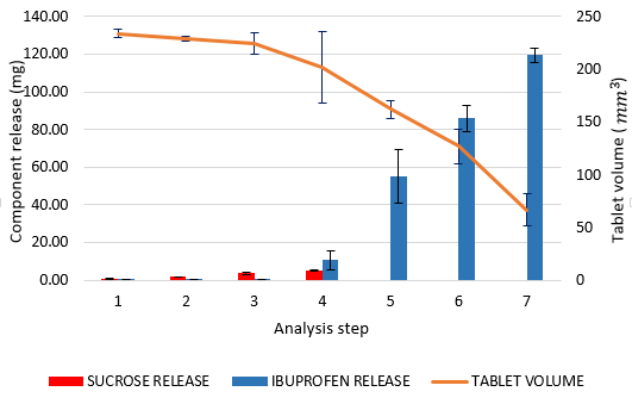
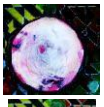


Figure 1. *Correlation between tablet volume and release of sucrose and ibuprofen after each experimental step.*

Table 2. *3D models of the sample under analysis obtained after each sample exposure.*

Dissolution steps	Top view	Lateral view	Dissolution steps	Top view	Lateral view
Native sample			Fourth		
First			Fifth		
Second			Sixth		
Third			Seventh		

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CONCLUSIONS

Our method enabled 3D modelling of ibuprofen sugar coated tablets after each exposure to phosphate buffer at pH 2.1. From these, the volumes of the sample were measured. 3D models of the formulations revealed a small volume displacement induced by the dissolution of the sucrose outer layer, followed by a significant variation of tablet volume after exposure of the product components underlying the outer sugar layer. These measurements were in agreement with the HPLC analysis of the recovered solvent, used to quantify components release. Volumetric analysis revealed that diffusion controlled the initial stages of the dissolution process, followed by erosion.

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