The Electronic Conference on Pharmaceutical Sciences
ECPS2011

sciforum
e-conferences
www.sciforum.net

Communication

Surface Roughness on Film Coated Extrudates Investigated Using Photometric Imaging

Mette Høg Gaunø [1,2,]*, Niklas Sandler [3], Crilles Casper Larsen[4] and Jukka Rantanen[2]

[1]Pharmaceutical Drug Development, International PharmaScience Center, Ferring Pharmaceuticals A/S, Copenhagen, Denmark
[2]Department of Pharmaceutics and Analytical Chemistry, Faculty of Pharmaceutical Sciences, University of Copenhagen, Denmark
[3]Laboratory of Pharmaceutical Sciences, Åbo Akademi University, Åbo/Turku, Finland
[4]Process Development & Pilot Plant, Ferring International Center SA, St-Prex, Switzerland

E-Mails: mgj@ferring.com (M. G.); niklas.sandler@abo.fi (N. S.); clr@ferring.com (C. L.); jtr@farma.ku.dk (J. R.)

* Author to whom correspondence should be addressed; Tel.: +45 28787160; Fax: +45 28176160 International PharmaScience Center, Ferring Pharmaceuticals A/S, Kay Fiskers Plads 11, DK-2300 Copenhagen S

Received: 19 February 2011 / Accepted: / Published:

Abstract:
The purpose of this study was to investigate the effect of four selected film coating process parameters on extrudate surface roughness measured by a photometric imaging technique. The four process parameters investigated were; coating amount, concentration of polymer in coating solution, spray rate of coating solution and fluidising airflow rate. The film coating was performed in a typical lab system coater equipped with a Wurster insert by using a full factorial design resulting in 16 batches.
The coated extrudates were presented to the photometric imaging instrument in a continuous feed and were imaged through a glass window. Two digital images were taken at each measurement and from the digital image information extrudate surface roughness values were calculated based on change in grey scale values in the surface images. Two roughness values were used to describe the extrudate surface roughness i.e. Ra and Rt. An increased coating amount decreased the Ra roughness and the same effect was observed by increasing the spray rate of coating solution whereas an increased fluidising airflow rate increased the Ra surface roughness. The concentration of ethyl cellulose in the coating solution did not have any effect on Ra roughness whereas an increased concentration decreased the Rt roughness. The suggested approach is a promising tool for evaluating surface roughness of film coated extrudates in a continuous manner.

Keywords: Film coating; extrudate surface roughness; photometric imaging.

---

1. Introduction

Development of controlled multiple release dosages forms requires thorough understanding of the formulation and process parameters as well as robust process control solutions which should be fast and non destructive. Surface roughness has been shown to have an effect on the final quality of the dosage form and various publications has investigated and monitored the surface roughness of film coated tablets (1-3). The surface roughness of film coated tablets has previously been measured by imaging techniques (4, 5) and the aim of this study was therefore to investigate the effect of four selected film coating process parameters on the surface roughness of coated extrudates by a photometric imaging technique.

2. Materials and methods

2.1. Materials

Uncoated extrudates containing 5-aminosalicylic acid (Syntese A/S, Denmark) as active pharmaceutical ingredient and Povidone (ISP, United Kingdom) as binder. Ethyl cellulose (Ethocol standard 45 premium, Colorcon, United Kingdom) was used as film polymer and ethanol (anhydrous 99.9 vol Ph.Eur, Kemetyl, Denmark) as solvent.

2.2. Methods

2.2.1. Experimental design and film coating

On the basis of results from preliminary experiments a complete 2^4 full factorial design was performed resulting in a total of 16 experiments. The following four process parameters were varied on two levels e.g. coating amount (%), concentration of ethyl cellulose in coating solution (w/w %), spray rate of coating solution (g/min) and fluidising airflow rate (m^3/h). The experiments were performed in a randomised order. The film coating experiments was performed in a typical lab system coater (GPCG2 lab system coater, Glatt, Germany) equipped with a Wurster insert. The coating solution was sprayed into the moving extrudates by a two-fluid nozzle (Glatt two component spray nozzle 1-050-00190 X171, Germany).

2.2.2. Measurement of surface roughness

The coated extrudates surface roughness was measured by a FlashSizer 3D (Intelligent Pharmaceutics Ltd, Finland). The photometric stereo imaging technique allows the reconstruction of three-dimensional images of the extrudates surface using two white light sources in illumination (6). The two light sources was placed 180°C from each other in a horizontal plane. The extrudates were presented to the instrument in a continuous feed and were imaged through a glass window and for each measurement two images were taken. Approximately 270 extrudates were measured per one feeding cycle and each batch was measured on average 15 times resulting in measurement of roughly 4000 extrudates per batch. The batches were measured in a randomised order.

2.2.3. Calculation of surface roughness

From the two digital images taken during measurements two matrices of grey scale values are formed and the difference between them is calculated. The grey values correspond to the average transmitted beam from the extrudates surfaces and is characterised by a number in the range from 0 – 255 where 0 is totally black and 255 is completely white. The extrudate surface roughness is then calculated and is based on differences in these grey scale values (6). Different roughness parameters can be calculated based on the digital image information and in this study both the arithmetic average of the roughness profile (Ra) and the maximum roughness height (Rt) has been used to describe the coated extrudate surface roughness. The Ra was calculated by equation 1 and Rt was calculated based on equation 2.

$$\textit{Arithmetic average of the roughness profile, } R_a = \frac{1}{n}\sum_{i=1}^{n}|yi| \qquad \text{Equation (1)}$$

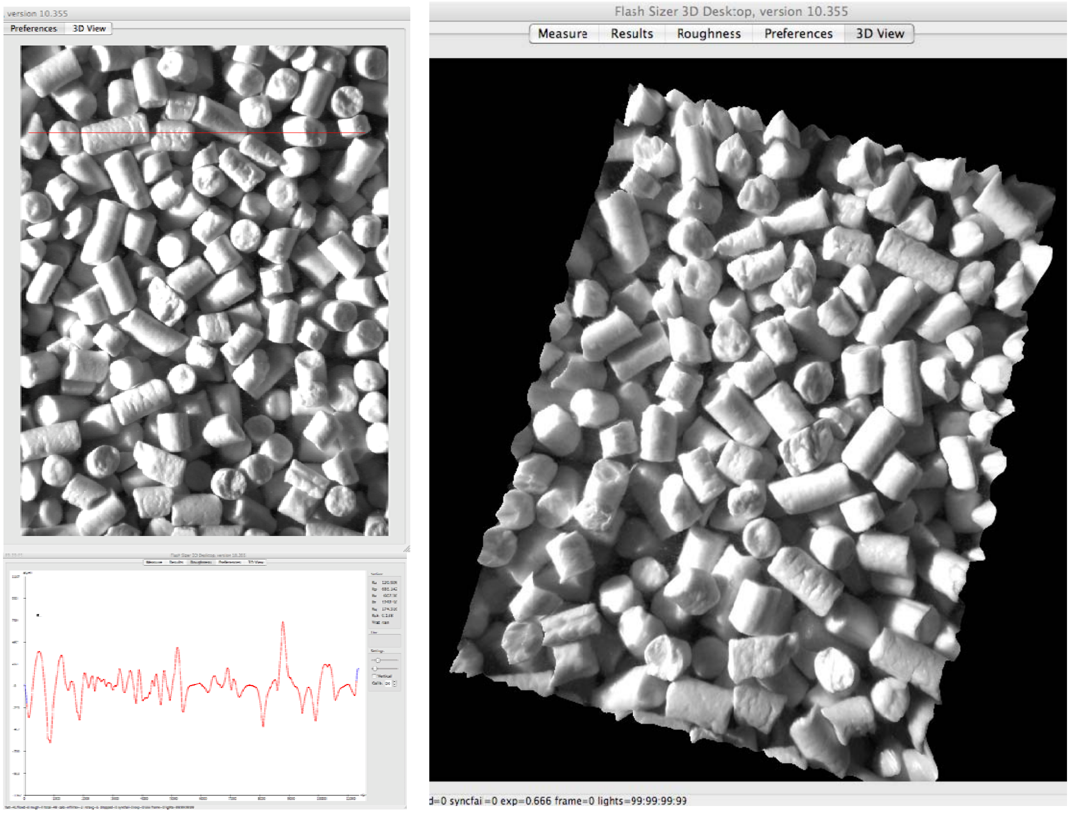
Y_i is calculated as $Y_n - Y^-$ where Y_n is the height value of one measuring point and Y^- is the mean value of all the height data points.

$$\textit{Maximum height of roughness profile, } Rt = (\max_i \times y_i) - (\min_i \times y_i) \qquad \text{Equation (2)}$$

3. Results and discussion

During each measurement digital images were taken and an example of an image can be seen in figure 1. As mentioned earlier the changes in grey scale values were used to calculate the roughness and in the software process window these differences in grey scale values was converted to a roughness profile line, also illustrated in figure 1. All information in the digital image were used which means that also the voids between each extrudates was included in the calculation of the roughness. The packing density is therefore a factor which should be accounted for when using this method for measuring roughness. It is believed that the batches investigated in this study have a comparable packing density and that the effect from difference in density therefore is considered to be small. The packing density can be applied as part of a control system during continuous measuring of roughness where a difference in flow of extrudates would results in difference in measured amount of voids. The two digital images are used for reconstruction of a 3D image of the measured extrudates and an example of this is illustrated in figure 1.

Figure 1. 2D-image (top left) showing a typical roughness profile line (bottom left) and a 3D reconstruction of an image for batch 14



The average Ra and Rt roughness values was calculated for each batch and the results is presented in table 1. The average Ra was in the range from 133 – 153 AU (arbitrary unit based on variations in pixels grey scale values) while the average Rt was in the range from 1761 – 1833 AU.

Table 1. Matrix of the coating factorial design and Ra and Rt results of the study

Experiment No.	Coating amount [%w/w]	Concentration of Ethyl cellulose in ethanol [%w/w]	Spray rate of coating solution [g/min]	Fluidising airflow [m^3/h]	Average Ra [AU]	Average Rt [AU]
1	1.6	1	15	80	149	1817
2	1.6	1	15	120	153	1817
3	1.6	1	25	80	146	1821
4	1.6	1	25	120	150	1812
5	1.6	3	15	80	146	1793
6	1.6	3	15	120	149	1771
7	1.6	3	25	80	147	1761
8	1.6	3	25	120	149	1800
9	3.8	1	15	80	144	1809
10	3.8	1	15	120	149	1804
11	3.8	1	25	80	139	1792
12	3.8	1	25	120	142	1803
13	3.8	3	15	80	141	1788
14	3.8	3	15	120	148	1771
15	3.8	3	25	80	133	1833
16	3.8	3	25	120	145	1781

Analysis of variance (ANOVA) has been used for studying the significance of the process parameters effect on these extrudate surface roughness values. By applying a high ethyl cellulose coating amount the resulting extrudate surface Ra roughness decreases ($p<0.001$). The same effect was observed for spray rate of coating solution where a high spray rate resulted in a decrease in surface Ra roughness ($p<0.01$), whereas increasing fluidising airflow increased the extrudate surface Ra roughness ($p<0.001$). The Ra surface roughness was also effected by the interaction between coating amount and spray rate ($p<0.05$), where the effect of coating amount is largest in combination with a high spray rate. The ethyl cellulose concentration did not significantly effect the Ra roughness value whereas an increased ethyl cellulose concentration decreased the Rt roughness value ($p<0.05$). None of the other film coating parameters significantly affected the Rt values.

4. Conclusions

The investigated roughness variables has shown to be able to detect difference in extrudate surface roughness induced by applying different settings of four selected film coating process parameters. Three of the selected parameters i.e. coating amount, fluidising airflow rate and spray rate had a significantly effect on the Ra roughness while ethyl cellulose concentration had an effect on Rt roughness value. The photometric imaging tool has shown to be a promising tool for evaluating surface roughness of film coated extrudates in a continuous manner.

References

1. Rowe, R.C. The effect of some formulation and process variables on the surface roughness of film coated tablets. *Journal of Pharmacy and Pharmacology* **1978**, *30*, 669-672.
2. Seitavuopio, P.; Rantanen, J.; Heinämäki, J.; Yliruusi, J. Monitoring tablet surface roughness during the film coating process. *AAPS PharmSciTech* **2006**, 7(2), Article 31
3. Rohera, B.D.; Parikh, N.H. Influence of Plasticizer Type and Coat Level on Surelease® Film Properties. *Pharmaceutical Development and Technology* **2002**, *7(4)*, 407-420.
4. Krogars, K.; Antikainen, O.; Heinämäki, J.; Laitinen, N.; Yliruusi, J. Tablet film-coating with amylose-rich maize starch. *European Journal of Pharmaceutical Sciences* **2002**, *17(1-2)*, 23-30.
5. Ruotsalainen, M.; Heinämäki, J.; Guo, H.; Laitinen, N.; Yliruusi, J. A novel technique for imaging film coating defects in the film-core interface and surface of coated tablets. *European Journal of Pharmaceutics and Biopharmaceutics* **2003**, *56(3)*, 381-388.
6. Sandler, N. Photometric imaging in particle size measurement and surface visualization. *International Journal of Pharmaceutics* **2010**, *In Press, Corrected Proof.*