European Journal of Pharmaceutics and Biopharmaceutics xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

European Journal of Pharmaceutics and Biopharmaceutics

journal homepage: www.elsevier.com/locate/ejpb

Research paper

Evaluating the effect of coating equipment on tablet film quality using terahertz pulsed imaging

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ARTICLE INFO

Article history:
Received 7 September 2012
Accepted in revised form 17 March 2013
Available online xxxx

Keywords:
Terahertz pulsed imaging (TPI)
Film coating
Delayed release
Dissolution
Image analysis
Unit operation

ABSTRACT

In this study, terahertz pulsed imaging (TPI) was employed to investigate the effect of the coating equipment (fluid bed and drum coater) on the structure of the applied film coating and subsequent dissolution behaviour. Six tablets from every batch coated with the same delayed release coating formulation under recommended process conditions (provided by the coating polymer supplier) were mapped individually to evaluate the effect of coating device on critical coating characteristics (coating thickness, surface morphology and density). Although the traditional coating quality parameter (weight gain) indicated no differences between both batches, TPI analysis revealed a lower mean coating thickness (CT) for tablets coated in the drum coater compared to fluid bed coated tablets ($p < 0.05$). Moreover, drum coated tablets showed a more pronounced CT variation between the two sides and the centre band of the biconvex tablets, with the CT around the centre band being 22.5% thinner than the top and bottom sides for the drum coated tablets and 12.5% thinner for fluid bed coated tablets. The TPI analysis suggested a denser coating for the drum coated tablets. Dissolution testing confirmed that the film coating density was the drug release governing factor, with faster drug release for tablets coated in the fluid bed coater (98 ± 4% after 6 h) compared to drum coated tablets (72 ± 6% after 6 h). Overall, TPI investigation revealed substantial differences in the applied film coating quality between tablets coated in the two coaters, which in turn correlated with the subsequent dissolution performance.

1. Introduction

Film coating of solid dosage forms in pharmaceutical development and manufacturing is carried out using a range of equipment designs, process parameters and coating formulations to manufacture the desired product. Besides immediate release coatings used for aesthetic reasons or taste masking, film coatings are mostly applied to modify the dissolution behaviour of active pharmaceutical ingredients (APIs) [1]. The purpose of the film coating dictates the quality requirements. In order to meet the requirements of a particular product, it is not only important to choose an appropriate coating polymer formulation [2], but it is also crucial to understand and optimise the complex coating process [3,4].

Currently, a number of coater types are used in pharmaceutical industry, including drum, fluid bed, rotary and continuous coaters. Heat and mass transfer as well as flow pattern of the material between different coater types differ and variation in the film coating quality including coating thickness, coating uniformity and surface morphology can be observed. Hence, changes in the coating equipment may severely affect the final product performance, including the critical quality attribute, drug release (i.e. dissolution), which is of particular importance if different coater types are used for scale-up [5]. Therefore, differences in the coating characteristics as a result of the coating equipment employed need to be identified and eliminated in order to prevent process and product failures.

At present, the end-point of a coating process is usually defined by the amount of coating dispersion applied and the weight gain of the coated dosage forms. However, these measurements provide little information on coating quality parameters such as the coating thickness, uniformity and density and thus render them largely

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http://dx.doi.org/10.1016/j.ejpb.2013.03.019

unsuitable to predict drug release performance. Other monitoring and controlling techniques, including light and scanning electron microscopy (SEM), laser-induced breakdown spectroscopy (LIBS), near infrared (NIR) and Raman spectroscopy are able to access certain aspects of the applied film coating quality but are limited in their ability to determine complex coating structures (e.g. distinction between coating layers within tablets), or the methods are destructive in order to study the coating structure (e.g. microscopy and LIBS) [6–11].

A more recently established non-destructive technique to better understand film coating properties is terahertz pulsed imaging (TPI). Terahertz radiation is part of the far-infrared region of the electromagnetic spectrum (approximately 2–120 cm^{-1}). Most of the well-established polymer formulations used in tablet coatings are transparent or semi-transparent to terahertz radiation [12]. Therefore, a terahertz pulse can penetrate several millimetres into or through a sample (depending on the opacity of the material) [12], and reflections are observed at each interface at which the refractive index (RI) changes. The time delay between the initial pulse (e.g. from the surface of a dosage form) and subsequent reflections provides information about distances between these interfaces and hence coating thickness (CT). Information may also be gained about other physical properties, such as the coating surface roughness and film coating density (by measurement of the terahertz electric field peak strength (TEFPS)) and variation at the coating/core interface (by measurement of the terahertz interface index (TII)). Finally, potential critical areas on coated tablets (e.g. coating defects) can be visualised non-destructively. These advantages of TPI measurements have been the basis for several studies on film coatings applied to tablets [13–19]. The TPI setup allows for rapid image acquisition of samples of different shapes and sizes, and its high measurement precision makes TPI a powerful tool for pharmaceutical tablet coating quality and process control [13]. Recently, TPI was applied as an in-line coating process control method where it was possible to determine CT of individual tablets in real-time during a production scale coating process [20].

In this study, the TPI parameters CT, TEFPS and TII were used for coating quality analysis in order to discriminate between the coating performance under recommended coating conditions in the two most commonly used types of tablet coating devices, the fluid bed and drum coater. Tablets, containing acetylsalicylic acid (ASA) as a model drug, coated with an enteric coating (Eudragit® L30 D-55) under recommended operating conditions were imaged using TPI. The TPI results were validated by scanning electron microscopy (SEM) and correlated to the drug release behaviour of the coated tablets.

2. Materials and methods

2.1. Materials

Acetylsalicylic acid (ASA) (Rhodia Organique, France), microcrystalline cellulose (MCC) (Avicel PH102, FMC BioPolymer, UK), magnesium stearate (Fagron, The Netherlands) and talcum (Fagron, The Netherlands) were used as received. Eudragit® L30 D-55 (Evonik Röhm GmbH, Germany) was redispersed in water and stabilised with sodium hydroxide. The final coating dispersion was prepared according to the recommendations of Evonik [21] for all coating experiments.

2.2. Compression of tablets

ASA was mixed with MCC at a mass ratio of 86:14. The powder blend was then mixed with a 9:1 (w/w) mixture of magnesium stearate and talcum at a 5:95 (w/w) ratio for 3 min at 32 rpm using a Turbula mixer (WAB AG, Germany) and compacted on an instrumented single punch tablet press (Diaf II, Denmark) by using biconvex 9.5 mm tooling. The ASA loaded tablet cores had a mean weight of 350 mg.

Table 1
Recommended coating conditions [21].

Process parameter	Fluid bed (Combi Coata)	Drum coater (Hi-Coater)
Inlet air temperature (°C)	40	74
Product/outlet temperature (°C)	33	34–36
Airflow rate/drum rotation speed	5.5 psi	20 rpm
Spray rate (g/min)	2.7	1.7
Amount of coating formulation applied (g)	61	61

2.3. Coating experiments

2.3.1. Fluid bed coater

A lab scale fluid bed coater (Combi Coata, Model CC1/LAB, Niro Atomizer, Denmark) was used to coat 250 ASA loaded tablet cores (FB-ASA). The coating experiment was carried out under conditions recommended by the coating polymer supplier [21] (Table 1). An inlet air temperature of 40 °C was used and the product temperature (outlet temperature) was 33 °C. Tablets were kept in motion by a constant airflow (monitored with a pressure difference over the orifice of 0.38 bar). The redispersed coating liquid was applied using an atomisation pressure of 1.6 bar; a nozzle with a diameter of 1 mm and a spray rate of 2.7 g/min. The coating process was stopped after the entire amount of coating formulation was used (61 g). The coated tablets were then cured for a 2 h period at 40 °C as recommended [21].

2.3.2. Drum coater

Similar to the coating experiment carried out using the fluid bed device, a lab scale drum coater (Hi-Coater, HCT 20, Lödige Maschinenbau GmbH, Germany) was used to coat 250 ASA tablet cores (DC-ASA). A total of 250 (85 g) tablet cores used for both coating runs, fluid bed and drum coating, were chosen according to the maximum capacity of the drum coater. Besides the tablet weight, the size of the tablets was considered in order to facilitate an optimal filling level of the equipment. The coating process was carried out under recommended operating conditions [21] (Table 1). The inlet air temperature was 74 °C, and the product temperature (outlet temperature) was 35 °C. A pan rotation speed of 20 rpm kept the tablet bed in motion while the coating liquid was applied using an atomisation pressure of 1 bar; a nozzle with a diameter of 1 mm and a spray rate of 1.7 g/min. After the application of 61 g of coating formulation, the coating process was stopped and tablets were cured for 2 h at 40 °C [21].

2.4. Terahertz pulsed imaging measurements

A total of six randomly chosen tablets of every batch were imaged individually using the TPI Imaga2000 (TeraView Ltd., Cambridge, UK). The detailed imaging setup employed in this system was described previously [16]. Terahertz scans were acquired in a point-to-point scan mode with a 150 μm step size in both the *x*- and *y*-directions and a 1 mm optical delay in air in the axial direction (*z*-direction). The average time required for acquisition of the tablet images in this study was 60 min for all surfaces, 21 min per tablet side and 18 min for the centre band. Data analysis was carried out using TPIView imaging software (TeraView Ltd., UK, version 3.0.5). The CT was directly calculated from the time delay between the reflection of the initial signal from the tablet sur-

Please cite this article in press as: M. Haaser et al., Evaluating the effect of coating equipment on tablet film quality using terahertz pulsed imaging, Eur. J. Pharm. Biopharm. (2013), http://dx.doi.org/10.1016/j.ejpb.2013.03.019