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Infrared thermography — A new approach for in-line density measurement of ribbons produced from roll compaction

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ABSTRACT

The ribbon relative density is one of the key quality attributes during roll compaction/dry granulation, as it primarily determines the granule porosity and granule size distribution. In this study, a new approach to measure the ribbon relative density in-line was investigated. A thermographic camera was used to record freshly produced ribbons as they left the gap. In a first step a principal correlation of the measured ribbon temperature and the ribbon density was proven. Furthermore, the cooling rate after compaction was identified as an additional characteristic that can be used to determine the ribbon density. Interestingly the thermographic images also revealed temperature distributions within the ribbon that could be matched with density distributions measured by X-ray micro-computed tomography. In the following, additional characteristics that are equally important for the practical application as an in-line measuring tool were further investigated. The technique showed short reaction times to changes in the process and in a long term experiment no temperature drift over time could be detected. This study demonstrated the applicability of a thermographic camera as an in-line analytical tool for the determination of ribbon relative density.

1. Introduction

1.1. Roll compaction/dry granulation

Roll compaction/dry granulation (RCDG) is the preferred agglomeration technique for APIs that are unstable to heat or hydrolysis. In recent years it has also become one of the most important granulation techniques in general [1]. This new popularity can primarily be assigned to the fact that roll compaction/dry granulation is a highly energy efficient process, as no heating or drying is needed [1,2]. As energy costs are increasing, many companies try to avoid energy expensive drying steps and hence focus on dry granulation. The rise in significance can be illustrated with recent proposals for a manufacturing classification system, in which dry granulation is considered to be the granulation technique of choice, while all wet granulation techniques are secondary [3]. Furthermore, RCDG is a continuous process and as continuous manufacturing moves into a focus area of interest, continuous processing techniques do so, too.

Roll compaction/dry granulation is a quite simple process. Powders are compressed between counter-rotating rolls and subsequently milled down to granules. Commercially available roll compactors use force feeding systems, in which a tamping auger forces powder between the rolls. To avoid leakage of non-compacted powder, two types of sealing systems can be used: a side-plate assembly ("cheek plates") and rimmed rolls [4]. More detailed descriptions of the process and roll compactors can be found in other literature and will not be further discussed here [2,5].

In terms of further processing, the most critical quality attributes of dry granules are granule porosity and granule size distribution [6,7]. Both are predominantly determined by the ribbon porosity, which makes it the most important quality attribute during roll compaction [2,8]. Furthermore, it is easily accessible than the granule porosity, which additionally increases the significance of this characteristic number. Following the Quality by Design concept and especially for the use in continuous manufacturing it is highly desirable to measure the ribbon porosity in-line.

1.2. Density distribution in ribbons

It has been described in literature many times that porosity is not distributed homogeneously over the ribbon. The porosity in the center differs from the one near the edges. How the porosity is distributed across the width depends primarily on the sealing system used during production [9–12]. Most authors in this field do not describe the

Abbreviations: API, active pharmaceutical ingredient; RCGD, roll compaction/dry granulation; NIR, near infrared; XμCT, X-ray micro-computed tomography; SCF, specific compaction force; FFT, fast Fourier transform; rpm, revolutions per minute; PAT, process analytical technology.

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distribution of ribbon porosity, but use the complementary quantity, the relative density or solid fraction (= 1 – porosity). Hence, the term relative density will be used in this paper.

When using cheek plates, it was shown that the relative density is the highest in the center of the ribbon, while it decreases near the edges [9,13–15]. Furthermore it was found that the region of the highest density follows a periodical pattern in form of a sinusoidal curve along the ribbon length [5,13,16]. This phenomenon is usually explained as a result of the rotating tamping auger, which is thought to cause one sinusoidal period by every rotation [13]. For ribbons produced with rim rolls, descriptions of the density distributions are rare. Wöll described that the density is distributed more homogeneously than in cheek plate ribbons, with higher density near the edges and a lower one in the center [12]. Along the ribbon length the density is described to fluctuate in a periodical pattern. Unlike in cheek plate ribbons, the region of the highest density does not follow a sinusoidal curve, but is constantly high on the edges with periodically appearing circular regions of lower density in the center [17].

1.3. Methods to determine ribbon density

1.3.1. Overall ribbon density

The ribbon density is usually determined using classical pycnometry techniques. Mercury pycnometry is the most used technique in this field and commonly accepted as a reference method [6,16]. An alternative method based on the same principle is powder pycnometry [18,19]. In this case, free flowing silica powder instead of hazardous mercury is used to envelope the sample. A simple method to approach the ribbon density is the oil absorption technique [20,21]. The ribbons are weighed, placed in a Petri dish containing liquid paraffin and weighed again afterwards. All three techniques have the disadvantage that closed pores, voids, and cracks, which oftentimes appear in laminating ribbons, cannot be detected and thus the density is underestimated. Also they naturally cannot be applied in-line.

In recent years more complex techniques have been used to study the ribbon density. NIR spectroscopy [19,22] as well as NIR chemical imaging [21,23]. Both have the advantage that the technique does not only provide information on the relative density, but also on the chemical composition. The most important advantage of both techniques is their applicability as an in-line tool. Both have been implemented in experimental production lines of roll compaction/dry granulation and tablet compression [20,21]. Terahertz spectroscopy [24,25] and ultrasonic imaging [10] are further imaging techniques that have been applied to determine ribbon densities in-line.

1.3.2. Density distribution

Several approaches to measure the density distribution within ribbons have been described in literature. The simplest technique is to break the ribbon into pieces and to determine the relative density of each piece (sectioning method) [14,15]. An alternative approach that has been described by several authors is to use the surface hardness as a surrogate for the relative density [9,12]. The surface hardness can easily be determined at several positions on the ribbon and allows density mapping in higher resolution. More precise determinations of the density distribution in even higher spatial resolutions were conducted in the last years, using X-ray micro-computed tomography [15,17], NIR chemical imaging [23], terahertz spectroscopy [24,25], and ultrasonic imaging [10]. Even though some of these techniques have measurement times short enough to allow real time imaging, none of it has been used to determine ribbon density distributions in-line. Furthermore all of the techniques require highly expensive equipment that is usually also too large to be easily implemented into a roll compactor. A more detailed overview of the listed techniques was given elsewhere and will not be repeated here [17].

1.3.3. X-ray micro-computed tomography

X-ray micro-computed tomography (XμCT) is a non-destructive high resolution 3D imaging technique. X-ray images are obtained from multiple angles and the data is subsequently reconstructed to a three dimensional image. The absorption of X-rays in materials depends (among other quantities) on the elementary composition and the material density [26]. Hence, this technique is suitable to detect density distributions within porous compacts. In recent years, XμCT has been used more and more in the field of pharmaceutical sciences. Since two excellent overviews on its pharmaceutical applications have been published by Hancock and Mullarney [27] and Zeitler and Gladden [28], the technique will not be described in further detail here.

1.3.4. Infrared thermography

Infrared radiation is electromagnetic radiation of wavelength between 0.78 μm and 1000 μm [29]. It is emitted from the surface of every object whose temperature is above 0 K [30]. The intensity and the wavelength of the emitted radiation depend on the surface temperature. Consequently, the surface temperature can be derived from the infrared radiation. For the majority of thermographic applications, the bandwidth between 7.5 and 13 μm is used [31].

The calculations of the temperature are classically based on the assumption of an ideal black body, i.e. all radiation leaving the object originates from emission (emissivity = 1). Real objects have emissivity values below 1. The radiation leaving the object is the sum of emission (ε), reflection (ρ), and transmission (τ) (see Eq. (1)) [30].

$$\varepsilon + \rho + \tau = 1 \tag{1}$$

Obviously, ribbons are no ideal black bodies. However, the assumption can be made that no infrared radiation transmits through the ribbon. Hence, the infra-red radiation detected by the camera consists of emitted and reflected radiation. To measure precise temperatures, the emissivity of the object has to be taken into account. If no value is known, the measured absolute temperatures will be biased. The measurement of relative temperature changes however, is still valid.

Infrared thermography has been used in several fields of pharmaceutical sciences, for example to investigate thermic stress during tablet compression or drying [32–37]. In 2015 Omar et al. applied a thermographic camera to roll compaction. They produced ribbons from several types of lactose and determined the surface temperature to investigate the inner friction of the materials during compaction [38]. The same group also used the camera in a study regarding determination of the nip angle [39].

1.4. Objectives

The aim of this study was to test the suitability of a thermographic camera as an in-line analytical tool for the determination of ribbon density. Furthermore the ability of this technique to detect density distributions within the ribbon should be investigated and the practical applicability checked.

2. Materials and methods

2.1. Preparation of ribbons

2.1.1. General

Microcrystalline cellulose (MCC) (Vivapur 102, JRS Pharma, D) was roll compacted on a Gerteis Minipactor (Gerteis Maschinen und Prozessengineering AG, CH) at five different specific compaction forces (2, 3, 4, 5, 7 $kN*cm^{-1}$). Smooth rolls (diameter: 250 mm, width: 25 mm) were used, the gap was automatically controlled at 2.0 mm and the roll speed was set to 2 rpm. These experiments were conducted once with cheek plates and once with rim rolls. The experiments were conducted under controlled climate conditions of 21° C and 45 % humidity.

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