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Measurement of surface color as an expedient QC method for the detection of deviations in tablet hardness

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Abstract

The objective of this study was to investigate whether a correlation exists between the surface color of tablets and their tensile strength. Theophylline powder blends with and without red dye were directly compressed into 600 mg tablets. Applied compression pressure ranged from 9.3 to 271.2 MPa. Colorimetric parameters: lightness (L^*), chromaticity (a^*, b^*), chroma (Cab), hue (hab) and color intensity (CI), were measured and recorded for both sides of each tablet using ColorQuest XE colorimeter in reflectance specular included mode. The tensile strength of the tablets was measured using a TA.XTPlus Texture Analyzer. A linear correlation was observed between the chroma (Cab) parameter and the tensile strength for each formulation of the tablets. For white tablets, the linearity was observed between Cab values ranging from 2.6 to 3.76 and tensile strength values ranging from 2.96 to 6.86 MPa. For red tablets, the linearity was observed between a chroma range from 21.76 to 30.75 and tensile strength from 2.51 to 6.52 MPa. A similar correlation was observed between the CI of red tablets and tensile strength. It was concluded that chroma could be used as suitable QC parameters to detect deviations in tablet hardness during bulk manufacturing.

Keywords: Color; Hardness; Tristimulus colorimetry; CIE $L^*a^*b^*$; Chroma; Hue

1. Introduction

Tablet hardness is an important quality control (QC) parameter that is usually measured during bulk tablet manufacturing. The role of hardness in disintegration and dissolution is well documented (Kitazawa et al., 1975). The current practice for its determination includes contact testing, either manual or automated. The major implications of the current method of hardness testing are delayed batch-release and labor-intensiveness, which may add expenditure to the manufacturing process. As a result, the Food and Drug Administration (FDA) introduced the process analytical technology (PAT) initiative, which is revolutionizing the manufacturing scenario by shifting attention from off-line to on-line testing and predictable variation in the processing parameters. FDA's document titled "Guidance for Industry: A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance" defined PAT as "a system for designing, analyzing and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring product quality" (FDA, 2003; Cogdill et al., 2005). In view of in-process measurement required by PAT, near infrared spectroscopy (NIR) was proposed and used for on-line determination of hardness. This non-destructive and non-invasive technique eliminated some of the errors encountered by the traditional hardness testing instruments, such as incorrectly indicating the true applied load and inconsistency in use between the operators (Morisseau and Rhodes, 1997). It also reduced the number of personnel involved and expedited the measurement of large number of tablets, which allowed for optimal statistical analysis and pattern-recognition.

In the NIR technique, two modes of detection are used to determine hardness, diffuse reflectance and diffuse transmission. Similar to the NIR technique, tristimulus method of color detection utilizes reflectance and transmittance mode and falls under the purview of PAT definition as a quality control variable. Therefore, tristimulus colorimetry could theoretically be used as an alternate and less expensive method to NIR for the

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on-line measurement of hardness, and more precisely, as a quality control tool for the detection of deviations in tablet hardness by observing subtle changes in the colorimetric parameter measured from the surface of the tablets.

Conventionally, color has been used as a marker of aesthetics, identification and stability in diverse fields. Its historic applications in paints, textile, plastic, food and pharmaceutical industries are well known (Bogdansky, 1975). For example Wie and Bitgood (1990) distinguished egg shells on the basis of color intensity. Chromaticity, a colorimetric parameter, has been used by Arias et al. (2000) to evaluate the lycopene content as well as to establish a relationship between color and the different stages of tomato development. In the pharmaceutical industry, color has traditionally been used as an index of tablet stability and in tablet color matching (Bogdansky, 1975). The determination of discoloration kinetics of tablets due to poor storage conditions or interaction amongst its different ingredients has been documented by Berberich et al. (2002). Of particular relevance is a study by Benavente et al. (2003), which demonstrated that gloss and polish of stones can affect surface coloration. In this study both qualities, gloss and polish, were correlated to surface roughness. It was suggested that surface topography affect color measurement by influencing the angle by which light is reflected from surfaces (Kim et al., 2003). This conclusion is further corroborated by a study in which a change in color measurement and reflectance was attributed to the roughness of split-core surfaces (Blum, 1997). In view of these studies on color, which is ubiquitous in almost all tablet ingredients, we hypothesized that a change in compression pressure and thereby tensile strength may cause a change in the surface characteristics of tablets. This, in turn, may influence the different colorimetric parameters measured from the surface of the tablet. Therefore, the objective of this work was to investigate whether a correlation could be established between tensile strength and tristimulus colorimetric parameters measured from the surface of uncoated flat-faced tablets.

2. Materials and methods

2.1. Materials

Theophylline anhydrous powder (grade 200M) was obtained from BASF (Mount olive NJ). Microcrystalline cellulose (MCC), grades Avicel® PH-101 and Avicel® PH-200 was supplied by FMC BioPolymer (Newark, DE). Magnesium stearate was provided by Amresco Inc. (Solon, OH). Talc was purchased from Spectrum Chemicals (Gardena, CA). D&C Red 30 Alum Lake was obtained from Sensient Technologies Corp. (Milwaukee, WI). All items were used as supplied without further modification.

2.2. Tablet preparation

Four powder blends, two with D&C Red 30 lake and two without, were prepared using two grades of microcrystalline cellulose (Avicel® PH-101 and PH-102). The composition of the four powder formulations is given in Table 1. Initially, theophylline anhydrous and magnesium stearate were passed through sieve no. 40 (0.425 mm) and 80 (0.180 mm), respectively. For each formulation, accurately weighed powders, with the exception of magnesium stearate, were transferred into a container and mixed with the aid of a Turbula blender type T2A (Chemical and Pharmaceutical Industries Co., New York, NY) at a rate of 72 rpm for 5 min. Magnesium stearate was then added to the powder blend and mixed for an additional 2 min. The same mixing procedure was used for each of the four formulations listed in Table 1. Tablets from each formulation were prepared by compressing 600 mg of the powder blend between the platen of a Carver press Model C (Carver Inc., Wabash IN) using 12.7 mm flat-faced punches. Tablets were prepared at nine different compression forces: 125, 250, 500, 1000, 1500, 2000, 2500, 3000 and 3500 kg force to provide an effective pressure range from 9.3 to 271.2 MPa. The diameter and thickness of each tablet was measured by a Fowler® electronic vernier caliper (Fred V. Fowler Co., Newton, MA). The relative solid fraction of each tablet at various compression pressures was calculated from its dimensions relative to the dimensions of the tablets that were prepared at maximum compression pressure.

Table 1
Formulation composition of the four tablet sets evaluated in this study

Ingredient (mg/per tablet)	White tablets		Color tablets	
	W101	W200	R101	R200
Theophylline	100	100	100	100
MCC Avicel® 101	467	0	466	0
MCC Avicel® 200	0	467	0	466
Magnesium stearate	1.2	1.2	1.2	1.2
Talc	1.8	1.8	1.8	1.8
Sodium starch glycolate	30	30	30	30
D&C Red 30 Alum Lake	0.0	0.0	1.0	1.0

2.3. Tensile strength

The diametric hardness of the tablets was determined from the force–distance profile obtained by a TA.XTPlus Texture Analyzer (Texture Technologies Corp., Scarsdale, NY/Stable Micro Systems, Godalming, Surrey, UK) fitted with a 1″ acrylic probe and a 50 kg load cell. Pressure was applied at a rate of 0.7 mm/s. A representative force–displacement profile of the compacts is given in Fig. 1. The tensile strength of the tablets was calculated by the following equation:

$$\mathrm{TS} = \frac{2\mathrm{CS}}{\pi \times D \times E}$$

where CS is the crushing strength (hardness), D the diameter, and E is the thickness of the tablet. All experiments were performed in triplicates.

2.4. Tristimulus colorimetry

2.4.1. Theory of color measurement

Color is a property of light of particular wavelength which is reflected or transmitted when falling onto opaque or transparent objects, respectively. At the atomic level, it is produced by changes in the electromagnetic energy in the electron orbital