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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

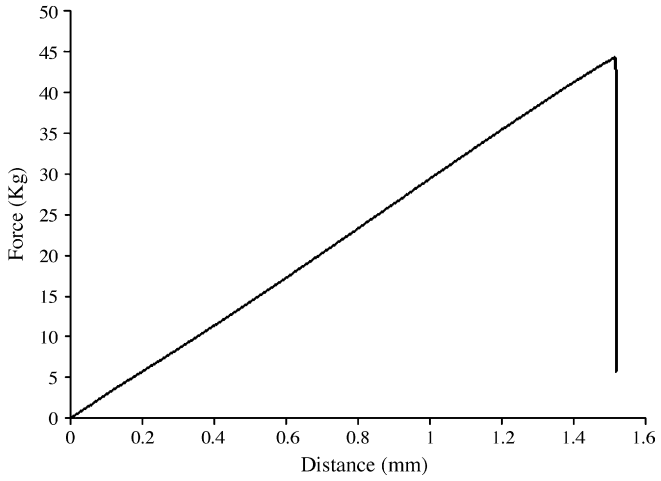

Fig. 1. A representative force–displacement profile of the compacts obtained from the TA.XTPlus Texture Analyzer.

due to photon absorption (Blum, 1997). In human eyes, the triple receptor systems in the retinal cone cell can perceive different color combinations that befall in the visible region of the electromagnetic spectrum (400–700 nm). Although subjective color perception is possible, it is not without limitations. Reproducibility of color description by the same individual is inconsistent and subtle color difference may not be exactly judged (Bogdansky, 1975). Therefore, subjective color measurement is not a viable option for qualitative and quantitative color description. As a result, color model and quantitative methods for color measurement were developed.

Color model is an abstract mathematical model designed to precisely describe different colors either in the form of numbers or color components. Color components or set of colors are called the color space (Fig. 2). The human color space is a horseshoe shaped cone, which extends from the origin to infinity. The outer rim of this space is occupied by the saturated (pure hue) colors. Saturation of color is determined by the amount of grey. If the amount of grey is more, the color would be less saturated. On the other hand, the lesser amount of grey, the color would be more saturated. Pure color has the least amount of grey. In other words, it can be generalized that saturation increases as one move from the centre of color space (grey)

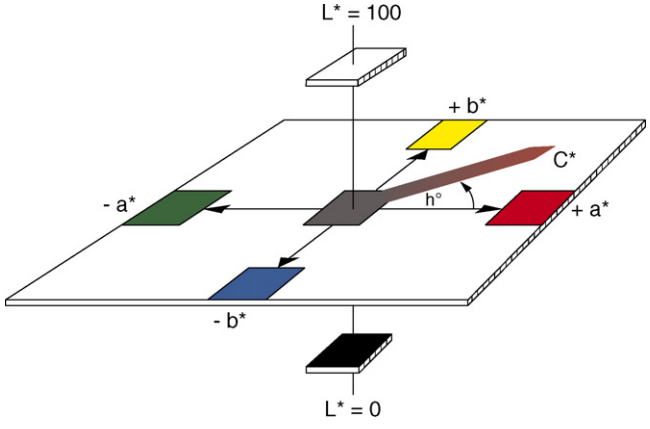

Fig. 2. CIE $L^*a^*b^*$ color space (courtesy of BYK Gardner, Columbia, MD).

towards extremes in X- and Y-direction of space. The centre of this cone is occupied by lightness extremes, such as white and black. The basic colors, such as red, green and blue or a combination of two basic colors, such as yellow green is called hue. Hue is also described by the average or strongest/dominant wavelength in the light spectrum irrespective of the range of wavelength present in the stimulus. Quantitatively color could be measured either by a spectrophotometer or a colorimeter. The colorimetric method of color measurement is used to quantify and physically describe human color perception (Ohno, 2000). This technique was developed by CIE (commission Internationale del'Eclairge/international commission on illumination) in 1931 based on the results of the visual experiments conducted individually by Wright and Gulild (Ohno, 2000), which were intended to improvise a color matching function. In these studies, red, green and blue (RGB) primaries were used to estimate the color matching function$\{\bar{r}(\lambda)\bar{g}(\lambda)b(\lambda)\}$, which was subsequently transformed to a new set of primaries called XYZ (Ohno, 2000). *XYZ* coordinates depict the specific location of the color in the Cartesian coordinate space (Berberich et al., 2002) and could be estimated by the following correlations:

$$X = K\int_{\lambda}\phi(\lambda)\bar{x}(\lambda)\,\mathrm{d}\lambda$$

$$Y = K\int_{\lambda}\phi(\lambda)\bar{y}(\lambda)\,\mathrm{d}\lambda$$

$$Z = K\int_{\lambda}\phi(\lambda)\bar{z}(\lambda)\,\mathrm{d}\lambda$$

where K is normalization constant and $\phi(\lambda)$ is the spectral distribution of light stimulus. The measurement of these integrated values of light stimuli to specify a color is called tristimulus colorimetry. *XYZ* coordinates can also be expressed by different inter-convertible scales, such as the CIE $L^*a^*b^*$ scale, which was employed in this study. These conversions can be expressed as follow: if (X/X_n), (Y/Y_n), $(Z/Z_n) > 0.008856$, then:

$$L^* = 116\left(\frac{Y}{Y_n}\right)^{1/3} - 16,$$

$$a^* = 500\left[\left(\frac{X}{X_n}\right)^{1/3} - \left(\frac{Y}{Y_n}\right)^{1/3}\right], \quad \text{and}$$

$$b^* = 200\left[\left(\frac{Y}{Y_n}\right)^{1/3} - \left(\frac{Z}{Z_n}\right)^{1/3}\right]$$

if (X/X_n), (Y/Y_n), $(Z/Z_n) < 0.008856$, then:

$$L^* = 903.29\left(\frac{Y}{Y_n}\right),$$

$$a* = 500\left\{7.787\left[\left(\frac{X}{X_n}\right) + \frac{16}{116}\right] - 7.787\left[\left(\frac{Y}{Y_n}\right) + \frac{16}{116}\right]\right\},$$

and

$$b^* = 200\left\{7.787\left[\left(\frac{Y}{Y_n}\right) + \frac{16}{116}\right] - 7.787\left[\left(\frac{Z}{Z_n}\right) + \frac{16}{116}\right]\right\}$$

where X, Y and Z are tristimulus values and X_n, Y_n and Z_n are tristimulus values for a perfect reflecting diffuser (white).

L^*, a^* and b^* values occupy the Z, X and Y plane in the CIE three-dimensional uniform color space, respectively (Fig. 2). The Z plane whose color ranges from white to black through grey is represented by L^* value. This value shows the lightness of an object. Color can be separated into bright and dark colors when their lightness is compared. Lightness is a perceptual response through which white objects are distinguished from grey objects and light objects from dark color objects (HunterLab manual, 2002). It is also a proportion of brightness of a colored surface with respect to the brightness of an area perceived as white. The relative sensation of the emitted or reflected light from a colored surface is called brightness. The different vertices of three-dimensional color space have different values to describe the color of an object. L^* has a maximum value of 100, which represents a perfect reflecting diffuser (white) and a minimum of zero, which represents black (a perfect absorber or non-reflecting object). The a^* and b^* values bear positive and negative signs to describe dark colored objects. Positive and negative a^* values depicts red and green whereas those for b^* values signify yellow and blue, respectively. Utilizing the L^*, a^* and b^* values, the color of an object can be specified by three parameters—chroma, hue and color intensity. Chroma (Cab), which expresses the degree of color for an area viewed in relation to its brightness, could be mathematically estimated from the following equation:

$$\text{Cab} = \sqrt{(a^2 + b^2)}$$

While chroma represents the location of a point in a two-dimensional planes, the exact direction of the locus of this point from the central grey is represented by hue angle (hab), which is mathematically expressed as:

$$\text{hab} = \text{Arc tan}\frac{b^*}{a^*}$$

The difference in color (ΔEab) between any two points in the color space can be obtained from the following correlation:

$$\Delta\text{Eab} = \sqrt{\Delta L^{2*} + \Delta a^{2*} + \Delta b^{2*}}$$

The difference in color between a point and a central axis in the Lab color space (100, 0, 0); however, is termed CI or color intensity (Berberich et al., 2002). Therefore, color intensity could be estimated from the following equation:

$$\text{CI} = \sqrt{(100 - L^*)^2 + a^{2*} + b^{2*}}$$

2.4.2. Method of color measurement

Three tablets at each compression pressure were prepared. After standardization of the instrument, the color of both surfaces of each tablet was recorded using a HunterLab ColorQuest XE tristimulus colorimeter (Hunter Associates Laboratory Inc., Reston, VA). Measurements were made in reflectance specular included mode (RSIN) with a 10° observer and a D_{65} illuminant. The reflectance included mode measures total light reflectance, i.e., both diffuse and specular reflectance. The specular portion is that portion of light that produces gloss whose angle of incidence is equal to the angle of reflection. From the recorded data, the Hunter scale coordinates L^*, a^* and b^* were obtained and were used to calculate different colorimetric parameters as described above. In each study the reported color data is the average of six measurements obtained from both faces of each of the three tablets, unless otherwise specified.

3. Results and discussion

3.1. Tensile strength

Four sets of flat uncoated tablets were prepared at different compression pressure, as described in the methods section. These sets differ in the grade of incorporated MCC (Avicel® 101 and Avicel® 200) and the presence or absence of D&C Red 30 dye. The formulation composition of the four tablet sets is given in Table 1. The average tensile strength of the tablets at different compression pressure is given in Fig. 3. As shown in the figures, the tensile strength of the tablets increased with an increase in compression pressure up to 155 MPa after which it reached a plateau. It is well documented that an increase in compression pressure increases the solid fraction of the pow-

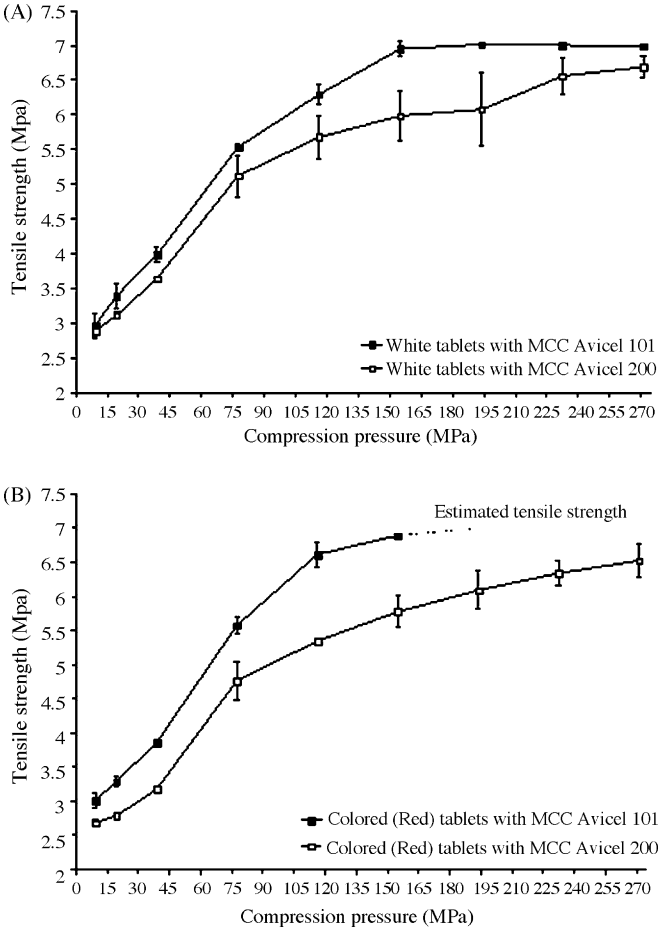

Fig. 3. Correlation between tensile strength and compression force for white (A) and colored/red (B) tablets.

Table 2
Primary color parameters (Lab) measured for white tablets

Compression pressure (MPa)	L^*		a^*		b*		Solid fraction[a]
	Average	S.D.	Average	S.D.	Average	S.D.	
W101 (Avicel® 101)							
9.3	93.570	0.031	0.544	0.016	3.070	0.022	0.873
19.4	93.640	0.013	0.548	0.013	3.135	0.021	0.893
38.7	93.720	0.027	0.557	0.014	3.232	0.039	0.909
77.4	93.800	0.034	0.582	0.012	3.533	0.034	0.962
116.2	94.090	0.126	0.600	0.018	3.795	0.069	0.979
155	94.530	0.062	0.598	0.019	3.947	0.074	0.991
193.7	95.090	0.063	0.600	0.009	3.973	0.031	1.000
232.4	95.270	0.054	0.607	0.010	4.032	0.018	0.999
271.1	95.410	0.049	0.597	0.015	4.038	0.013	1.000
W200 (Avicel® 200)							
9.3	96.088	0.057	0.528	0.074	2.713	0.052	0.873
19.4	97.953	0.281	0.619	0.056	2.779	0.044	0.893
38.7	97.155	0.075	0.458	0.010	2.928	0.122	0.909
77.4	96.490	0.109	0.473	0.020	3.257	0.116	0.962
116.2	96.218	0.060	0.478	0.012	3.452	0.074	0.978
155	96.813	0.098	0.583	0.044	3.520	0.055	0.991
193.7	95.920	0.068	0.488	0.010	3.607	0.103	1.000
232.4	95.858	0.090	0.487	0.014	3.622	0.160	0.999
271.1	94.432	0.178	0.517	0.048	3.733	0.070	1.000

[a]Solid fraction relative to the tablets compressed at 271.1 MPa.

der, decreases its porosity, and results in stronger inter-particular bonds (Olsson and Nystrom, 2001). Increase in tensile strength was more prominent in tablets incorporating MCC Avicel® 101. MCC Avicel® 101 particles are rod shaped with an average particle size of 50 μm, whereas MCC Avicel® 200 particles are larger and globular with an average size of 180 μm. The smaller particle size of Avicel® 101 allows the powder to pack more efficiently and provides larger surface area for inter-particulate bonding, which explains the higher values for tensile strength (Nazzal et al., 2002). No significant difference in tensile strength was observed between the white (W) and red (R) tablets incorporating the identical Avicel® type since the addition of minute quantities of dye is not expected to influence the compaction behavior of the powder blends. In general, the tensile strength of the four tablet sets, at different compression pressure, ranged from 2.7 to 7.0 MPa.

Table 3
Primary color parameters (Lab) measured for colored/red tablets

Compression pressure (MPa)	L^*		a^*		b^*		Solid fraction[a]
	Average	S.D.	Average	S.D.	Average	S.D.	
R101 (Avicel® 101)							
9.3	81.011	0.937	21.760	1.372	−0.108	1.372	0.878
19.4	80.218	0.377	22.645	0.804	−0.125	0.087	0.895
38.7	79.636	0.788	23.082	1.084	−0.138	0.067	0.912
77.4	78.536	1.174	26.441	1.500	−0.095	0.094	0.976
116.2	75.182	1.343	27.900	2.014	−0.062	0.100	0.993
155	74.500	0.974	28.215	1.4135	0.002	0.155	1.000
193.7	73.278	2.106	29.298	2.477	0.097	0.228	1.000
232.4	74.924	0.833	30.035	1.175	−0.008	0.073	1.000
271.1	74.142	0.970	30.753	1.331	0.105	0.099	1.000
R200 (Avicel® 200)							
9.3	83.793	0.293	16.277	0.373	0.850	0.074	0.868
19.4	83.583	0.093	16.663	0.165	0.813	0.088	0.885
38.7	82.578	0.237	17.757	0.324	0.745	0.075	0.902
77.4	80.253	0.301	19.893	0.382	0.690	0.041	0.965
116.2	78.428	0.203	21.595	0.272	0.677	0.039	0.982
155	76.982	0.366	22.888	0.408	0.658	0.038	0.989
193.7	76.613	0.210	23.178	0.287	0.638	0.028	0.995
232.4	75.923	0.256	23.950	0.347	0.578	0.037	0.995
271.1	75.338	0.332	24.580	0.399	0.572	0.016	1.000

[a]Solid fraction relative to the tablets compressed at 271.1 MPa.

3.2. Tristimulus colorimetry

The L^*, a^*, b^* values for both sides of each tablet were recorded and further used to calculate other color descriptive parameters; mainly chroma, hue and color intensity. The average L^*, a^*, b^* color data are summarized in Tables 2 and 3 for white and red tablets, respectively. These data were used as the initial step to establish the utility of the colorimetric method in this study. As given in the tables, average L^* values for white tablets were higher than their red counterpart. The average L^* values were 94.3 and 96.3, for W101 and W200, respectively, and 79.3 and 76.8, for R101 and R200, respectively. The effect of Avicel® type on L^* was insignificant ($P > 0.10$). Observed L^* data are in agreement with the general theory of color measurement whereby white tablets should have greater lightness and least a^* and b^* values in the color space in comparison to the red tablets. The a^* values, which represent the degree of redness within the color space, were insignificant and approximated zero for white tablets. For red tablets a^* values increased with an increase in compression pressure from 21.76 to 30.75 and from 16.27 to 24.58 for R101 and R200 tablets, respectively. Since Avicel® 101 particles are smaller in size with a larger overall surface area than the Avicel® 200 particles, the red dye added to the formulation is expected to spread more evenly on the surface of the smaller particles with lesser amount entrapped in the voids between the particles, which explains the higher a^* values observed with tablets prepared with MCC Avicel® 101. Increase in compression pressure forces the dye out of the voids and onto the surface of the tablet, which increases the intensity of surface coloration and thereby increases the observed a^* values. Higher a^* values could also be the result of an increase in solid fraction of the compacts with increasing compression pressure. The increase in solid fraction (also a decrease in voids or porosity) results in a relative increase in dye concentration since the same weight of dye would occupy a smaller volume of powder. The b^* value of red tablets was overshadowed by the redness of the surface and therefore approximated zero. b^* values; however, increased with an increase in compression pressure for white tablets. This increase indicates a slight shift in color from white to yellow. This might be due to the increase in solid fraction of the compact and a decrease in the number of voids with compression. This in turn increases the concentration of Avicel® particles in a lower volume and results in a yellow appearance of the compacts. The recorded b^* values for white tablets were in the range from 2.7 to 3.13 for the W200 tablets and from 3.07 to 4.03 for the W101 tablets. Out of these L^*, a^* and b^* values Cab, hab and color intensity (CI) data were derived as described above.

3.3. Derived colorimetric parameters

3.3.1. Chroma (Cab)

Cab values were calculated as given in the introduction section. For the four tablet sets, Cab increased with an increase in compression pressure. The correlation between Cab and compression pressure is graphically represented in Fig. 4. For W101 and W200, Cab increased from 3.11 to 4.08 and from 2.76 to 3.76, respectively. For R101 and R200 tablets, Cab increased

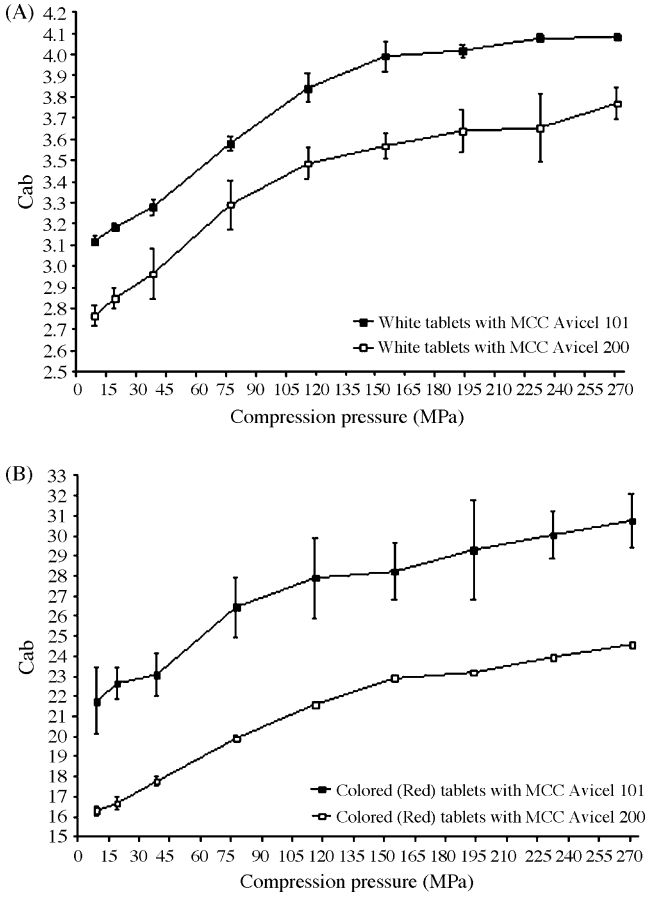

Fig. 4. Correlation between chroma (Cab) and compression force for white (A) and colored/red (B) tablets.

from 21.76 to 30.75 and from 16.29 to 24.58, respectively. Changes in Cab values with a change in compression pressure and the differences observed in Cab between the tablets prepared from different MCC grades is easily explained by the fact that Cab values are mathematically derived from a^* and b^* parameters discussed above, with a^* primarily contributing to the change in Cab values for red tablets and b^* primarily contributing to the change in Cab values for white tablets. This observation supports the broader claim that Cab could be used as a universal QC parameter when color is used as a measure of tablet hardness. The observed increase in Cab values with an increase in compression pressure could also be explained on the basis that an increase in compression pressure results in smoother and denser surfaces, assuming that compression pressure does not induce deformities on the surface of the tablets. With increased compression pressure, the increased smoothness or decreased asperities on the surface of the tablets, as observed by the increase in solid fraction, increases the specular component of the reflected light. The specular portion is that portion of light whose angle of incidence is equal to the angle of reflection. Since the color was measured in reflectance specular include mode (RSIN) an increase in the specular component of the light leads to an increase in the perceived chroma (Cab) values (Benavente et al., 2003). Higher Cab values observed for the tablets prepared with Avicel® 101 suggests they have smoother

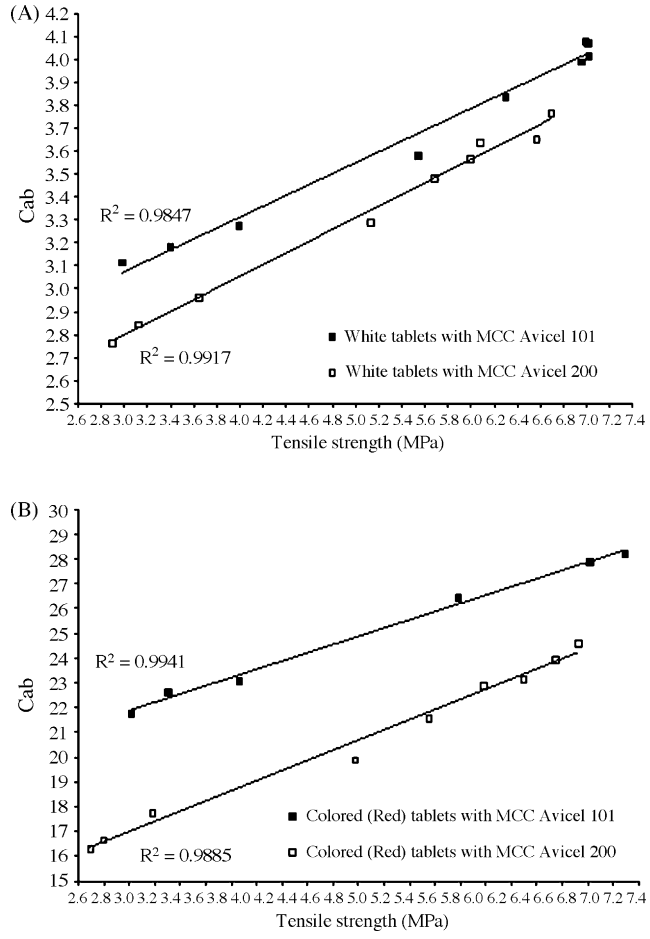

Fig. 5. Correlation between chroma (Cab) and tensile strength for white (A) and colored/red (B) tablets.

surfaces than those prepared with Avicel® 200. This conclusion is supported by a study in which surface roughness of tablets was measured as a function of the Avicel® grade used as a filler (Nazzal et al., 2002). In this study, a stylus profilometer was used to measure the Ps roughness parameter, which is a measure of the distance between grooves primarily caused by granules of variable sizes. It was observed that the Ps values increased with an increase in MCC particle size suggesting an increase in surface roughness (Nazzal et al., 2002).

After observing the pattern in color data, Cab values were correlated with the tensile strength data. The correlation between tensile strength and Cab values is graphically represented in Fig. 5. The Cab values increased with an increase in tensile strength, irrespective of tablet color or the grade of MCC used. This trend was observed uniformly for all four tablet sets. Linear regression analyses were performed on the data. For simplicity, regression coefficients (R^2) values, which reflect the linearity of the correlation, are given in Fig. 5. The linear correlation between Cab and tensile strength suggest that chroma could be used as a measure of hardness. Cab is an attractive parameter because it only considers the degree of color saturation omitting the brightness of the compact. Color; however, is also a function of tablet composition as evident by the different Cab values for the different MCC grades. Therefore, the tensile strength of an unknown tablet cannot be estimated unless a calibration curve is established between Cab and tensile strength for the given tablet formulation. Cab value is therefore more useful as a non-destructive QC measure of a deviation in tablet hardness from preset hardness specifications.

3.3.2. Hue angle (hab)

Hue angle indicates the location of a particular point in a two-dimensional (*X–Y*) color space. This two-dimensional space, also called chromaticity, is represented by a^* and b^*, whereby a^* represents the color scale from green (−value) to red (+value) while b^* represents the color scale from blue (−value) to yellow (+value). The hue angles for the white tablets were higher than the red tablets. The value for the angle obtained for W101 and W200 tablets ranged from 79.9 to 81.5 and from 76.9 to 82.1, respectively. Hue angle values for R101 and R200 tablets ranged from 2.98 to 1.33 and from (−) 0.281 to 0.190, respectively. The narrow hue angle observed for the red tablets indicates that the color is located very close to the *X*-axis, which represents the red color. No significant differences were observed in the hue angle values within each tablet category, i.e., between white tablets prepared with Avicel® 100 and 200, and between colored tablets prepared with Avicel® 101 and 200.

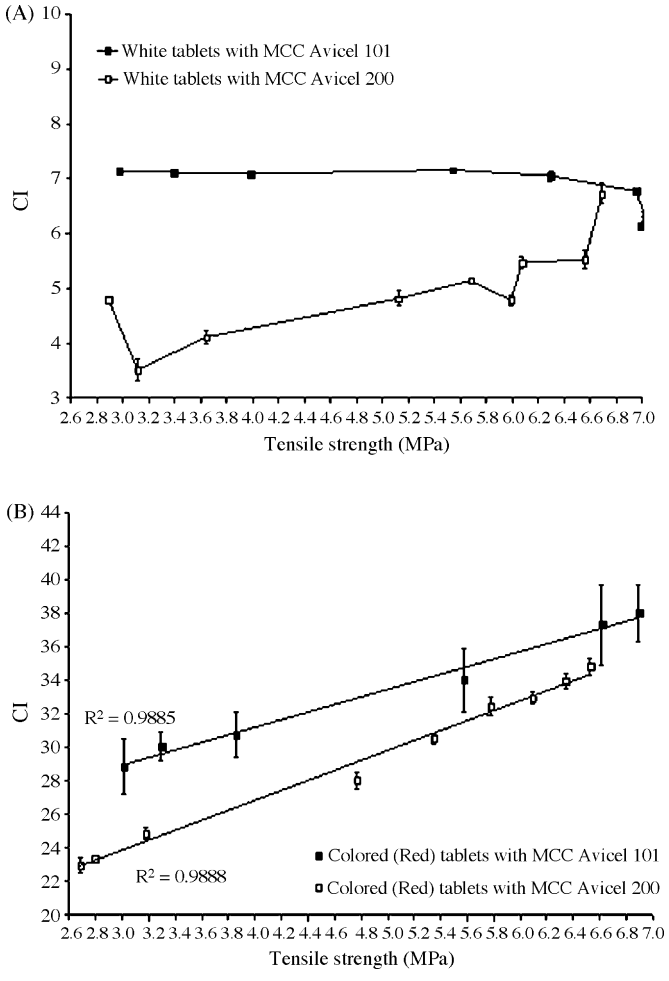

Fig. 6. Correlation between color intensity (CI) and tensile strength for white (A) and colored/red (B) tablets.

3.3.3. Color intensity (CI)

Color intensity is a colorimetric parameter which describes the relative location of a point in the color space from the absolute white (100, 0, 0). CI was calculated as given in the introduction section. For W101 and W200, CI values varied from 7.1 to 6.1 and from 4.8 to 6.7, respectively. For R101 and R200 tablets, CI increased from 28.9 to 40.2 and from 23.0 to 34.8, respectively. CI values were correlated with the tensile strength data. This correlation is graphically represented in Fig. 6. Unlike chroma, there was no correlation between CI values and the tensile strength of the white tablets. A linear correlation as reflected by the regression coefficient (R^2) values however was only observed between tensile strength and CI of red tablets, irrespective of the MCC grade used. This is due to the fact that red tablets have a higher contribution of the a^* value to the measured chroma and color intensity. This explains the similarity in the observed correlation between Cab or CI values with tensile strength. White tablets; however, have low chroma and high lightness values. Therefore, the color intensity of white tablets is mostly a measure of their lightness. Absence of a correlation between CI and tensile strength for white tablets implies that lightness is a poor QC parameter and should not be considered appropriate when handling samples with low chromaticity.

4. Conclusion

Data presented in this study demonstrated that colorimetric parameters, such as chroma, and color intensity, offer sensitive and non-destructive means to monitor and potentially control changes in the mechanical properties of tablets during manufacture. The colorimetric parameters were shown to be capable of detecting changes in the tensile strength and hardness of the tablet with changing compaction pressure and hence solid fraction. Furthermore, the colorimetric parameters were sensitive to differences in the particle size between excipient grades of the component powders within the compacted tablet. Of the two parameters, chroma appears capable of application to a broader range of tablet types than color intensity since the former parameter was linearly correlated with changes in tensile strength for both red and white tablets while the latter parameter only correlated linearly with red tablets. The presence or absence of talc and other light reflective ingredients, as well as the influence of picking, sticking, capping or lamination on the surface characteristics and color properties of tablets was not considered in this study. Colorimetric based control of tablet properties will require that a calibration curve is established for each drug product. However, it is reasonable to conclude that tristimulus colorimetry can provide a convenient, low cost, sensitive, on-line quality control tool for the rapid detection of changes in tablet hardness during manufacture.

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