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USE OF RAMAN MICROSCOPY AS TOOL TO EVALUATE IMPACT OF POLYMER BLENDS USED ON SURFACE ROUGHNESS OF FILM-COATED TABLETS

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ABSTRACT

This study was focused on understanding impact of different polymers and their blends in Film Coating formula on Surface characteristic of coated tablets. Surface roughness of tablet coated with polymer bends were successfully measured using Raman microscopy equipped with Atomic Force Microscopy and laser light to guide the microscope through an optical fiber (WITec alpha 300RA+). In this study, various analytical tools (correlogram analysis, multivariant analysis and one-way ANOVA test) were used to assess statistical similarity between tablets coated with two different polymer blends in optimized composition (PVA: PVA-PEG and HPMC: PVA-PEG samples). Data generated with optical profilometry was used to understand the formulation variables (type and concentration of polymer blends, pigment versus non-pigmented formulation and influence of talc) and impact of these variables on surface roughness. Based on analysis, results provided an evidence that, HPMC: PVA-PEG polymer blend performed better and gave most robust results compared to another blend.

KEYWORDS: Polyvinyl Alcohol, PVA-PEG graft copolymer, Hypromellose, Raman microscopy, Atomic force microscopy, Optical profilometer.

INTRODUCTION

Film coating is a process that has been utilized in the pharmaceutical industry for over half a century, however, it remains a complex process in which all technical issues (appearance attributes) and their impact is not always fully appreciated. Although, the appearance attributes of a film coated tablet such as colour, film opacity and gloss have no therapeutic

advantages, however, it has psychological importance especially in securing patient co-operation in taking the medicine. In addition, gloss of film-coated tablets has been connected to dissolution rate, permeability, surface roughness and stability of the product on storage (Allan et al., 1995; Podczeck, 1998; Eber, 1986; Parikh, 2002).

Many of technical problems can occur, therefore, with the increased use of film coating there has been an increased awareness of need for a fundamental understanding of the various film defects seen on coated tablets. Film coating defects can generally be divided into two groups; the first includes defects like picking (isolated areas of film pulled away from surface), blistering (film becomes locally detached forming a blister) and orange peel (film rough and non-glossy surface like skin of orange), can usually be overcome by optimizing the coating process conditions, whereas the second, includes defects like cracking (film cracking across the crown of the tablet), splitting (film splits usually around the edges of the tablet) and bridging (film pulls out of intagliation forming a bridge across the mark), usually requires a more fundamental approach which may involve reformulation of the tablet core or film coating formulation (Rowe,1992). Although, there are various proactive approaches that have been taken for optimization of film coating formulation (Forse and Rowe, 1980; Forse and Rowe, 1981) and fundamental analysis of film coating operation (Khinast et al, 2010; Muliadi and Sojke, 2009; Aulton et al, 1991) to troubleshoot and make defects free film coating application for oral solid dosage forms is of utmost significance.

Gloss can be defined as that attribute of a surface that causes it to have a shiny or lustrous appearance and it is used for the description of coated tablet. In physical terms gloss can be ascribed to the specular reflection of light by the surface and it is this property that is measured to assess gloss (Rowe, 1985). It has been observed that for film coated tablets, the measured gloss can be correlated to its inherent surface roughness measurement (Rowe, 1985). Therefore, in the present work it was decided to use surface roughness measurement as a direct measure of gloss. Surface measurement was monitored visually as well as using analytical tool.

Various analytical tools have been reported for surface characterization of core and coated tablets such as laser profilometer (Brown et al, 1999), near-infrared spectroscopy (Drennen and Kirsch, 1995; Andersson et al, 1999; Larena et al, 2002), optical scanning profilometer (Bhatia et al, 2017), scanning electron microscopy (SEM) and energy dispersive X-ray (EDX) (Belu et al, 2002; Byrne and Deasy, 2002; Hussain et al, 1988). Raman spectroscopy

and near infrared spectroscopy reported to be used in detection of active pharmaceutical ingredients in tablet formulation (Rowe, 1985; Dgardin et al, 2010) Ideally, these and other spectroscopic methods give information about the material properties of tablet but not about the surface roughness. When a probe wave with optical wave lengths are used one can consider surface roughness as a source of noise, which is usually manifested in cases where coherent laser radiation is utilized.

In the present work optical profilometry or surface microscopy of film-coated tablets was performed with a Raman microscopy equipped with Atomic Force Microscopy and laser light to guide the microscope through an optical fiber (WITec alpha 300RA+). The objective of present work is to unravel the impact of variables and understand the interplay between coating formulation and type of polymer blend. This study focuses on measuring the surface roughness of coated tablets in which coating formulation were prepared from varying the concentration of polymer blend with different proportions of additives.

MATERIALS AND METHODS

Materials

The polymers and plasticizers used in this study are Poly vinyl alcohol (PVA; Manufacturer: Nippon Gohsei (Gohsenol GL-05FS), Lot No.: 64M52T, Viscosity: 5.3 cP), Polyvinyl alcohol - Polyethylene glycol graft copolymer (PVA-PEG; Manufacturer: BASF (Kollicoat IR), Lot No.: 38230468E0, Viscosity: 120 cP), Hydroxypropyl methylcellulose (HPMC 6cP; Manufacturer: DOW [Methocel E6 Premium LV], Lot No.: D011G4CL02, Viscosity: 5.9 cP for 2% aqueous solution), Triethyl citrate (TEC; Manufacturer: Vertellus, Lot No: 0000157958). Additives used in this study are Titanium dioxide (TiO_2) (Manufacturer: Brentag Specialties, Lot No: 0001161), talc (Manufacturer: Luzenac, Lot No: S.180/18) and FD&C Blue #2 Lake (Indigo Carmine) (Manufacturer: Colorcon, Lot No: WP781738:AX8281). Partially pregelatinized starch (Starch 1500) (Manufacturer: Colorcon, Lot No: IN532309), Cab-o-Sil (Manufacturer: Cabot, Lot No: GAR486516), Magnesium stearate (Manufacturer: Akcros, Lot No: GAR487248).

Compression of Placebo Tablets

The tablets were prepared by compressing a standard placebo blend, consisting of lactose monohydrate (69%), Cellulose powder (15%), Starch 1500 (15%), Magnesium stearate (0.5%) and Aerosil 200 (0.5%), using 20 station tablet press (Cadmach, CU-20, Ahmedabad) fitted with 10.1 mm plain, round, standard concave tablet tooling. Tablets were manufactured

by direct compression method at target weight of 360mg/tablet and having hardness of 9 to 11 kP.

Preparation of Coating Formulation Systems

In this study polymer blend of PVA: PVA-PEG (90:0) and HPMC 6Cp: PVA-PEG (90:10) was selected. Coating formulation systems (pigmented and non-pigmented) were prepared by mixing in domestic blender at 90:10 ratio polymer blend followed by addition of additives at different ratios (Polymer: diluent ratio; 20:80, 30:70, 40:60, 50:50, 60:40, 70:30, 80:20 and 90:10 ratio respectively) TiO_2, FD&C Blue# 2 Lake, Talc and plasticizer (Triethyl Citrate), as given in below Table 1.

Coating of Compressed Tablets

Placebo tablets were coated with coating formulation (T1 to T16 as depicted in Table) at 3% weight gain. The coating dispersion (20% solids in purified water) was prepared by slowly adding coating formulation to the water under stirring into the vertex. Continued the stirring for 45 minutes Total 16 batches were coated, and each coating batch comprised 0.3 kg of placebo tablet cores. Coating was performed using 8.5" pan of O'Hara LCM 5 side-vented coater with Schlick ABC 970 gun equipped with 0.8 mm nozzle. For each coating, process parameters were adjusted as follows: atomization and pattern air pressure of 1.5 bar, rotating speed of pan 10-15 rpm, bed temperature 44-47 ° C, gun to bed distance 6 cm and spray rate of 3-4 g/min. After being sprayed, tablets were dried for 5 minutes at 40 ° C in the coating pan.

Surface Roughness Measurement

The instrument used in this study was a Raman microscopy- WITec alpha 300RA+ (WITec GmbH, UIm, Germany). This instrument incorporates the features of the Raman microscopy system alpha300 R for powerful chemical imaging along with Atomic Force Microscopy (alpha300 A) for high-resolution nanoscale surface characterization. This instrument works based on Raman effect i.e. inelastic scattering of excitation light by the molecules of gaseous, liquid or solid materials. The interaction of a molecule with photons causes vibrations of its chemical bonds, leading to specific energy shifts in the scattered light that can be identified in its Raman spectrum. In this instrument, the laser light is guided to the microscope through an optical fiber. Further it can be focused to a diffraction-limited spot and therefore acts as a point light source. This light is focused onto the sample using a dichroic beam splitter that reflects the exciting laser beam but is fully transparent for the frequency-shifted Raman light.

The Raman scattered light is collected with the same objective and is focused into the core of another optical fiber that is connected to a spectrometer. The light is dispersed inside the spectrometer and the spectra are acquired with an ultra-sensitive, back-illuminated CCD camera. Further topographic confocal Raman imaging was applied to measure the surface characteristics of tablet (core and coated).

The Tablet samples were placed on glass slide which was fixed using double sided tape. The full tablet images were acquired using 10x (digital image size 13000 x 13000 µm) while using 20x true surface objective the image size was 4000 x 4000 µm. The surface profilometric images were collected using 20x true surface objective. The image size and position of collection of images were fixed which was 400 x 2000 µm acquired from center of the tablet. The sensor probe can resolve an elevation difference of 3 mm with a step size of 120 nm along the z-axis. ~400 x 2000 µm tablet surface was irradiated and was rasterized at a step size of 5 x 5 µm along the x and y-axis using an integration time of 0.05 s with 1 scan accumulations. Post-scan analysis was conducted using the image statistics dialog as a part of the operating software (WITec Project Plus 5.0) to give the common roughness parameters. In this study, the surface roughness amplitude values, Sa, (arithmetic mean height) were used as a measure of contact surface roughness. In this study statistical analytical tool (correlogram analysis, multivariant analysis and anova test) was used based on data generated with optical profilometer to understand the formulation variables (type and concentration of polymer blends, pigment versus non-pigmented formulation and influence of talc) and its impact on surface roughness.

RESULTS

Novel coating Formulation

Novel coating formulations prepared with polymer blend (PVA: PVA-PEG; 90:10 and HPMC 6cP: PVA-PEG; 90:10) have a significant impact on fundamental mechanical properties of film. Further presence of plasticizer and other additives in the coating formulation enhance flexibility, lower the Tg, minimize the formation of cracks or defects and improve the aesthetic appearance of the final product.

Visual Observation of Coated Tablets

In present work, all coatings were performed using distinct types of coating formulations (T1 to T16) with similar type of coating process parameters and similar type of core tablets, therefore, defects observed on coated tablets are mainly related to either coating formulation

or coating process parameters. Figure 1, visual observation of coated tablets indicated that, for PVA: PVA-PEG polymer blend, the coating formulations T1, T2 and T3 prepared with lower concentration of PVA 18%, 27% and 36% respectively, the coated tablets have smooth surface without any defects. However, in case of other coating formulations i.e. T4, T5, T6, T7 and T8 having comparatively higher concentration of PVA (45%, 54%, 63%, 72% and 81% respectively), coated tablets showed roughness, non-glossy film appearance. In all pigmented formulation (T1 to T6) the quantity of FD&C Blue #2 was fixed whereas TiO_2 quantity was varied, which resulted in shade of coated tablets changes from darker blue to lighter blue as the quantity of TiO_2 decreases in the coating formulation. In case of T7 and T8 (non-pigmented formulation), FD&C Blue #2 and TiO_2 was not added, therefore, coated tablets had white to off-white appearance as initial core tablets is white in color.

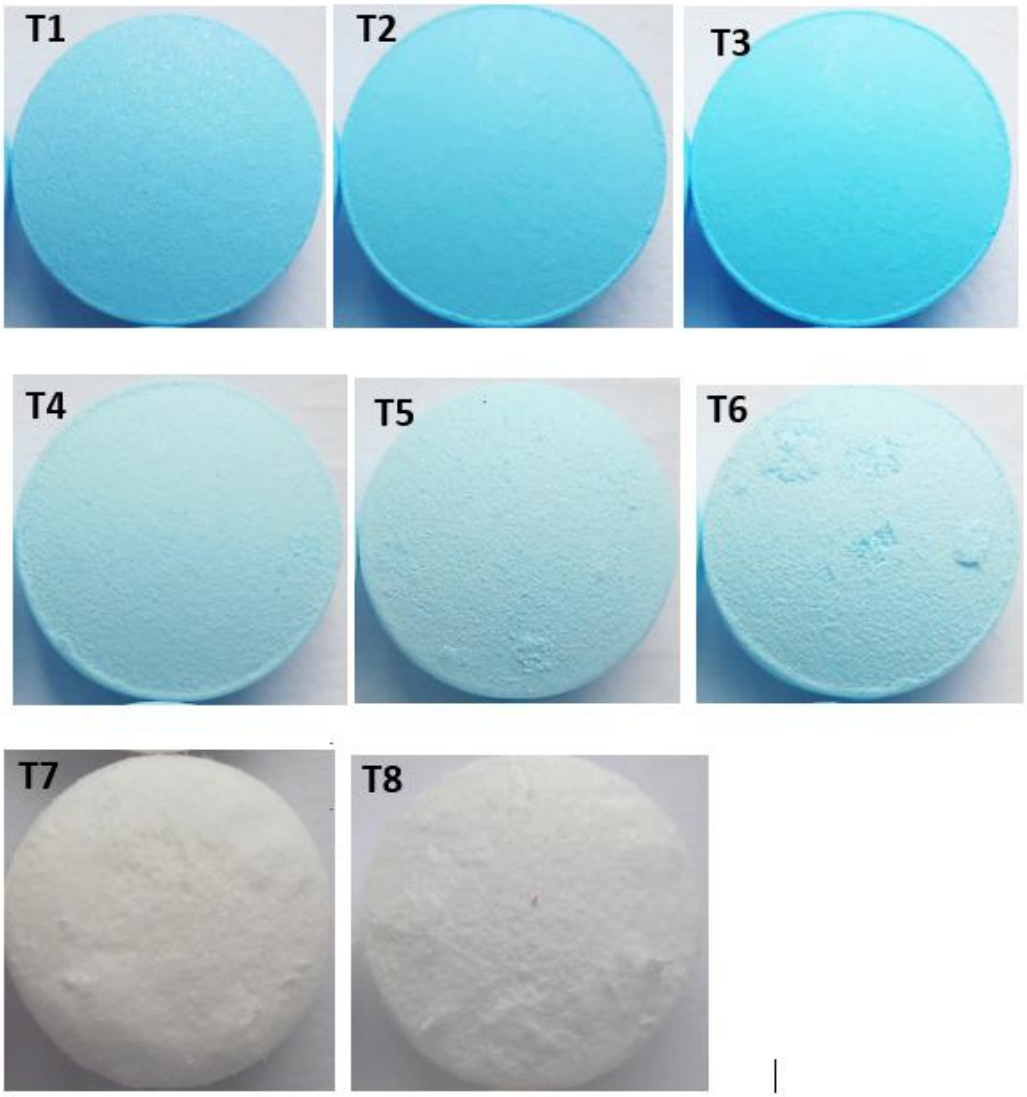

Figure 1: Photographs of coated tablets (T1 to T8).

In case of HPMC based polymer blends (HPMC 6cP: PVA-PEG; ratio 90:10) and corresponding their coating formulation systems (T9 to T16) both pigmented and non-pigmented showed coated tablets have overall smooth surface, however, in case of T12 to T16, coated tablets have slight roughness (Figure 2).

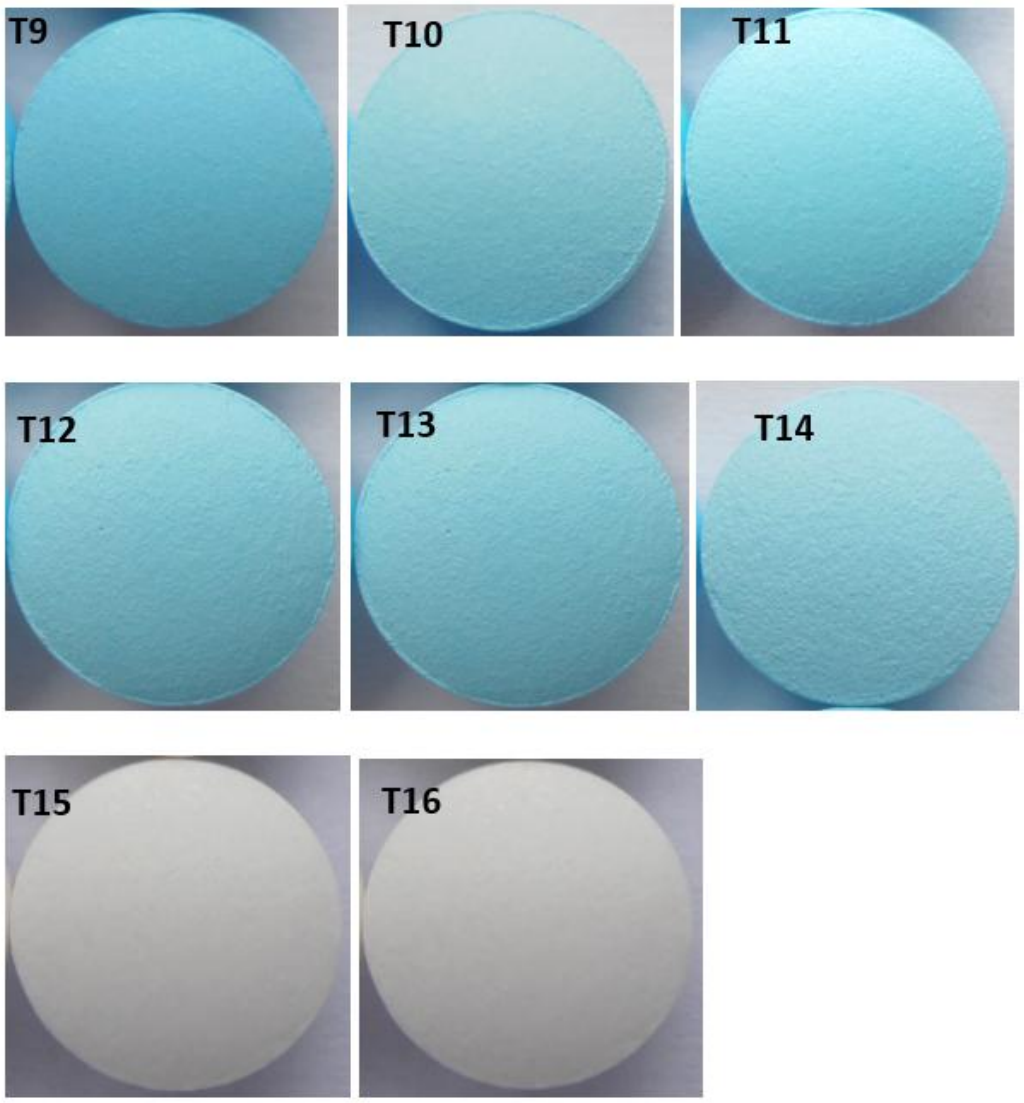

Figure 2: Photographs of coated tablets (T9 to T16).

Optical Profilometry

Surface roughness measurement was performed for tablets coated with T1 to T16 (pigmented and non-pigmented formulation) with optical profilometer to compare the tablet coating components and subsequent its impact on roughness value. Figure 3 showed microscopic images at different micron levels under optical profilometer for tablets coated with T1 and T9. Figure 4 showed comparison of surface roughness amplitude values, Sa (arithmetic mean

height) for HPMC versus PVA polymer blends. Bivariate analysis was found to showed significant differences between samples that contained opacifier as well as pigment versus samples that did not contain TiO_2 and colorant. This is in-line with visual observation of coated tablets, PVA based polymer blend showed comparatively higher surface roughness values and these values increases with increase in concentration of PVA and decrease in concentration of talc in coating formulation (T4, T5, T6, T7, T8 and T8). However, for HPMC based polymer blend showed lower value in surface roughness irrespective of concentration of polymer and talc present in coating formulation. Slightly higher roughness value was observed with T15 and T16 containing higher concentration of HPMC + PVA-PEG (80% and 90% respectively).

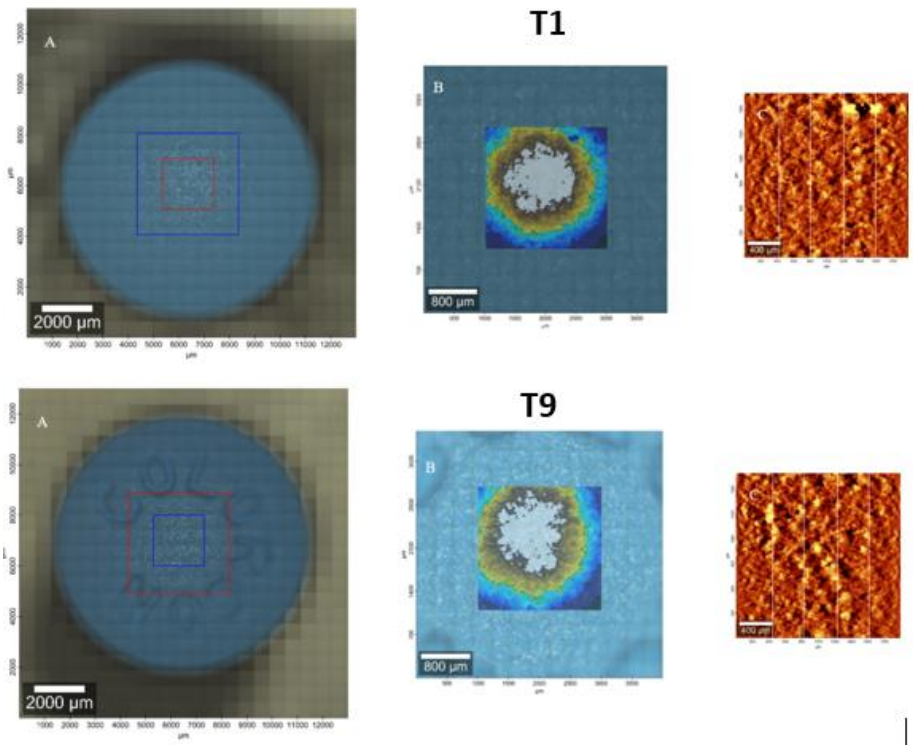

Figure 3: Microscopic images of tablets (T1 and T9) under optical profilometer.

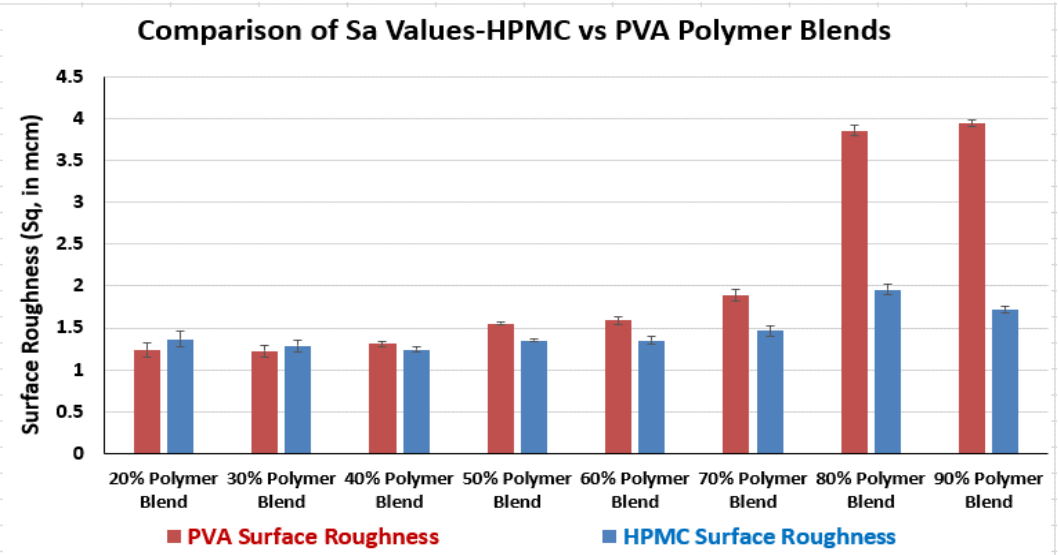

Figure 4: comparison of Sa values for HPMC versus PVA polymer blends.

Statistical analysis

Box plot: From the boxplot (Figure 5), it is inferred that the spread of the PVA based polymer coating has a wide range of surface value results. Presence or absence of additives in coating formulation was found to immensely influence the PVA polymer than the HPMC based polymer blend.

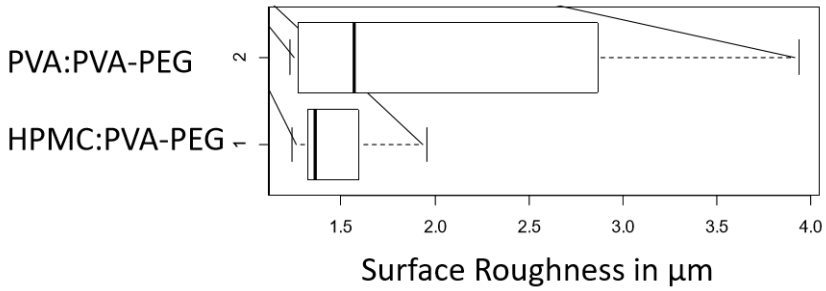

Figure 5: Boxplot for comparison of PVA versus HPMC.

Multi-plot analysis, Correlogram analysis: Figure 6, multi-plot analysis of formulation variables (type and concentration of polymer blends, pigment versus non-pigmented formulation and influence of other additives talc, TEC) versus Sa values indicated that, indicates that there are more than one factor contributing to the surface roughness. Correlogram analysis (Figure 7) was performed to highlight the most correlated variables. Correlation matrix was reordered according to the degree of association between the variables. Correlation coefficient values range from "-1" to "0" to "+1". The values close to "-1" is highly correlated negatively whereas values close to "+1" is correlated positively. On

the other hand, values close to "0" are not correlated or does not influence the variables. The distribution of each variable is shown on the diagonal. On the bottom of the diagonal: the bivariate scatter plots with a fitted line are displayed. On the top of the diagonal: the value of the correlation plus the significance level as stars (*). Each significance level is associated to a symbol: p values (0, 0.001,0.01, 0.05, 0.1) <=> symbols ("***", "**", "*", ".").

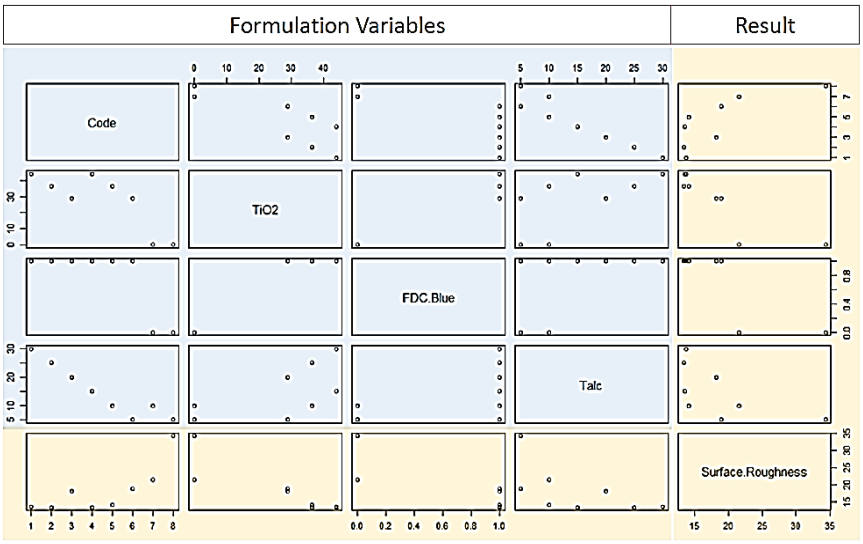

Figure 6: Multi-plot analysis, formulation variables versus Sa.

Correlogram analysis demonstrated that, surface roughness is positively correlated to polymer to additive ratio whereas it is negatively correlated to titanium dioxide, colorant, as well as talc concentration. Both polymers (PVA and HPMC) and surface roughness are less influenced by the presence TEC. PVA polymer blend formulation are more positively correlated to surface roughness as compared to that observed with HPMC polymer blend. From this analysis, multicollinearity between the variables exist, therefore, multivariate data analysis was performed like Principal Component Analysis (PCA).

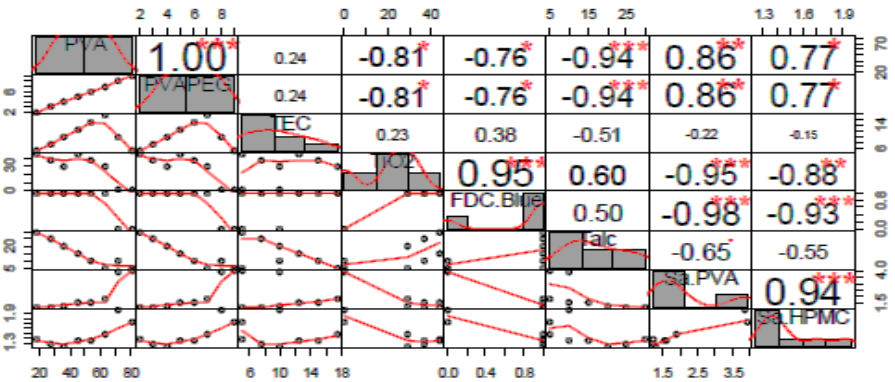

Figure 7: Correlation between variables and measurements (Sa).

Principal Component Analysis: PCA was carried out which reduces the dimensionality of a set of variables (y data structure) while retaining the maximum variability in terms of the variance covariance structure where the x, y dataset transformed to a new set of coordinate systems which is lesser in dimension than the number of original variables.

Multivariate data analysis of PVA polymer blend using PCA provides majorly 4 plots as shown in Figure 8 A-D. Plot of scores (Figure 8 A) for the first two principal components with 95 confidence indicating, no data point lies outside this ellipse. There is clear pattern in the data, i.e., the roughness increases as the polymer to additive concentration as well as polymer to additive composition changes. Three groups based on surface roughness is obtained i.e. 1 75 µm, 1 75 2 5 µm and 2 5 µm. Figure 8 B shows the correlation loadings plot for; group 1 (independent variables) for FDC Blue and TiO_2, group 2 (independent variables) for talc and group 3 (dependent variable) for surface roughness or measurement response, group 4 (independent variable) for polymer (PVA polymer blend) and group 5 (independent variable) for TEC. Summary described with respect to the group 3 i.e. dependent variable which is surface roughness. This is indicating that, polymer and roughness parameters are positively correlated such that increase in polymer composition will increase Sa and vice versa. Polymer, colorant, TiO_2 and talc are negatively correlated, that is there presence reduces the roughness as well higher the concentration lowers the roughness. TEC is close to mid-point line indicating its presence or absence will not influence roughness value. Figure 8 C, since data points are within the red point region, it means there are no noise or outliers similar to results from Figure 8 A. The plot 8 D is used to ascertain how many components are required to interpret the influence of formulation variables on the surface roughness and the results indicate two PC's are enough as plateau reached and any more inclusion leads to over fitting the model, in summary, two to three PC's explain 98 variability in the data.

Similar PCA was performed for HPMC polymer blend samples (Figure 9 A-D). Plot of scores (Figure 9 A) for the first two principal components with 95 confidence indicating, no data point lies outside this ellipse. Figure 9 B shows the correlation loadings plot for the first two principal components which is similar to observed with 8 B plot. Figure 9 C, since data points are within the red point region, it means there are no noise or outliers similar to results from Figure 8 A. The plot 9 D is used to ascertain how many components are required to interpret the influence of formulation variables on the surface roughness and the results

indicate three PC's are enough as plateau reached and any more inclusion leads to over fitting the model, in summary, two to three PC's explain 98 variability in the data. In comparison to the PVA polymer blend plot, only the directions have changed otherwise the patterns both in scores and loading are the same.

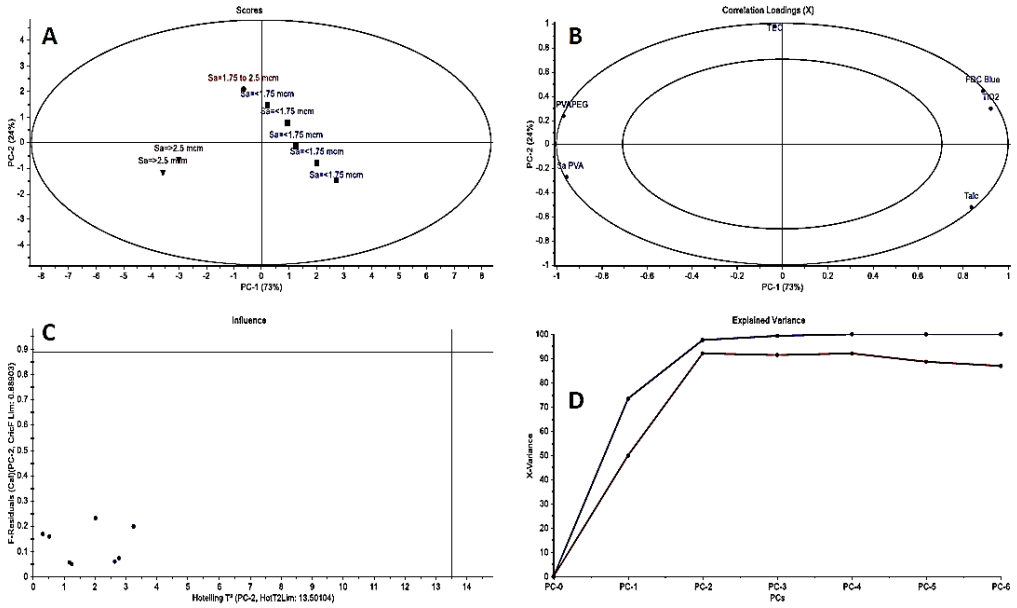

Figure 8: PCA for PVA polymer blend samples.

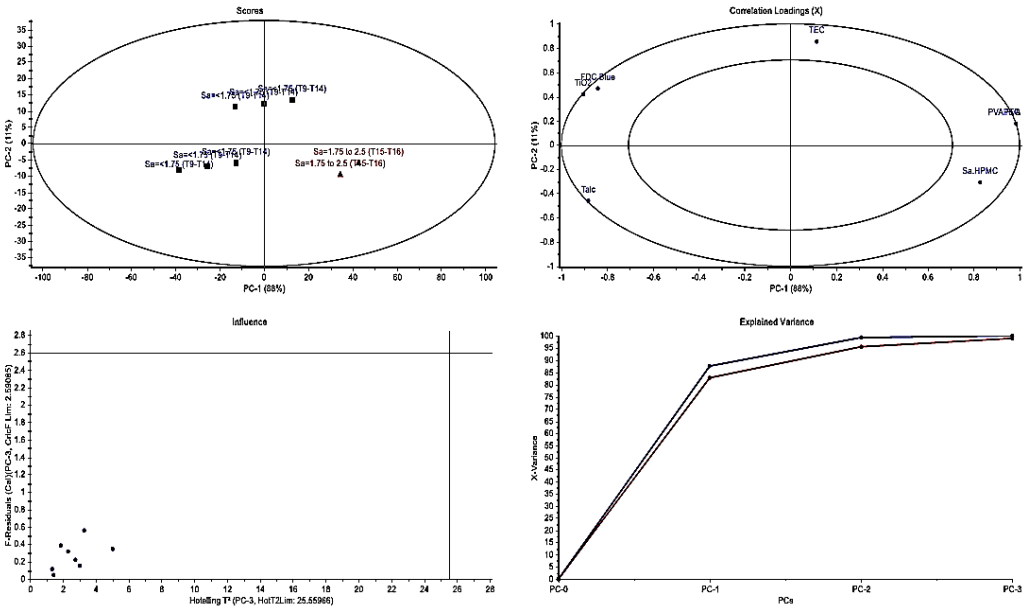

Figure 9: PCA for HPMC polymer blend samples.

Partial Least Squares Regression (PLSR): PLSR was performed for both PVA polymer band and HPMC polymer blend, refer to Figure 10 (A-D) and 11 (A-D) respectively. This plot

helps to understand the influence of formulation factors on the surface roughness. In case of PVA, plots of PLSR scores (Figure 10 A) and PLSR loadings (Figure 10 B) are interpreted similar to PCA scores and loadings (refer Figure 8 A and 8 B, respectively). Figure 10 C is similar to the correlogram and/or loading lots of PCA/PLSR, that is, graphical points above 0 indicate a positive correlation with the surface roughness or 'Y variable' or 'dependent variable' while values below zero demonstrate a negative correlation. Plot 10 D is the prediction vs reference plot and is used to measure the validity of the PLS model. There is a linear correlation with R-Square of >0.95 and a very low root mean square error (RMSE) indicates the model is valid in >95 instances.

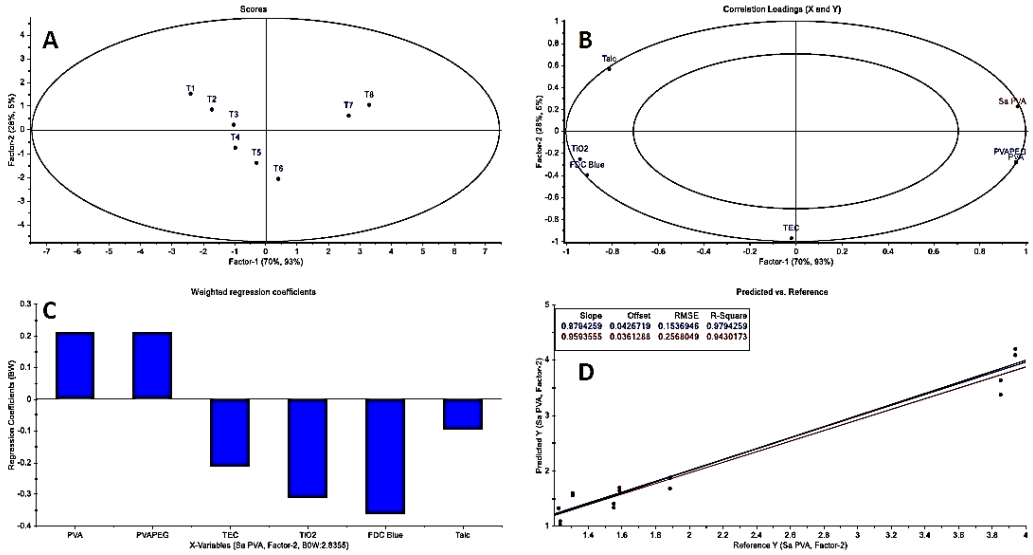

Figure 10: PLSR for PVA polymer blend samples.

Similarly, PLSR plot described for HPMC polymer bend (Figure 11 A-D). PLSR scores (Figure 11 A) and PLSR loadings (Figure 11 B) are interpreted similar to PCA scores and loadings (refer Figure 9 A and 9 B, respectively). Figure 11 C is similar to the correlogram and/or loading lots of PCA/PLSR, that is, graphical points above 0 indicate a positive correlation with the surface roughness or 'Y variable' or 'dependent variable' while values below zero demonstrate a negative correlation. Plot 11 D is the prediction vs reference plot and is used to measure the validity of the PLS model. There is slightly weaker linear correlation with R-Square of >0.76. However, the root mean square error (RMSE) of <1 indicates the model is valid in >75 instances.

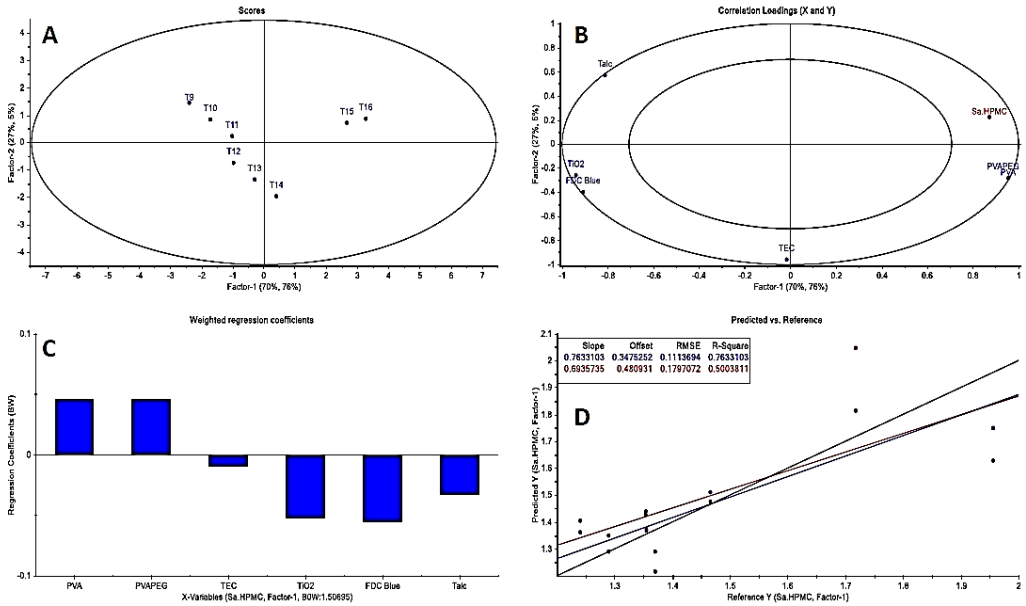

Figure 11: PLSR for HPMC polymer blend samples.

From boxplot, correlogram analysis, PCA, PLS it is established that the HPMC polymer blend (HPMC: PVA-PEG) performed better than the PVA polymer blend (PVA: PVA-PEG). In order to determine if there are any significant differences between the surface roughness values (Sa) of HPMC and PVA polymer blend in the various formulation conditions, one way ANOVA test was carried out. ANOVA test was carried out in R studio using generic R function aov () and summary.aov () which is used to summarize the model. The model predicted that, p value is less than the 5% significance level (p value < 0.05), therefore, it can be concluded that there are significant differences in the surface roughness values between the two polymers within the studied formulation ranges.

Table 1: Coating Formulation System.

Polymer blend	Name of Ingredients	Polymer bend to Additives ratio							
		20:80	30:70	40:60	50:50	60:40	70:30	80:20	90:10
		T1	T2	T3	T4	T5	T6	T7	T8
		Total polymer concentration							
		20%	30%	40%	50%	60%	70%	80%	90%
		Pigmented coated system						Non-pigmented	
		Quantities (%)							
PVA: PVA-PEG (90:10)	PVA	18	27	36	45	54	63	72	81
	PVA-PEG	2	3	4	5	6	7	8	9
	TEC	5	7.5	10	12.5	15	17.5	10	5
	TiO_2	44	36.5	29	21.5	14	6.5	0	0
	FD&C Blue#2 lake	1	1	1	1	1	1	0	0
	Talc	30	25	20	15	10	5	10	5
Total (%)		100	100	100	100	100	100	100	100
		T9	T10	T11	T12	T13	T14	T15	T16
		Pigmented coated system						Non-pigmented	
HPMC 6Cp: PVA-PEG (90:10)	HPMC 6cP	18	27	36	45	54	63	72	81
	PVA-PEG	2	3	4	5	6	7	8	9
	TEC	5	7.5	10	12.5	15	17.5	10	5
	TiO2	44	36.5	29	21.5	14	6.5	0	0
	FD&C Blue#2 lake	1	1	1	1	1	1	0	0
	Talc	30	25	20	15	10	5	10	5
Total (%)		100	100	100	100	100	100	100	100

DISCUSSION

Impact of polymer blend

A novel coating formulation using polymer blend demonstrated an example of ideal coating system having ability to produce hard and tough film without being brittle. In this polymer blend, hydrophilic graft-copolymer (PVA-PEG) get distributed uniformly within the macromolecular network of another polymer such as PVA, HPMC 6cP when applied in aqueous dispersion. Visual observation of coated tablets showed smooth uniform surface indicating no phase separation of polymer from the blend when coated on placebo tablets. In this coating system there is interactions between plasticizer molecules (TEC) and two polymer molecules of polymer blend which have impact on improving the mechanical properties of coated film. This interaction is mainly due to presence of hydroxyl group in plasticizer (TEC) which forms hydrogen bonding with carboxyl hydrogens of the polymer as a result there is increase in molecular mobility of polymer chain and reduction in tensile strength of film.

Other insoluble additives were included in this novel coating formulation to provide both color and photolytic protection, enhance appearance, and act as processing aids.

Impact of additives on polymer properties

PVA has an inherent tackiness, therefore, presence of anti-tacking agent (talc) and plasticizer in film coating formulation play a significant role in making smooth and uniform film. The talc is a glidant, and it helps to improve the smoothness of the final coating since the talc facilitates the tumbling of tablets over one another during coating process. Literature survey indicated that, for PVA talc has the unique effect of enhancing the ability of films to undergo stress release and hence relieve stress build-up (Gibson et al, 1989) which ultimately resulted in formation of smooth uniform film.

Impact of surface roughness based on additives and polymer type

Literature survey indicated that, other factors also affect the roughness and gloss on film coated tablets including initial roughness of the tablet core, the film thickness, type and concentration any added additives (pigment or fillers) (Rowe,1978; 1981 and 1985). In coating formulation T1, T2 and T3, the quantity of anti-tacking agent (talc) is on higher side as compared to that of present in T4, T5, T6, T7 and T8 also quantity of PVA is on higher side in T4, T5, T6, T7 and T8 as compared to that of present in T1, T2 and T3. This resulted in overall tendency of surface roughness (visual) on coated tablets was increased in the order of T1<T2<T3< T4<T5<T6<T7<T8 as the quantity of talc decreases and PVA quantity increases respectively.

In case of HPMC based system, slight roughness observed in T12 to T16 is mainly due to presence of higher content of polymer blend in coating formulations which resulted in increase in viscosity of coating dispersion and droplets are too viscus to spread when they reach to tablet surface which causes rough film formation on tablet surface.

The overall physical interaction of HPMC and PVA based polymer blends differs with respect to presence of other additives in coating formulation. HPMC polymer does not have tacking issue like PVA therefore, HPMC polymer blend showed, lower tendency of formation of surface roughness on coated tablets as compared to observed with PVA polymer blend.

Interpretation of statistical analysis

Boxplot analysis indicated that the spread of surface roughness (Sa) values for PVA: PVA-PEG polymer blend was broader than the HPMC:PVA-PEG polymer blend. Univariate data analysis was able to only extract the impact of surface roughness (Sa) on placebo coded

tablets due to pigmentation, i.e., the pigmented tablets displayed less surface roughness than the non-pigmented tablets. Univariate data analysis was seriously limited to understand the interaction between different formulation variables. Multivariate data analysis like PCA was employed and there was a trend in the data observed which extracted the influence as well as the interaction of various formulation parameters on the surface roughness. Multivariate regression models were developed to extract the influence of various parameters on the regression and a significant correlation for PVA polymer blend was obtained whereas slightly weaker correlation was obtained for HPMC polymer blend. In summary, within the studied protocol of various composition the polymer PVA was found to be influenced and a better multivariate linear model was obtained whereas the HPMC polymer was found to resist the changes to the surface roughness. Statistical significance was carried out using One Way ANOVA test, p value was found to be less than the 5% significance level (p value < 0.05), hence concluded that there are significant differences in the surface roughness values between the two polymers within the studied formulation ranges. In summary, based on the chemometric data analysis as well as the ANOVA results provided evidence that HPMC: PVA-PEG polymer blend performed better with respect to surface roughness values. These results are to be correlated with the formulation performance tests.

CONCLUSION

Visual observation of coated tablets indicated that, the tendency of surface roughness (visual) on coated tablets was increasing in the order of T1<T2<T3< T4<T5<T6<T7<T8 as the quantity of talc decreases and PVA quantity increases respectively. However, Hypromellose polymer blend showed, lower tendency of formation of surface roughness on coated tablets.

Surface microscopy study of coated tablets with optical profilometry (WITec alpha 300RA+) was successfully performed to predict the surface roughness (Sa) values. Tablets coated with PVA based polymer blend having higher concentration of polymer (PVA) and lower quantity of talc resulted in lower Sa value. HPMC based polymer blend showed lower value in Sa irrespective of concentration of polymer (HPMC) and talc present in coating formulation.

Statistical analysis was successfully applied to understand the impact of pigment versus non-pigment, presence of other additives (TiO_2, talc and TEC) and their concentration on influence of Sa of coated tablets. For PVA polymer blend, the surface roughness measured value is 1.778 whereas the regression model predicts the surface roughness values as 3.0407 µm. Therefore, the hypothesis that the presence of either other additives (talc) may reduce the

surface roughness was found to be evident and valid. For HPMC polymer blend, the surface roughness measured value is 1.4436 whereas the regression model predicts the surface roughness values as 1.6925 µm which is a closer to prediction. So, in summary, based on the chemometric data analysis as well as the ANOVA results provided evidence that HPMC: PVA-PEG polymer blend performed better with respect to surface roughness values.

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