Developing a Photometric Method to Determine the Amount of Film-Coating Material Applied onto Individual Tablet Cores

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Purpose

The dissolution property of a tablet, coated with a functional film-forming polymer depends strongly on the coating level. A variation in content uniformity leads directly to a high standard deviation in dissolution results. In the realm of Quality by Design (QbD), it is therefore essential to know the coating levels on individual cores, the variation within a batch and its influence on the dissolution profile of the dosage form.
Various analytical methods can be used to determine either the content of applied polymer or pigment onto a core [1, 2, 3]. However, the tests are either complex or costly. The aim of this work was to evaluate a colorant which can be determined photometrically, even at low concentrations. The application of this colorant was tested for a formulation based on the functional coating agent Kollicoat® Smartseal 30 D [4].

Materials and Methods

Materials

For the core formulation (Table 1) the following components were used: Caffeine (gran. 0.2–0.5), Ludipress® LCE, Kollidon® CL-F, Kollidon® VA64 fine (all BASF) and magnesium stearate (Baerlocher).
For the coat formulation (Table 1) the following excipients were used: Kollicoat® Smartseal 30 D and iron oxide red (all BASF), triethyl citrate (Jungbunzlauer Ladenburg), buthylene hydroxy toluene (BHT) (Sigma-Aldrich), talc (Merck).
As colorants, FD&C Blue No. 1, Riboflavin, Ponceau 419, Tartrazine and patent blue (all BASF) were tested.

Table 1: Composition of the cores

Ingredients	Quantity [%]
Caffeine, gran. 0.2–0.5	15.5
Ludipress® LCE	74.0
Kollidon® CL-F	5.0
Kollidon® VA64 fine	5.0
Magnesium stearate	0.5

Table 2: Composition of the coat

Ingredients	Quantity [%]
Kollicoat® Smartseal 30 D	51.75
Triethyl citrate	6.73
BHT	0.52
Talc	38.00
Colorant	2.00
Indicating colorant	1.00

Equipment

The UV/VIS spectrometer Agilent 8453 assembled with a 1 cm cuvette was used for the analytical tests.

Methods

Tablets were dissolved in 15–25 ml solvent (depending on the amount of indicating colorant), passed through a 0.45 µm filter (Sterivex™, Millipore) and then put into UV/VIS measuring.

Results and Discussion

When determining the amount of coating material borne by a single core by means of photometric measurement, several things have to be considered: the method has to be quick and simple enough to be performed for a large number of tablets (in order to allow statistical calculations such as standard deviation). At the same time, the sensitivity must allow the determination of relatively small differences in coating levels.
The colorant that is used as an indicator should have a high specific absorption rate. The excipients in the formulation are not to interfere with the determination of the colorant or the active ingredients.

Colorant

FD&C Blue No. 1 presented an absorption maximum at about 630 nm which was separated markedly from the spectrum of caffeine with its maximum at about 275 nm (Figure 1). With detectable concentrations of 1.0 mg/L the sensitivity was found to be sufficient. Riboflavin showed an absorbance spectrum in the wavelength range of caffeine (Figure 2). Due to this overlap, Riboflavin cannot be used in combination with caffeine in the test.
The absorbance maxima of Ponceau 419 (Figure 3) and Tartrazine (Figure 4) were separated sufficiently from caffeine, but due to the poor specific absorption, these two colorants have to be disregarded as well.
Patent blue showed a similar performance as FD&C Blue No. 1 (Figure 5). Both absorption maximum and position were identical (about 630 nm). Conversely, at 275 nm the spectra presented a distinctive signal. Therefore, FD&C Blue No. 1 was selected for further tests.

Solvent for sample preparation

In spite of the good solubility of Kollicoat® Smartseal in organic solvents (e.g. methanol, acetone, THF) these liquids could not be used for the test. Lactose, as one component of the core formulation, is not soluble in these solvents. However, a tendency of colorant absorption in the filter cake could be seen if lactose was not dissolved. Mixtures with water could not be applied, as the solubility of Kollicoat® Smartseal was dramatically reduced.
Kollicoat® Smartseal 30 D is a coating agent for taste masking and moisture protection. The coat is not soluble in water, but dissolves rapidly in acid media (< pH 5.5). Therefore, acidic aqueous solvents could be used for sample preparation.
FD&C Blue No. 1 was tested in this media. It was found that the absorbance was reduced at a pH-value of 1.1. However, after adjusting the pH-value with NaOH, the absorbance could be increased again (Figure 6). Therefore, before the UV-measurement of the colorant, the pH-value had to be adjusted to gain reliable results.
High colorant concentrations are desirable in order to reduce the analytical error. Therefore, the analytical test was conducted in a sample volume of 15 ml (for low weight gain) up to 25 ml (for high weight gain).
Coats based on Kollicoat® Smartseal 30 D were found to be insoluble in HCl 1 mol/L. However, in HCl 0.08 mol/L the coat dissolved rapidly, but this solution caused clogging when it was passed through a filter (0.45 µm).
Acetic acid 50 % (w/w) dissolved Kollicoat® Smartseal rapidly but caused a modification change of iron oxide as well which passed the filter again, causing a turbid sample that could not be measured. Therefore, iron oxide ought not to be contained in the coating formulation.
Finally, a mixture of acetic acid 50 % and NaOH (1 mol/L) in the ratio 7:8, which resulted in a pH-value of 4.5 was found to be ideal. All other ratios caused either high viscosities or modification changes of the iron pigments, both resulting in sample not usable.

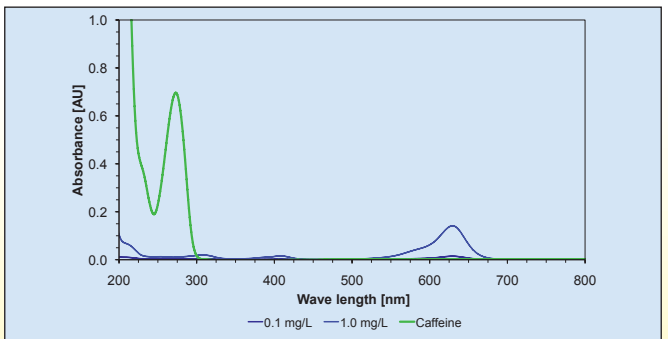

Figure 1: Absorption spectra of different FD&C Blue No. 1 concentrations in comparison to caffeine

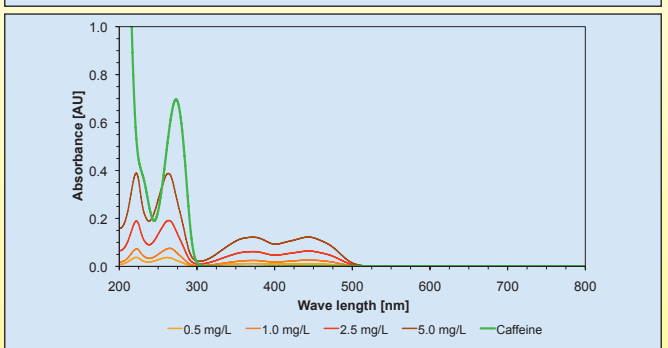

Figure 2: Absorption spectra of varying Riboflavin concentrations in comparison to caffeine

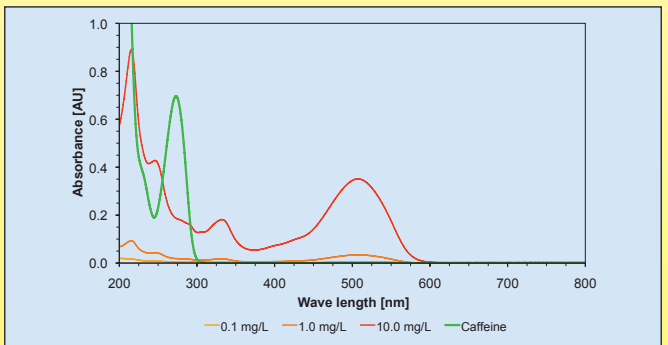

Figure 3: Absorption spectra of varying Ponceau 419 concentrations in comparison to caffeine

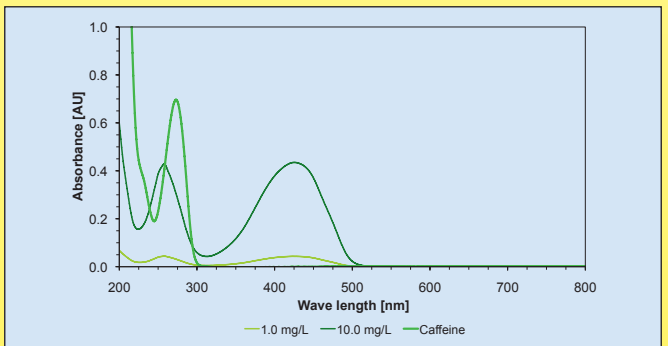

Figure 4: Absorption spectra of varying Tartrazine concentrations in comparison to caffeine

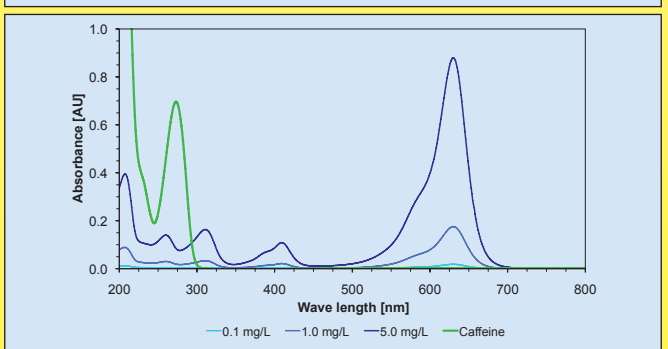

Figure 5: Absorption spectra of varying Patent blue concentrations in comparison to caffeine

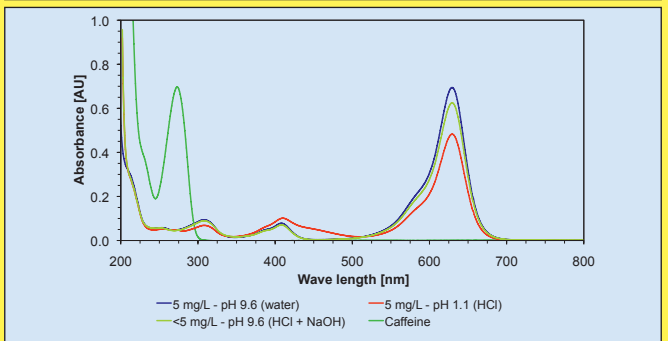

Figure 6: Absorption spectra of FD&C Blue No. 1 at different pH-values in comparison to caffeine

Stability of the liquid sample

Light stability of FD&C Blue No. 1 was found to be depending on the sample media (Figure 7). However, stability in the selected media acetic acid in the combination with NaOH (1 mol/L) in the ratio of 7:8 showed very good results.

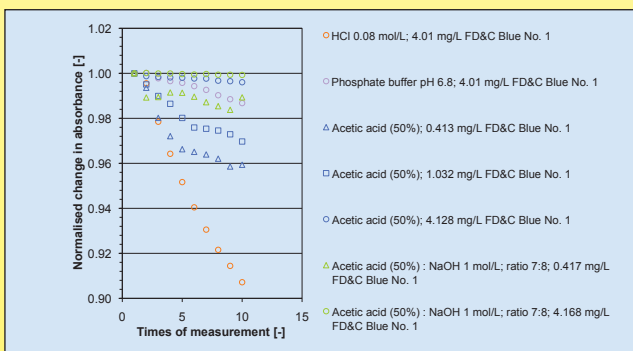

Figure 7: UV-light stability of FD&C Blue No. 1 determined in the photometer by repeating the measurement 10 times

Validation

Specific amounts of FD&C Blue No. 1 were given to samples containing either un-coated cores or coated cores with Kollicoat® Smartseal 30 D but without additional colorant. In all cases, the various individually dosed amounts of FD&C Blue No. 1 could be detected with an acceptable error of about 2 %.

Conclusion

FD&C Blue No. 1 is a suitable indicator to determine coating levels on individual tablets.
The sample preparation requires the disintegration of the tablets in 15–25 ml of acetic acid (50 %) and NaOH (1 mol/L) of the ratio 7:8. After filtration (0.45 µm hydrophilic PVDF filter), the retained solution could be measured directly using a photometer.

References

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