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PTR-102

Overcoming the Color Stability Issue Exhibited by Indigo Carmine in Film-coating Formulations

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Introduction

Colorants give pharmaceutical dosage forms a distinctive appearance. Coloring is needed for identifying pharmaceutical dosage forms, providing safety, a pleasing aesthetic appearance and potentially improving product stability. Parameters such as light, temperature and humidity affect the color stability of tablet film coatings. Indigo carmine (E132, FD&C Blue #2) is an indigoid dye frequently used in tablet coating that is known to be less stable in light[1]. The objective of this study was to investigate the color stability under different storage conditions of tablets that were coated with different coating formulations containing indigo carmine as a colorant.

Experimental Methods

Light, temperature and incompatibility of the ingredients are some of the main reasons for discoloration in tablet film coatings. Discolorations of tablets that were coated with different coating materials and stored in different conditions were compared. All coating materials were formulated with the same amount of the globally acceptable colorants yellow iron oxide and indigo carmine (E132, FD&C Blue #2), which is less stable than other colorants [1]. To compare color stability, placebo tablets were coated with standard HPMC-based coating formulations and with copovidone-based Aquarius™ Preferred HSP film-coating system.

Plasticizers are used to increase the flexibility of coating films. Studies done in the past have shown that plasticizers may interact with the APIs or promote degradation on the tablet surface, which appears as discoloration [2]. Conversely, triacetin was found to minimize the discoloration in HPMC-based coatings for ranitidine tablets [2]. To evaluate plasticizer effects on color stability, HPMC-based coating formulations were prepared with two different plasticizers; polyethylene glycol (PEG), which is commonly used in coating systems, and triacetin, which is known to minimize discoloration of coated tablets. All three formulations were prepared with the same amount of colorants (Table 1).

Note: This work was presented at the annual meeting of the American Association of Pharmaceutical Scientists, October 25–29, 2015, Orlando, Florida.

Table 1. Coating Formulation Ingredients

Aquarius™ Preferred HSP	HPMC-based Formula with PEG	HPMC-based Formula with Triacetin
Hydroxypropyl methylcellulose	Hydroxypropyl methylcellulose	Hydroxypropyl methylcellulose
Polyethylene glycol	Polyethylene glycol	Triacetin
Plasdone™ S-630 copovidone	–	–
Polydextrose	–	–
Medium-chain triglycerides	–	–
Titanium dioxide	Titanium dioxide	Titanium dioxide
Yellow iron oxide (E172)	Yellow iron oxide (E172)	Yellow iron oxide (E172)
Indigo carmine (E132, FD&C Blue #2)	Indigo carmine (E132, FD&C Blue #2)	Indigo carmine (E132, FD&C Blue #2)

Lab-scale blenders were used to prepare coating formulations. An O'Hara Lab Coat IIX pan coater was used to coat the placebo tablets and a DataColor™ 600 color analyzer was used to measure the color of the samples at each time interval and calculate the color differences with respect to the initial samples. The standard HPMC-based coating formulation contains HPMC, polyethylene glycol or triacetin, titanium dioxide, indigo carmine (E132, FD&C Blue #2) and yellow iron oxide (E172). The Aquarius™ Preferred HSP formulation contains Plasdone™ S-630 copovidone, polydextrose and medium-chain triglycerides, in addition to these ingredients.

The coating formulations were reconstituted with deionized water at 12% solids content (standard HPMC-based coating) and 20% solids content (copovidone-based Aquarius™ Preferred HSP film-coating system). Solids contents of coating materials were chosen in order to prepare solutions with similar viscosities. Placebo tablets (11 mm diameter) were coated up to 3% weight gain in the O'Hara Lab Coat IIX with the parameters shown in Table 2.

Table 2. Coating Parameters

Parameter	HPMC-based Coating	Copovidone-based Coating
Pan Size	15 in	15 in
Solvent	DI WATER	DI WATER
Solid Content	12%	20%
Actual Weight Gain	3%	3%
Tablet Charge	2 kg	2 kg
Gun Type	Schlick gun model 970/7-1 S35	Schlick gun model 970/7-1 S35
Number of Guns	1	1
Gun to Bed Distance	15 cm	15 cm
Atomizing Air Pressure	1.3 Bar	1.3 Bar
Pattern Air Pressure	2.3 Bar	2.3 Bar
Drying Air Volume	250 m^3/h	250 m^3/h
Pan Speed	12–15 rpm	12–15 rpm
Pre-warm tablet Bed	54–56 °C	52–54 °C
Inlet Air Temperature	60 °C	55 °C
Tablet Bed Temperature	44–46 °C	42–44 °C
Spray Rate	12–15 g/min	12–15 g/min

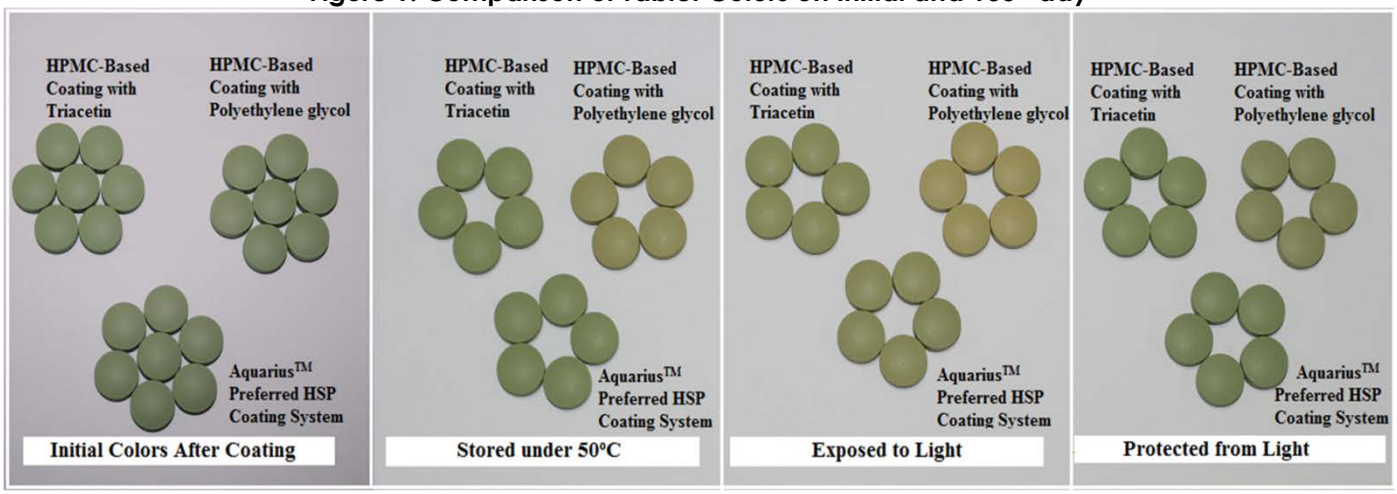
To evaluate the color differences of individual tablets, sample tablets were sequentially numbered from 1 to 15 and read into the DataColor™ 600. Each color reading was saved as a reference. To investigate the effect of light on color stability, five of the tablets were exposed to daylight directly and five were put in an opaque HDPE bottle and protected from light. The remaining five tablets were stored in an incubator at 50°C to demonstrate the effect of temperature on color stability. These tablets were read into the

DataColor™ 600 on the 1st, 5th, 30th, 45th, 60th and 100th days, using the initial measurements for reference to investigate the color change over time.

Results and Discussion

The Aquarius™ Preferred HSP film-coating system with copovidone has an apparent stabilizing effect on indigo carmine, compared with the standard HPMC-based coating formulations. The color change of tablets after exposure to light and temperature is noticeably greater in the HPMC-based formulations than in the copovidone-based formulation. Color differences in the tablets over time are shown in Figures 1 to 3.

Figure 1. Comparison of Tablet Colors on Initial and 100th day



It was also observed that triacetin has an additional contribution to color stability compared with polyethylene glycol when used as a plasticizer in HPMC-based film coating systems. When the colors of tablets that were protected from light or exposed directly to light were compared, it was observed that protecting tablets from light, as expected, significantly improved their color stability. However, the color change is much greater for the tablets coated with standard HPMC-based coating formulations than for the tablets coated with Aquarius™ Preferred HSP film coating system when the formulations were exposed to light.

Figure 2. Effect of Temperature on Color Stability

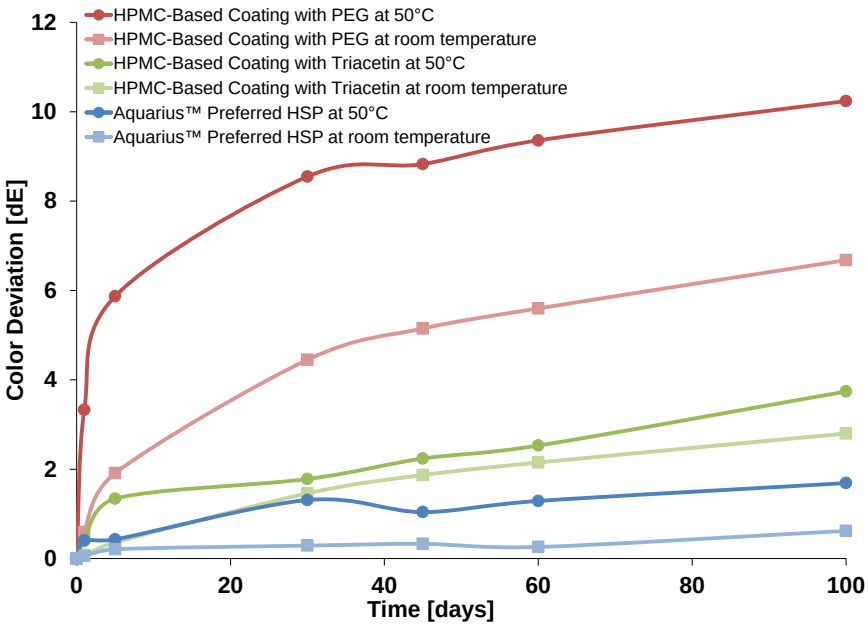
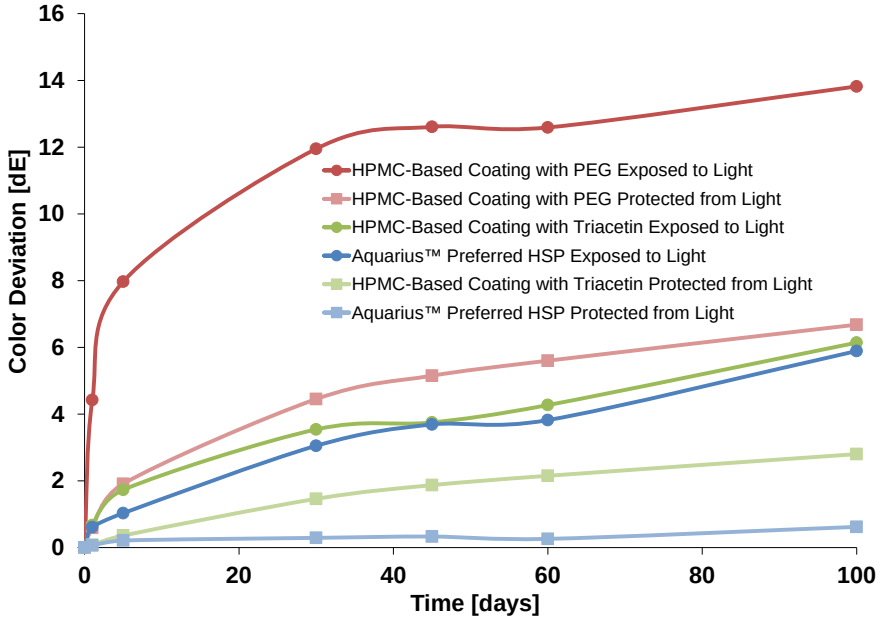


Figure 3. Effect of Light on Color Stability



Conclusion

As a result of this study, it can be concluded that both light and heat affect the color stability of coating formulations containing indigo carmine. For standard HPMC-based coating formulations, the use of triacetin instead of polyethylene glycol as a plasticizer improved color stability; however, the best color stability was obtained with copovidone-based Aquarius™ Preferred HSP film-coating system.

References

1. Allam, K.; Kumar, G. Colorants the Cosmetics for the Pharmaceutical Dosage Forms, Int J Pharm Pharm Sci, Vol 3, Suppl 3, 13-21 (2011).
2. US4880636, Film coated tablet of Ranitidine HCl, Robert M. Franz, May 13,1988