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Assessment of the Opacity of Titanium Dioxide Free Film Coating Formulations

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SUMMARY

Titanium dioxide (TiO_2) is widely used as an excipient in pharmaceutical film coating formulations. In August 2022, the European commission (EC) adopted a ban on the use of TiO_2 (E171) as a food additive. There is uncertainty around the implications of this decision on pharmaceutical products, and a potential need to find suitable alternatives to TiO_2. In this study, we evaluated the opacity of the different TF film coating systems by assessing the ability of TF film coatings to mask coloured tablet cores at varying weight gains. HPMC-based film coatings containing $CaCO_3$ demonstrated the best covering potential and were positively correlated to the amount of $CaCO_3$ present, while PVA-based film coatings containing $CaCO_3$ showed poor coverage, even at 9% weight gain.

INTRODUCTION

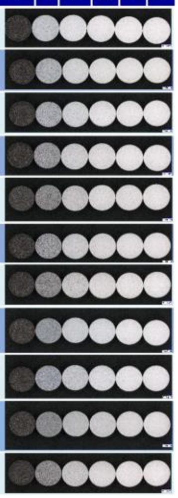
Titanium dioxide (TiO_2) is widely used as an excipient in pharmaceutical film coating formulations. TiO_2 acts as a colourant, opacifier and protection from UV light due to its high refractive index and light-scattering properties (Hughes, 2022). In August 2022, the European commission (EC) adopted a ban on the use of TiO_2 (E171) as a food additive (European Medicines Agency, 2021). This created uncertainty around the use of TiO_2 in pharmaceuticals, and potential need to find suitable TiO_2 alternatives with comparable opacity, whiteness, chemical inertness, and photoprotection to satisfy the replacement requirements.

In this study, we evaluate the opacity of the different TiO_2-free (TF) film coatings by assessing the ability of TF film coatings to mask coloured tablet cores at varying film coating weight gains, providing its aesthetics.

MATERIALS AND METHODS

Table 1. *Photographs of white-coated tablets using different TF film coatings at increasing weight gains.*

Coating name	Opacifiers and their quantity in film coating (%)	Pictures/Target weight gain(%)					
		0	1	3	5	7	9
TI	TiO_2: 25						
C38	$CaCO_3$: 38						
CM1	$CaSO_4$, $MgCO_3$						
CI	$CaCO_3$: 35, Isomalt: 30						
CM2	$CaCO_3$: 27, $MgCO_3$: 25						
C35	$CaCO_3$: 35						
RI	Rice starch: 35, Isomalt: 30						
CRI	$CaCO_3$: 25, Rice starch: 10, Isomalt: 10						
ZT	ZnO: 25, Talc: 10						
CP2	$CaCO_3$: 45						
CP1	$CaCO_3$: 25						



Ten TF film coating systems with different TiO_2 opacifier alternatives ($CaCO_3$, Rice starch, $MgCO_3$, ZnO, $CaSO_4$) were selected to coat black placebo

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tablets to assess their ability to mask coloured tablet cores at different coated weight gains (1%, 3%, 5%, 7% and 9%). CP1 and CP2 were PVA-based film-coating formulations while the rest were HPMC-based. TiO_2 – containing film coating acted as the control in this study.

Whiteness assessment was carried out on these film-coated tablets using the ColorFlex® EZ spectrophotometer. The L*, a* and b* values were measured and ΔE was calculated for each weight gain and film coating using the black tablet cores as reference (Fig. 1).

$$\Delta E = \sqrt{(L1 - L2)^2 + (a1 - a2)^2 + (b1 - b2)^2}$$

L1 – the L* value of reference colour (black tablet)
a1 – the a* value of reference colour (black tablet)
b1 – the b* value of reference colour (black tablet)
L2 - the L* value of sample colour
a2 – the a* value of sample colour
b2 – the b* value of sample colour

Fig. 1. *Equation for ΔE.*

RESULTS AND DISCUSSION

The ΔE values for each film coating at different weight gains are shown in Fig. 2. The higher the ΔE value, the easier it is for the human eye to perceive the colour difference between two samples. Human eye perception test is ongoing to understand the significance of ΔE values.

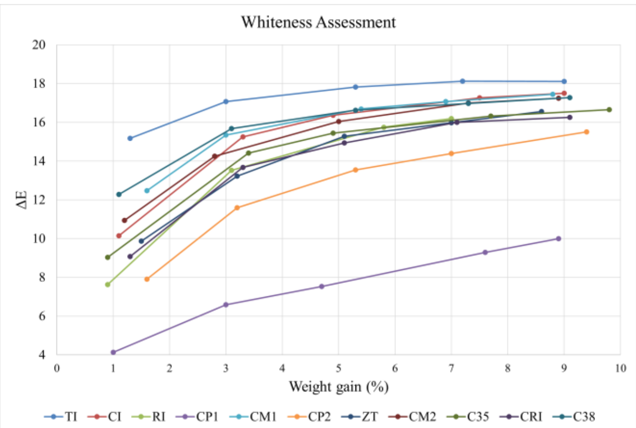

Fig. 2. *ΔE values calculated with respect to the black tablet cores as reference at different weight gains*

HPMC-based film coatings containing $CaCO_3$ demonstrated the best covering potential and were positively correlated to the amount of $CaCO_3$ present. This was followed by the TF film-coating containing both $CaSO_4$ and $MgCO_3$. However, these TF film coatings still required a weight gain of ≥7% to achieve similar coverage to TiO_2 at the standard 3% weight gain. In contrast, rice starch with isomalt did not show comparable whiteness to TiO_2. ZnO was initially thought to be the most promising alternative to TiO_2 due to its similarity in particle size (Radtke et al., 2021), however it did not exhibit good covering potential. ZnO may still possess good opacifying properties in terms of photostability, investigation into this is currently ongoing. Lastly, PVA-based film coatings containing $CaCO_3$ showed poor coverage, even at 9% weight gain.

CONCLUSIONS

In conclusion, HPMC-based TF film-coating formulations containing $CaCO_3$ provided the best covering potential. These were positively correlated to the amount of $CaCO_3$ present in the film coatings. PVA-based formulations containing $CaCO_3$ exhibited poor covering potential, even at 9% weight gain. Further studies assessing the ability of TF coating systems to protect against photodegradation are ongoing.

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