Colouring Orally Dispersible Tablets

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Introduction

Delivering active ingredients via orally dispersible tablets (ODTs) is a recent trend in the pharmaceutical industry. Due to the easy and fast application, patient's compliance is high for this kind of dosage form. To ensure a fast drug release, ODTs are typically not coated. Nevertheless, a product-specific appearance by means of colour might also be requested.
This work was to investigate possibilities of how a colorant might be added to an ODT avoiding a film coating process. Two methods were tested: firstly the direct compression (DC) and secondly the application of the colouring agents onto the powder blend in a fluid bed (FB) coating process.

Experimental Methods

Materials

Ludiflash® (based on mannitol (90 %), Kollicoat® SR 30 D (5 % solids) and Kollidon® CL-SF (5%)) from BASF SE, Ludwigshafen, Germany, were used.
As colouring agents, Indigotine 85 % E132 (Sensient, King's Lynn, UK) and riboflavin (BASF SE, Ludwigshafen, Germany) were used.
As flavours, peppermint (Bell Flavors & Fragrances, Leipzig, Germany) and banana (Symrise AG, Holzminden, Germany) were used.
As most suitable lubricant, sodium stearyl fumarate (PRUV®, JRS GmbH & Co. KG, Rosenberg, Germany) was used [1].

Formulations

Two colouring agents were tested in DC (Table 1, Table 2), whereas one was transferred to the FB process (Table 3).

Table 1: DC formulations tested (blue tablets)

	# 1	# 2	# 3
Ludiflash®	192.0 mg	191.0 mg	189.0 mg
Indigotine 85 %	1.0 mg	2.0 mg	4.0 mg
Peppermint flavour	3.0 mg	3.0 mg	3.0 mg
Sodium stearyl fumarate	4.0 mg	4.0 mg	4.0 mg
Total weight tablet	200.0 mg	200.0 mg	200.0 mg

Table 2: DC formulations tested (yellow tablets)

	# 4	# 5	# 6
Ludiflash®	195.2 mg	194.7 mg	193.7 mg
Riboflavin	0.5 mg	1.0 mg	2.0 mg
Banana flavour	0.3 mg	0.3 mg	0.3 mg
Sodium stearyl fumarate	4.0 mg	4.0 mg	4.0 mg
Total weight tablet	200.0 mg	200.0 mg	200.0 mg

Table 3: FB formulations tested (yellow tablets)

	# 7
Ludiflash®	192.0 mg
Indigotine 85%	1.0 mg
Peppermint flavour	3.0 mg
Sodium stearyl fumarate	4.0 mg
Total weight tablet	200.0 mg

Methods

Blender

As blender, the high shear mixer P1-6 (Diosna GmbH, Osnabruck, Germany) assembled with 2 L product bowl, 300 rpm, chopper off, was used for a blending time of 5.5 minutes.

Coating equipment

As fluid bed coater, the GPCG 3 (Glatt GmbH, Binzen, Germany) assembled with 5L product container and Wurster 7" bottom spray nozzle (d = 1.0 mm) was used.

Table 4: Process settings fluid bed coater.

Batch size	1,000 g
Coating suspension	5.0 g indigotine 85% in 71.0 g water
Inlet air quantity	50 m³/h
Inlet air temperature	45 °C
Spray rate	3 g/min
Spraying pressure	4.0 bar

Compression

The single punch press XP 1 (Korsch GmbH, Berlin, Germany) assembled with a set of plane punches (diameter 8 mm) was used for compression.

Results and Discussion

The aim of the trials was to optimise the colorants homogeneous distribution within the tablet rather than the actual characterisation of the tablet. All formulations were compressed into tablets by applying a compression force of about 2.5 kN. The tablets presented a hardness of about 38 N which led to a disintegration time of <10 seconds.

Direct compression

Visually, the colour of indigotine can be described as very intensive. Already small agglomerates of this colouring agent were found to be visible as dark spots within the tablet (Figure 1). Even at higher concentrations, the colour impression was not homogeneous. Dark blue as well as white spots could be recognised within the surface of the tablet.
Therefore, it was suggested to apply the colorant as a suspension in a coating process directly onto the granules to achieve an improved uniformity.
Conversely, riboflavin offered a distinctively lighter hue. Furthermore, the tendency to form agglomerates was less pronounced. This was the reason why tablets containing riboflavin had a homogenous yellowish colour impression (Figure 2) independent of the colorant's amount in the tablet.

Fluid bed coating

Homogeneously coloured agglomerates could be achieved by applying indigotine suspension directly onto Ludiflash® granules in FB. Interestingly, the coat could be applied without the need of additional film formers.
The tablets obtained from this precoated material showed a much more homogenous colour appearance compared to DC (Figure 3). Hardly any spots could be seen within the tablet's surface.
Independent of the process used for incorporating the colouring agent into the ODT, it should be taken into consideration that the amount of colouring agent is much higher compared to coloration via a film coat. In a coating process, the colour is applied onto the surface of the tablet whereas both approaches described in this paper led to a colouration throughout the whole tablet. Therefore, higher contents of colouring agent are required in this type of formulation. From the regulatory point of view (maximum daily intake of the colorant) this could be a critical aspect.

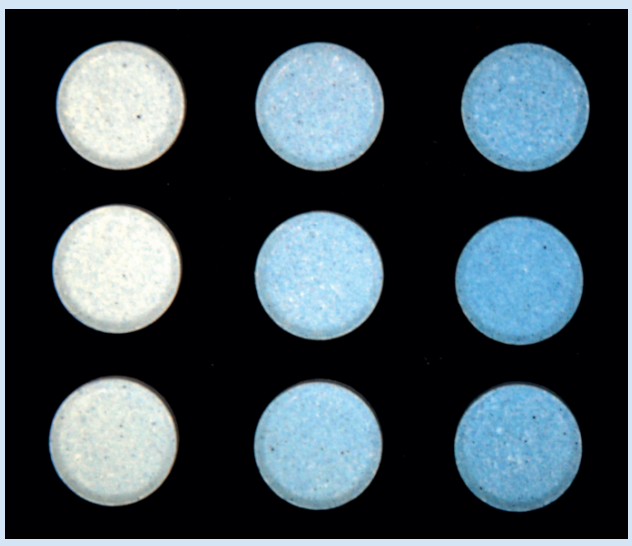

Figure 1: Visual appearance of tablets containing different amounts of indigotine – formulation #1 (left), #2 (middle) and #3 (right)

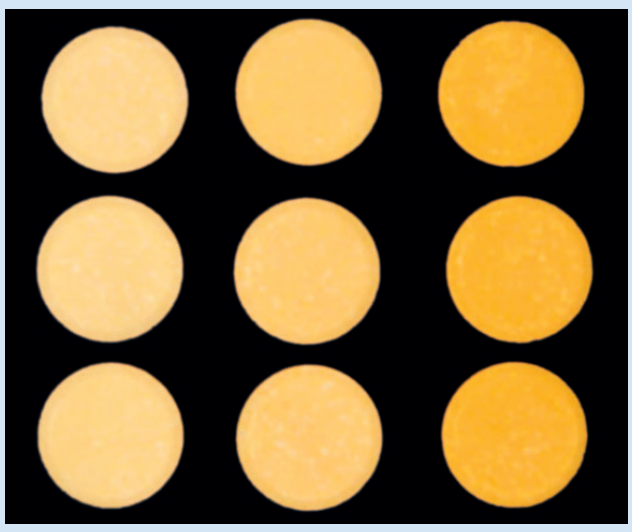

Figure 2: Visual appearance of tablets containing different amounts of riboflavin – formulation #4 (left), #5 (middle) and #6 (right)

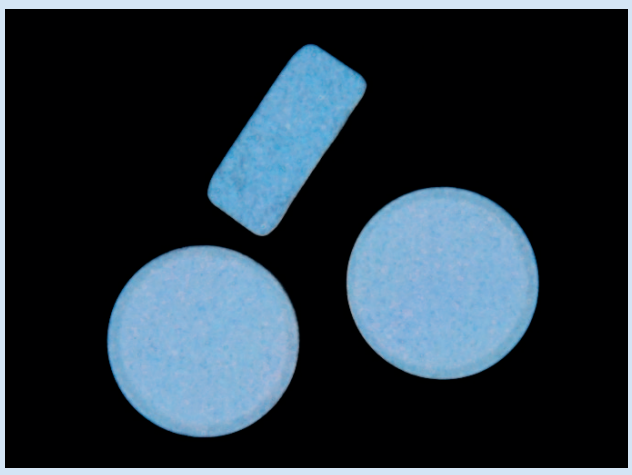

Figure 3: Visual appearance of tablets containing previously coated Ludiflash®

Conclusion

It could be shown that the colouration of the tableting blend is an alternative to the coating of ODTs which bares the risk of prolonging disintegration time. Whether the colouring agent can directly be added to the powder blend or has to be applied previously, is dependent on its nature and the expected hue.
However, coating of either Ludiflash® or the whole powder blend, including the API was found to be an efficient approach. For achieving a coloured DC material, it could even be considered to add the colouring agent directly to the Kollicoat® SR 30 D dispersion during the production of Ludiflash®.

References

[1] Kruse, S., Gebert, S., Meyer-Böhm, K., Maschke, A., Kolter, K.; Compression Characterization and lubricant sensitivity of orally disintegrating tablets based on Ludiflash®; APV World Meeting; April 7–10, 2008; Barcelona, Spain

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