Evaluation of a film-coating system for heat sensitive products

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INTRODUCTION

Aqueous film-coating systems based on PEG, PVA, and HPMC are recommended to be applied at temperature of about 40°C with a spraying time close to 1 hour. Tablets containing heat sensitive API or excipient cannot afford such conditions without causing chemical or physical degradation, degradation amplified by the presence of water. More, when coating tablets with moisture sensitive actives or excipients, an increase of the temperature is recommended to overcome the API's sensitivity. But for the majority of APIs and excipients the solubility increases with the temperature and accelerates the degradation phenomena. Film-coating at a process bed temperature lower than 25°C is now possible when using a new coating system, starch based. The goal of this study was to evaluate the feasibility and benefits of low bed temperature coating on heat sensitive tablets.

MATERIALS & METHODS

A new ready to use coating system (ReadiLYCOAT®, Roquette) based on modified pea starch polymer was used for all the trials.

First part of the study: evaluation of the benefits of a coating done at a process bed temperature lower than 25°C on the chemical and physical stability of tablets.
Three distinct heat sensitive tablets were selected and tested.

1- Tablets containing an API unstable at temperature higher than 30°C
2- Tablets containing a lipid based system melting at 35°C
3- Tablets containing a highly soluble excipient (sorbitol: water solubility increasing dramatically with temperature (20°C: 222g, 40°C: 354g and 60°C: 614g in 100 ml of water).

These tablets were coated using a fully perforated 2L coating pan (Labcoat M, O'Hara, pan size 12") equipped with a Schlick spray gun utilizing a 0.8 mm fluid tip and an anti-bearding cap.
For each formulation, coating trials were performed comparatively with and without heating:

- Standard coating conditions with a tablet bed temperature of 35°C (T1-1)
- Experimental coating conditions at ambient (20°C) temperature (T1-2 & T1-3).

The new starch based coating system exhibits a low viscosity in suspension and can be sprayed at high dry substance. Minimizing the water amount is of obvious interest in film-coating which is primary a drying process: 2 suspension dry substances 20% (T1-2) and 25% (T1-3) were tested.

Freund-Vector Laboratory Development Coating System (LDCS) with 4 liter coating pan

Second part of the study: evaluation of the quality of coating done at a process bed temperature lower than 25°C. 2.5 kilograms core tablets (800mg, mannitol based) were processed with 20% dry solids coating formulation (to 4% coating by weight) using a fully perforated 4L coating pan (LDCS, Freund-Vector Corporation) equipped with a Schlick spray gun utilizing a 1.0 mm fluid tip and an anti-bearding cap. Process conditions were controlled to achieve different tablets bed temperatures ranging from 40°C down to 20°C. Color uniformity was evaluated visually, and via spectrophotometric ΔE values (ΔE is a positive number expressing a difference between two colors) using a Konica Minolta CM-5 spectrophotometer. Film adhesion was evaluated using friability and disintegration USP methods.

RESULTS & DISCUSSION

First part of the study
The coatings with or without any heating were done successfully on the 3 tablet formulations (Table 1).

Parameters	Trial T1 -1	Trial T1-2	Trial T1-3
Batch Size (g)	900	900	900
Suspension dry substance (%)	20	20	25
Suspension viscosity (mPa/s)	98	98	163
Inlet Air Temperature (°C)	55	20	20
Tablet Bed Temperature (°C)	**35**	**17**	**18**
Inlet Air Flow (m^3/h)	100	100	100
Spray Rate (g/min/kg)	3 to 4.5	1.5 to 2.5	1.5 to 2.5
Atomization Air (bar)	1.0	1.0	1.0
Pattern Air (bar)	1.0	1.0	1.0
Pan Speed (rpm)	18	18	18
Weight gain %	3.0	3.0	3.0
Spray Time (min)	32	65	52

Table 1. Coating parameters of the first series of coatings.

It has to be emphasized that the drying is feasible without heating because the amount of cores is small (900g) and because the air used has a low relative humidity (inlet air regulated at 20°C and 50% relative humidity maximum).

- Tablets containing an unstable API: no degradation was observed on the low temperature coated tablets whereas tablets coated with heating were out of specifications on API content
- Tablets containing an excipient melting at 35°C: the low temperature coated tablets had exactly the same shape than the uncoated ones, whereas the heat coated tablets lost their shape due to the main excipient melting
- Tablets containing sorbitol (a highly soluble excipient) were coated successfully at low temperature and the initial logo was kept. On the heat coated tablets the logo disappeared partially (Figure 1). It was not due to a logo bridging defect but a consequence of the partial dissolution of sorbitol: the letters are clearly modified and not filled.

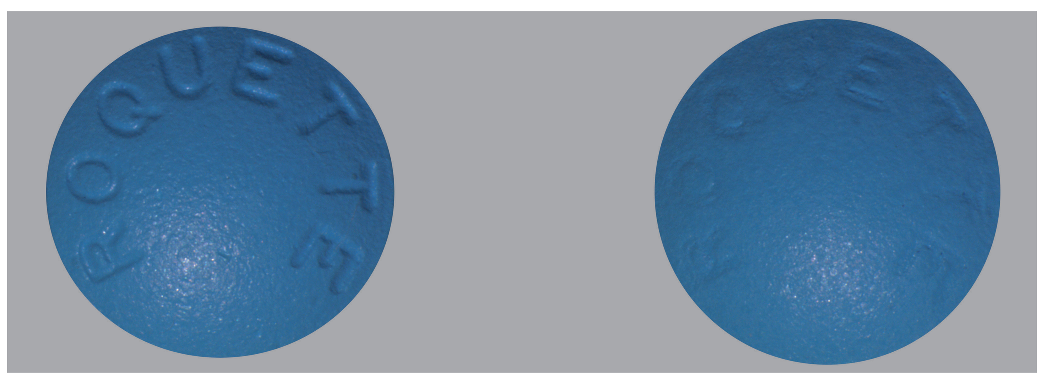

Figure 1. Tablets containing sorbitol coated at 18°C (left) and 35°C (right).

Second part of the study
The coatings were performed successfully at all temperatures (Table 2).

Parameters	Trial T2-2	Trial T2-3	Trial T2-4	Trial T2-5	Trial T2-6
Batch Size (g)	2.5	2.5	2.5	2.5	2.5
Inlet Air Temperature (°C)	57-60	60-62	42-47	37-42	30-35
Tablet Bed Temperature (°C)	**40-43**	**37-38**	**24-28**	**20-25**	**19-22**
Inlet Air Flow (m^3/h)	100	68	68	68	100
Spray Rate (g/min/kg)	10.0	10.4	10.4	10.5	8.2
Atomization Air (bar)	1.2	1.2	1.2	1.2	1.2
Pattern Air (bar)	1.2	1.2	1.2	1.2	1.2
Spray Gum to Tablet Bed (cm)	10.0	10.0	10.0	10.0	10.0
Final Coating (%)	4.0	3.9	4.1	4.0	4.0
Spray Time (min)	51.9	48.5	52.0	49.9	63.3
Pan Speed (rpm)	18	18	18	18	18

Table 2. Coating parameters for the second series of coatings.

To decrease the tablet bed temperature from about 40°C to about 20°C it was necessary to decrease the inlet air temperature from about 57/60°C to 30/35°C. A heating of the air was still required for a tablet bed temperature of 20°C as the drying is consuming energy with consequently a drop of temperature. The spraying time was only increased by 22% (63.3 min versus 51.9 min).
All tablets trials were visually appealing with very good color uniformity. There was no visible difference between the coated tablets whatever the coating conditions: ΔE values ranged from 0.5 to 1.0. So less than 1.5 this is the point from where a visible color difference is perceived by the eye (Figure 2).
Friability measurements resulted in 0% loss of tablet/coating weight. Disintegration times for coated tablets compared to uncoated tablets increased only 39 seconds (86 seconds to 125 seconds).

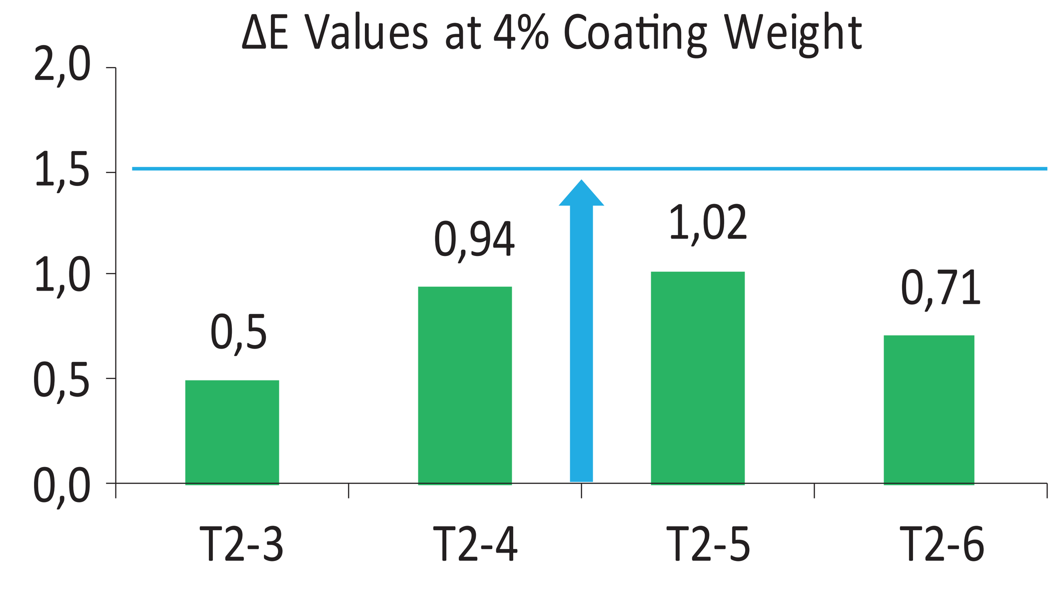

Figure 2. Second series of coatings – Color uniformity – Trial T2-3 tablets were used as the reference tablets for ΔE values – Blue line: limit of visible color difference.

CONCLUSION

The novel combination of ReadiLYCOAT®, ready to use coating system based on modified pea starch polymer, with high solids content of the coating suspension and low tablet bed temperature proved to be effective to coat heat sensitive products. It produces uniform coatings with zero visible defects while using standard film-coating equipment and only water as solvent.

REFERENCES

1-Barkley, A, Levine, S, Signorino, C: The Evolution and Evaluation of Tablet Coatings, Tablets & Capsules, (4), 2006.

2-Porter SC, Felton LA. Techniques to assess film coatings and evaluate film-coated products. Drug Dev Ind Pharm. 2010;36(2):128–42

3-Patent EP 1.684.731B1

4-Patent FR 2 862 654B1