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Aqueous pharmaceutical coating at low temperature processing – performance and scale up

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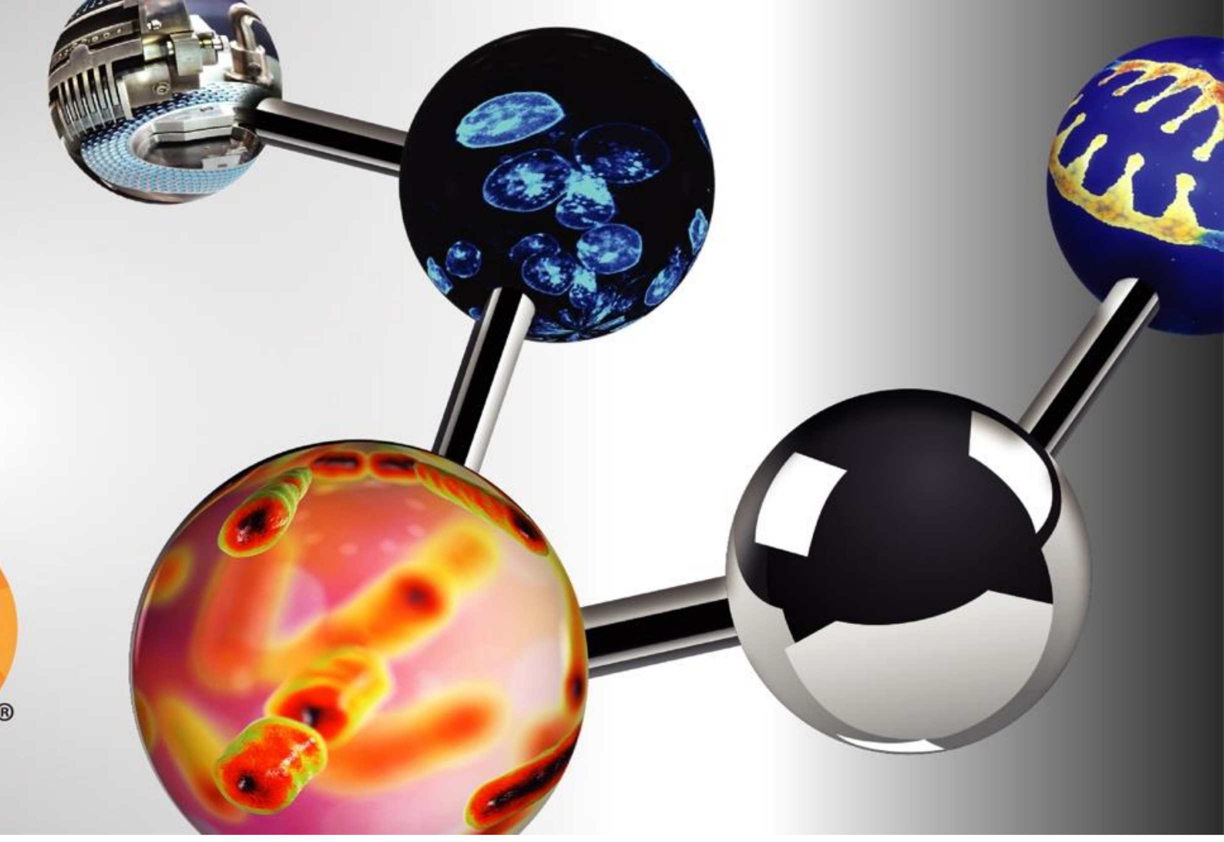


PURPOSE

Aqueous pharmaceutical coatings normally are applied in processes where tablet temperatures are maintained in 35-45ºC range. To the date there is no information available for aqueous coating formulations able to be applied while maintaining tablet bed temperatures lower than 30ºC.

Usual issues when trying to coat under low processing temperature include tablet sticking, bad appearance with increased roughness, and even tablet disintegration.

Present work describes the use of a new water dispersible coating product able to be applied at low tablet bed temperature which previously only could be achieved using organic coating dispersions.

Tested coating formulation, consists of a proprietary mixture of a polyol derived of Isomaltulose, cellulosic derivate and vinylic polymers as film forming agents.

Results of applications at laboratory and productive scale are included in order to verify the possibility of handling low temperature processes despite lot size.

Coating product performance was evaluated following difference in color evolution, in process observations and roughness on final coated tablets.

To the best knowledge of the authors there is no previously documented registration for aqueous coatings processed at temperatures lower than 30ºC

OBJECTIVE

The object of this work is to expose a new water dispersible pharmaceutical coating product able to be applied at tablet bed process temperatures lower than 30ºC.

METHODS

12 mm concave placebo tablets were coated with Gray EasyCoat® SP RAS1099 using equipment and working conditions shown in Table No. 1. Production scale trials were held at low (28-30ºC) and normal (35-40ºC) tablet bed Temperature.

Evolution of Color Difference (DE) was evaluated by measuring color (CIE L*a*b) of two out of 200 sampled tablets. Tablets measured for DE were the most distinct in color from each sample. Sampling was held each using 0.5% theoretical weight gain increment from 0.5 to 4.0. Color (L*a*b scale) was determined by Colorimeter CHN SPEC Model CS-10.

Appearance of final coated tablets was assessed by measuring Roughness (Ra) using Microscope Keyence model VR-5000 by digital image processing.

	Lab Conventional Pan 8"	***Lab Perforated Pan 8"***	***Productive scale Perforated pan – Freund-Vector VHC60M***	***Productive scale Perforated pan – Freund-Vector VHC60M***
Solvent	Water	Water	Water	Water
Dispersion solids content (%)	25	25	25	25-30
Tablets lot size (Kg)	**0.5**	**0.5**	**100**	**100**
Coating Weight gain (%)	4	4	4	4
Inlet air temperature (ºC)	40-45	40-45	45-50	65-70
Tablet bed temperature (ºC)	**28-30**	**28-30**	**28-30**	**40-42**
Spraying guns	1	1	2	2
Nozzle diameter (mm)	1.2	1.2	1.2	1.2
Atomizing air pressure (psi)	12	12	18	18
Pattern air pressure (psi)	12	12	18	18
Nozzle-bed distance (cm)	15	12	23	23
Drying air flow (cfm)	80	--	1600	1400
Pan speed (rpm)	15	15	6	6
Liquid flow (g/min)	4	5.3	300	300
Process time (min)	20	15	53	53

Table 1. Trials working conditions

RESULTS

Evolution of color difference.

Color difference during process is a good way to evaluate process performance on a coating process. The less weight gain required for obtaining uniform color, the better. Figure 1, shows 3% weight gain was enough in all cases to achieve DE>1, which indicates acceptable color uniformity. No significant difference was found comparing process at normal vs low temperature at production scale.

It is perceived that lab scale perforated pan achieves faster color uniformity compared with productive scale.

Tablet Roughness

Visual aspect of coated tablets was acceptable and similar across all trials. Roughness evaluation on a linear (Ra, Rk, Rz) and surface models (Spc, Sdr, Spd) were held to compare results from changing scale, and from process temperature change for a production scale unit. Table 2 shows that coated tables obtained from all trials are comparable, showing only minor appearance difference for finished product processed under low (28ºC) or normal (40ºC) coating temperature. Visual aspect of final coated tablets is very similar within all trials.

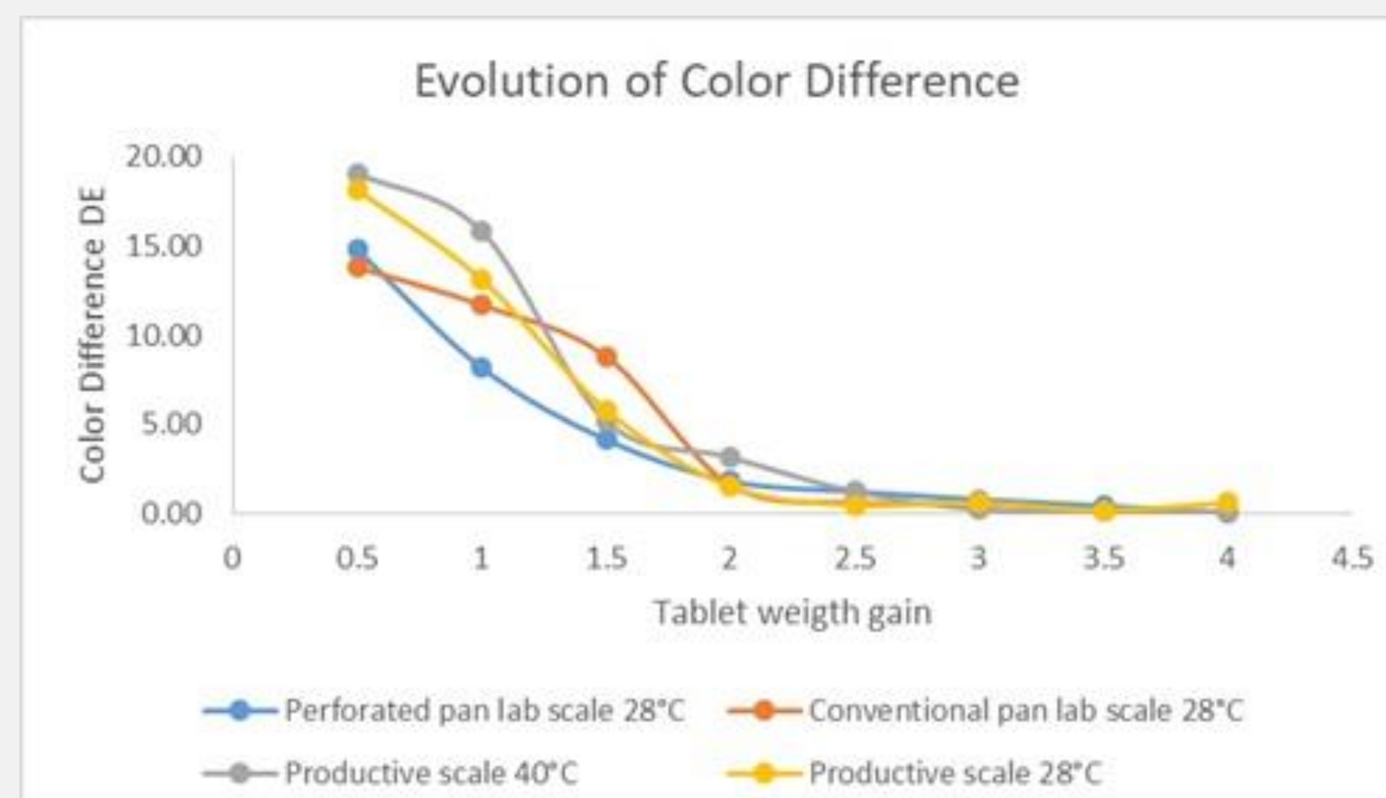


Figure 1. Evolution of color difference

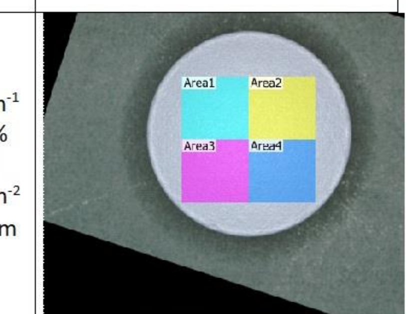
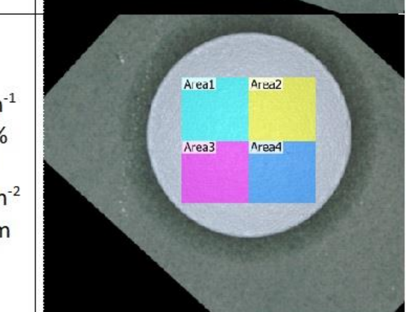
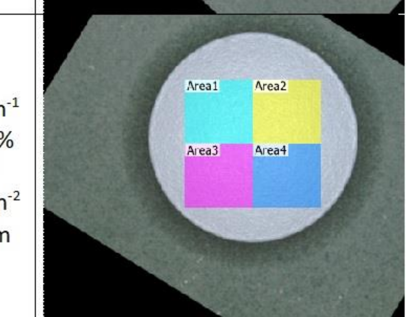
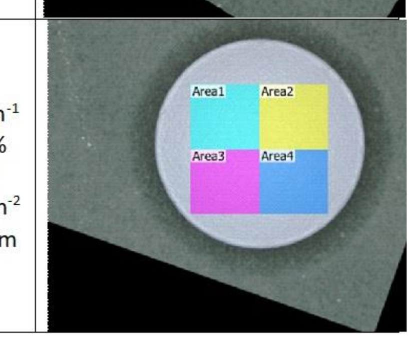
Process Equipment	Tablet bed process Temp (°C)	Lineal Roughness (mm)	Surface Roughness	Image
Lab scale Perforated pan	28-30	Ra: 1.511 Rk: 4.113 Rq: 1.895 Rz: 5.888 RzJIS: 3.566	Spc: 2.037 mm^{-1} Sdr: 5.897^{-3} % Sdq: 0.108 Spd: 3.170 mm^{-2} Sp: 215.123 µm	
Lab scale Conventional Pan	28-30	Ra: 1.778 Rk: 4.910 Rq: 2.096 Rz: 6.922 RzJIS: 4.617	Spc:2.248 mm^{-1} Sdr: 5.613^{-3} % Sdq: 0.105 Spd: 4.758 mm^{-2} Sp: 189.05 µm	
Productive scale Perforated Pan	28-30	Ra: 1.725 Rk: 5.395 Rq: 2.288 Rz: 7.260 RzJIS: 4.734	Spc: 1.420 mm^{-1} Sdr: 3.9415^{-3} % Sdq: 0.089 Spd: 3.836 mm^{-2} Sp: 155.93 µm	
Productive scale Perforated Pan	40	Ra: 1.587 Rk: 4.386 Rq: 1.834 Rz: 5.991 RzJIS: 3.844	Spc: 1.346 mm^{-1} Sdr: 3.608^{-3} % Sdq: 0.085 Spd: 3.037 mm^{-2} Sp: 163.345 µm	

Table 2. Tablet surface roughness

CONCLUSIONS

A new pharmaceutical water dispersible coating product has been formulated, which is useful for low temperature processes. Trials have been held at laboratory and production scale in order to assess equivalent finished coated product. During the coating process, the tablet bed temperature was maintained at temperatures lower than 30ºC.

Color evolution throughout the process, shows product uniformity at 3% theoretical tablet weight gain despite vastly different lot sizes (0.5 to 100 Kg).

Tablet appearance in terms of roughness (Ra) is also equivalent.

Aqueous coatings able to be applied at low temperature may be useful for processing temperature sensitive API´s. It is also an option; for designing robust coating processes where it is expected that coating process will run with diminished possibility of issues under a wider temperature range

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