Identification of critical parameters for an automatic film applicator to produce orodispersible hydrocortisone hemisuccinate films

L. Nobilet[a,1], B. Toussaint[a,b,1], M. Sauvat[a], A. Thouvenin[a,b], B. Andre-Nonque[a], P. Lamarque[c], E. De Landtsheer[c], A. Schweitzer-Chaput[c], V. Boudy[a,b]

a: Département de Recherche et Développement Pharmaceutique, AGEPS, APHP, Paris, France
b: UTCBS, CNRS, Inserm, Université Paris Cité, Paris, France
c: Pharmacie à Usage Intérieur, Hôpital Necker-Enfants Malades, APHP, Paris, France
1: These authors contributed equally to the work

COM25-69100

Introduction

Need for new pharmaceutical forms and dosages:

Patient-centered treatment → Swallowing disorders + several drugs + multiple dosages

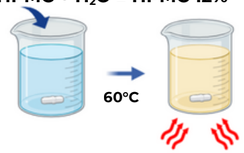
Industrial drugs shortage → Drug preparations → Development/organisational issues

Objective: Identify and evaluate the critical parameters of the manufacting process of orodispersible films (ODFs) containing 1.0 mg of hydrocortisone hemisuccinate (HCS) using an automatic film applicator (AFA)

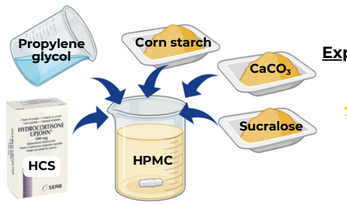
Materials and method

ODFs production

1) HPMC + H_2O = HPMC 12%



2) Adding excipient, HCS, H_2O



3) Solvent casting method: Automatic Film Applicator

4) Packaging in Medi-dose® blisters

Design of experiments (DoE): full factorial design

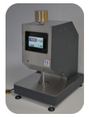
	Levels		
Factors	-1	+1	Center point (n=3)
Applicator's Height (µm)	300	700	500
Application Speed (mm/s)	5.0	25	15
Drying temperature (°C)	60	70	65
Drying time (min)	30	50	40

ODFs characterisations (DoE responses)

Expected dose (%): HPLC-UV

Column: Polaris C18 (250x4.6 mm ; 5 µm)
Mobile phase: 30/70% (v/v) acetonitrile/H_2O pH = 2
Flow rate: 1.0 mL/min
Injection: 50 µL
Analysis: 254 nm

Thickness (µm): Micrometer



Mass (mg): Precision scale

Residual moisture (%): Halogen moisture analyser

Dissolution in artificial saliva (min): Sotax USP IV (orodispersible tablet adaptator) + UV-vis spectrophotometer

Conclusion

- AFA is suitable for ODFs production
- Height and speed: major impact on mass uniformity and expected dose
- Applicator's height is not a relevant "dose adjustment" parameters
- Center point: respect ODFs mass uniformity and HCS content
- Stability of HCS in ODFs: reduced with high residual moisture

Results

Design of experiments

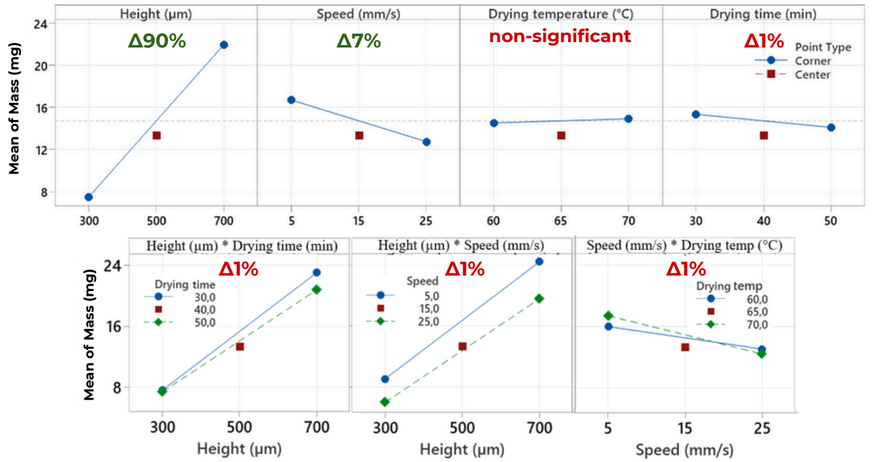


Fig. 1. Main effects and interactions plots for mass (R^2 = 99%). Δ = percentage of the total variation of the response explained by the factor or interaction

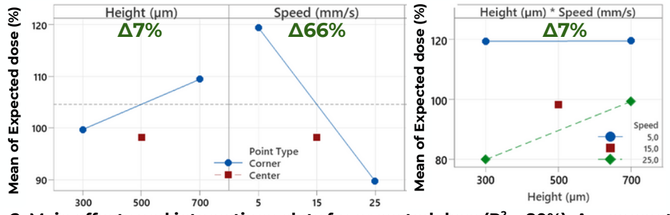


Fig. 2. Main effects and interactions plots for expected dose (R^2 = 80%). Δ = percentage of the total variation of the response explained by the factor or interaction

Applicator's height and application speed are the most contributive factors to control film weight and accuracy of the dose

Correlated data to film mass

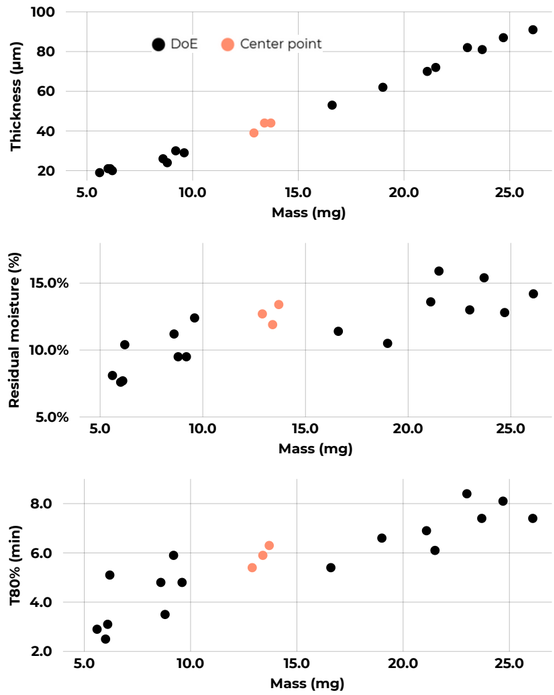


Fig. 3. Correlations of the weight with thickness, residual moisture and T80%

Thickness, residual moisture and dissolution kinetics are correlated to mass and thus give same DoE results

Mass uniformity

3 out of 4	Levels
Applicator's Height (µm)	700
Application Speed (mm/s)	5.0

All other levels

Expected Dose: 1.0 mg

Center point = 98.2 ± 4.5 %

Center point offers best results

Dissolution datas

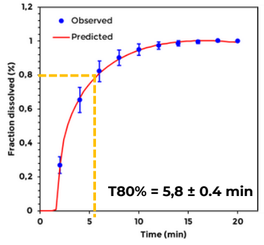


Fig. 4. Dissolution time for the center point using Peppas-Sahlin model

Setofilm®: T80% = 6 min

T80%: time to reach 80% of HCS's dissolution

Dissolution kinetics of center point and Setofilm® lead to similar results

Stability study

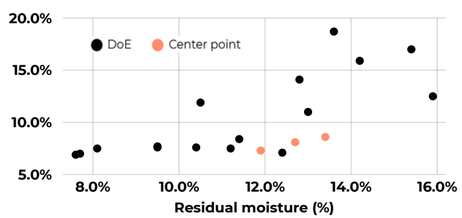
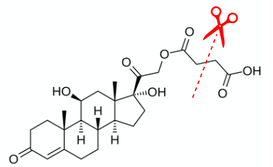


Fig. 5. HCT/HCS ratio (m/m) measured in FOD at 2.6 months



Hydrolysis:
Hydrocortisone hemisuccinate (HCS) ↓ Hydrocortisone (HCT)

HCS is more unstable in ODFs with high residual moisture

28e journées scientifiques européennes du GERPAC, 1-3 octobre 2025, Hyères, France.