T3093

Taste Masked Drugs For Pediatric Medicines Through Lipid Coating

Yvonne Rosiaux, Amandine Forest, Jean-Michel Girard, Carole Deleglise, Delphine Marchaud
Gattefossé SAS, France

CONTACT INFORMATION: yrosiaux@gattefosse.com

2017 AAPS ANNUAL MEETING & EXPOSITION

DEVELOPING SCIENCE. IMPACTING HEALTH.

PURPOSE

The need for age-appropriate formulations for the pediatric population is increasingly understood by the pharmaceutical industry. Nevertheless the development of suitable dosage forms with acceptable taste, smell and texture remains a huge challenge. Drug coating is a popular approach to provide palatability. But often efficiency is suboptimal and coating times long. **High shear mixing of potassium chloride with Precirol® ATO 5 was investigated as an alternative coating technology that enabled effective and convenient taste masking with high drug load.**

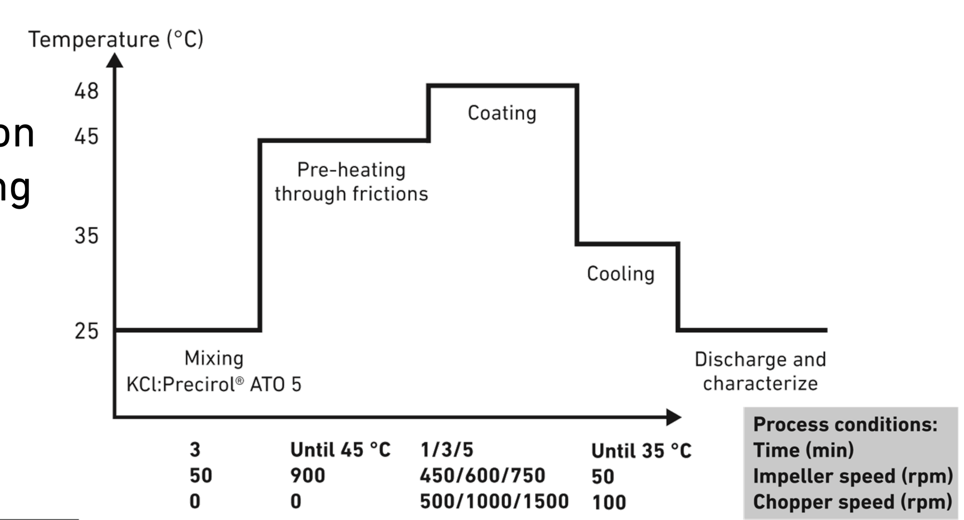
OBJECTIVES

1) Coat bitter potassium chloride with Precirol® ATO 5 for efficient taste masking to provide pediatric medicine.
2) Investigate a convenient coating technology that delivers high drug loading, easy scaling-up and reproducibility.

METHOD

A binary mixture of 80% potassium chloride (KCl, 280 g) and 20% glyceryl distearate (Precirol® ATO 5, 70 g) was placed into a 1 L (and 6 L for scale-up) high shear mixer (Diosna P1) and processed as indicated in Figure 1. Drug coating was investigated at varying impeller speed, chopper speed and coating times referring to the parameter combinations determined in a surface response experimental design (Figure 2).

Figure 1: Schematization of the high shear coating process steps.



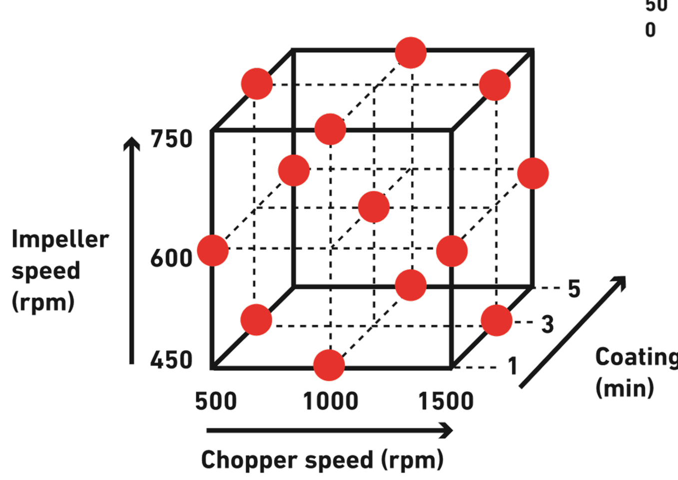


Figure 2. Box-Behnken response surface design for the investigation of effective coating parameters with Precirol® ATO 5 to mask the taste of KCl.

RESULTS

Taste masking efficacy of KCl coated with Precirol® ATO5

The drug was considered successfully taste masked using the process parameter combinations summarized in Table 1. Drug release from these samples was below the reported taste perception threshold of 0.03 M (Hough et al. 1982) corresponding to 2.2 mg/mL KCl. Drug release measurements were conducted in 3 mL of demineralized water at 37 °C under gentle stirring for 5 min.

Table 1: Process parameter combinations for efficient taste masking

Impeller speed (rpm)	450	450	450	600	600	750
Coating time (min)	3	5	3	1	5	1
Chopper speed (rpm)	500	1000	1500	500	1500	1000

Convenient coating technology

Taste masking of KCl via high shear mixing is an efficient and convenient coating technology. A binary drug:excipient mixture was coated without heating and without solvents. High drug loading of 80% was achieved with 88% of the coated particles passing the sieve of 1250 µm. Scaling-up from 350 g to 2.1 kg was readily achieved by simply adjusting the impeller speed. For example, instead of 450 rpm in the 1 L bowl the speed was set to 349 rpm in the 6 L bowl (same ratio of inertial to gravity forces of the powder blend = Froude number). Coating time and chopper speed were not altered. The process yield of the larger scale production was higher with 97% (Figure 3) and drug release was similar as shown in Figure 4. Product reproducibility could be ensured when process conditions and parameter combinations were kept the same.

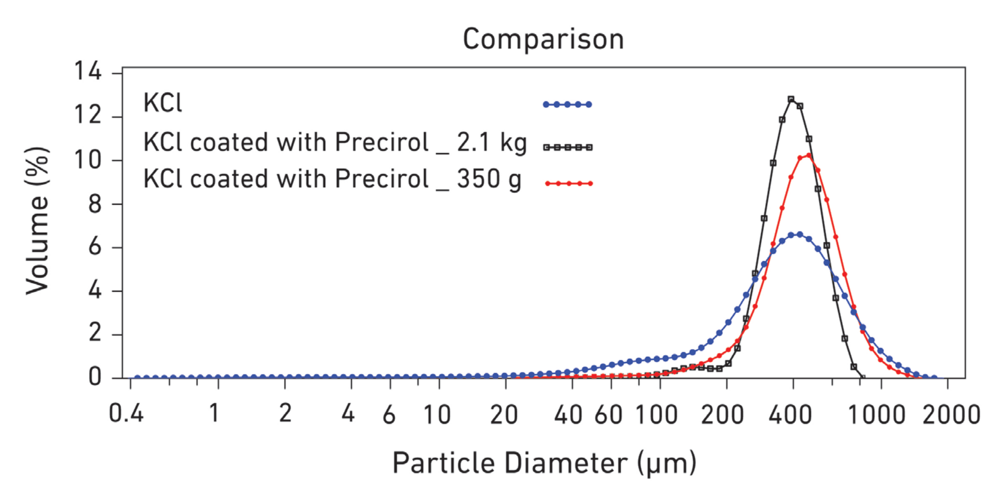


Figure 3. Particle size distribution of KCl before and after coating with Precirol® at small and larger scale and sieving through 1250 µm.

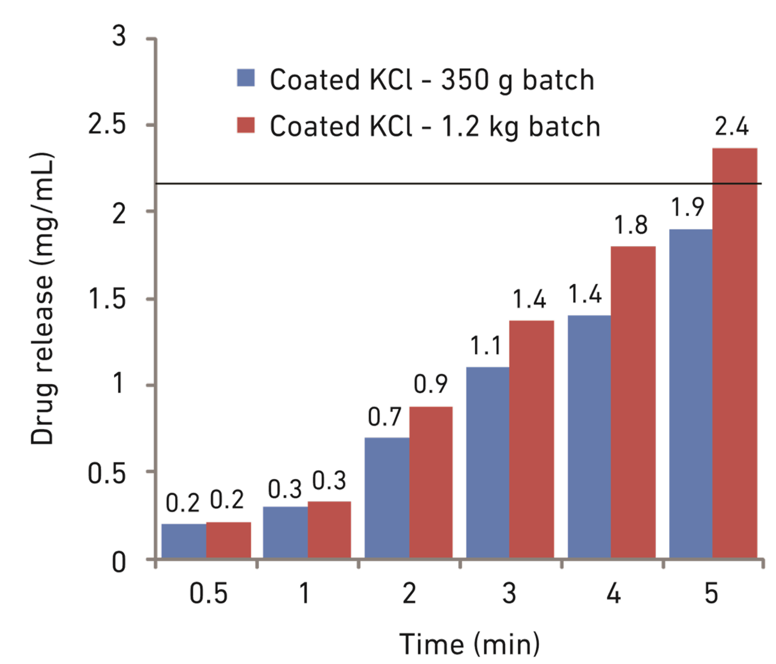
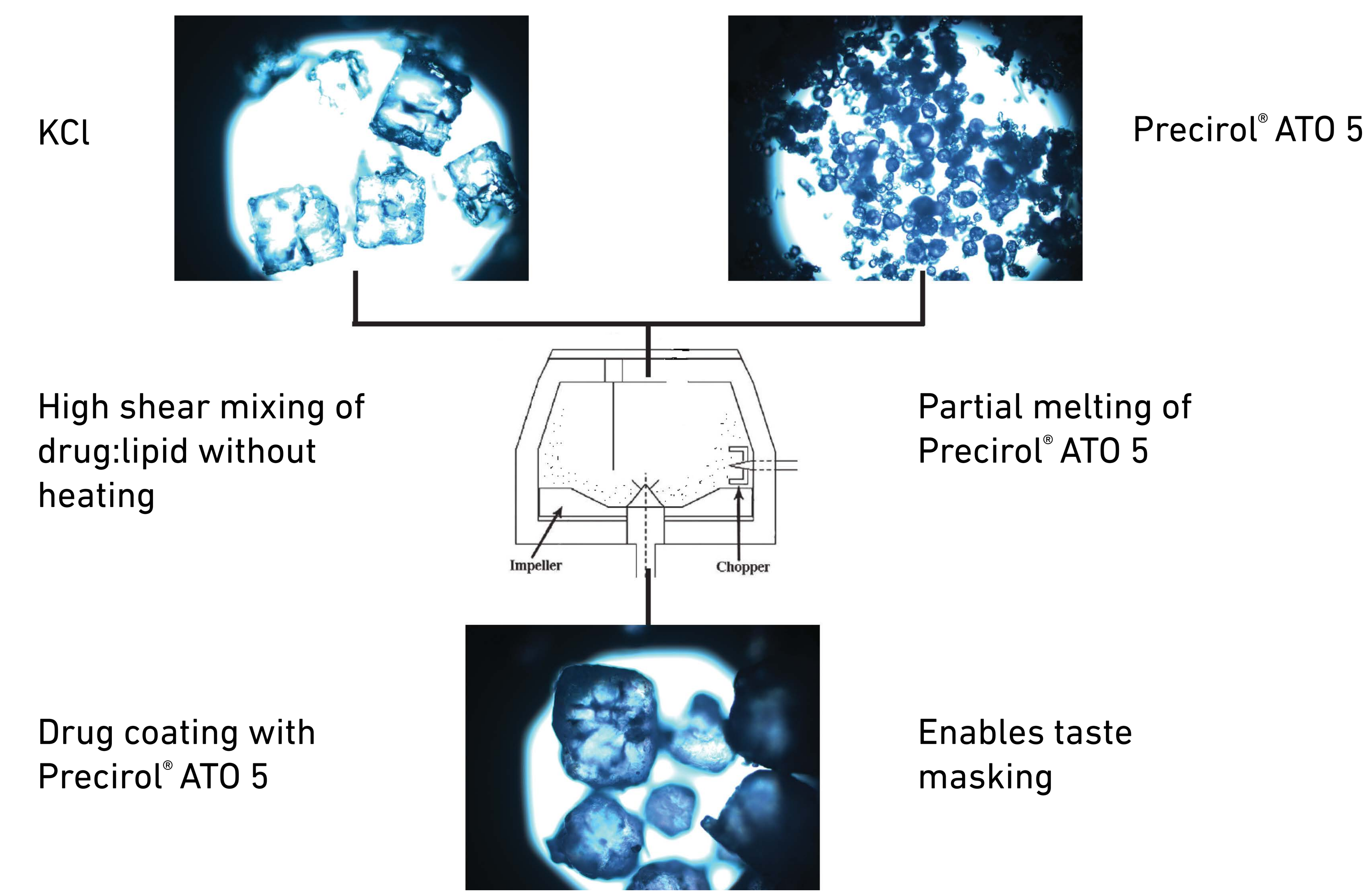


Figure 4. Comparison of drug release from KCl coated with Precirol® ATO 5 at small and larger scale (bitter perception threshold indicated by the solid line).

PRINCIPLE OF THE INVESTIGATED COATING METHOD



CONCLUSION

Child-appropriate dosage forms with acceptable taste can be formulated when a basic high shear mixer is used for taste masking. Precirol® ATO 5 was chosen due to its precedence of use in pediatric hard gelatin capsules of acetaminophen and plant extracts. Friction heat induced softening of Precirol® ATO 5 that enabled the formation of a protecting film around the bitter tasting drug particles. The absence of external heating provides a robust and simple process allowing for successful scale-up and good reproducibility. **The huge advantage of this technology lies in 1) its simplicity 2) the minimum use of excipients with high drug load and 3) the effective masking of bitter drugs.**

REFERENCE

J.S. Hough et al. (1982). Malting and Brewing Science: Hopped Wort and Beer. Volume 2. p. 849. Springer US

GATTEFOSSÉ