



HIGH SHEAR COATING: A VERSATILE TASTE-MASKING PROCESS

In this article, Cécile Morin, Technical Communication Executive, Pharmaceuticals, and Yvonne Rosiaux, PhD, Innovation Application Manager, both of Gattefossé, discuss taste-masking, covering the advantages of Precirol® ATO 5 and how Gattefossé’s high shear coating process presents an appealing alternative to standard fluid bed techniques.

INTRODUCTION

Many processes exist to circumvent the bad taste of drugs (Figure 1). As such, the challenge for formulators looking to taste-mask a drug is finding the most appropriate method to do so.^{1,2}

The process of coating a drug consists of building a physical barrier onto the drug particles with a film coating, which can be polymer or lipid based. The coated particles

can then be used in sachets or capsules, or transformed into tablets.

The primary advantage of using a lipid-based coating over polymer-based one is that, with lipids, organic solvent and water are absent during the coating process. The preferred lipid for this coating process is Precirol® ATO 5 (glyceryl distearate), due to its moderate melting point and rapid recrystallisation. Moreover, it has US FDA GRAS status and precedent for use, including in paediatric dosage forms.

Using a fluid-bed coater for lipid coating is a well-known technique.^{3,4} The process consists of fully melting Precirol® ATO 5 and spraying it on the drug

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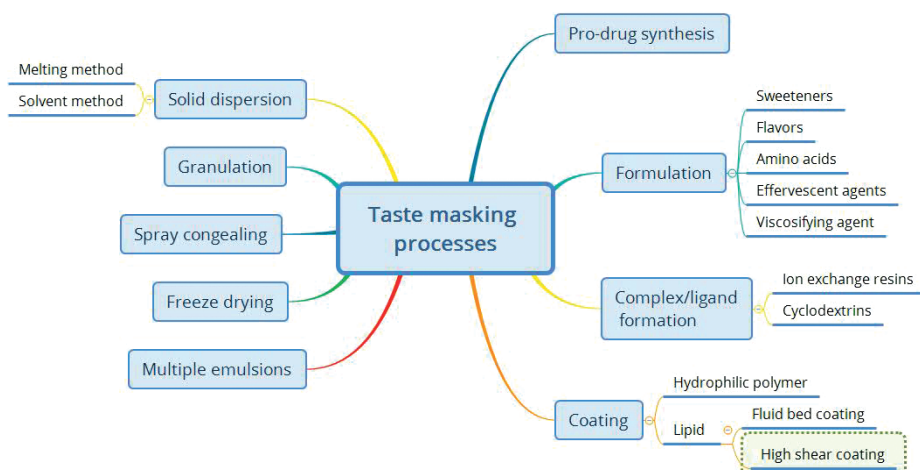


Figure 1: Different taste-masking processes.



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particles. However, insulation of the pipes and the nozzle is required to prevent early lipid crystallisation. As such, Gattefossé aimed to develop a simpler process for taste masking, using a standard high shear coater and Precirol® ATO 5, whereby partial melting of the lipid excipient is driven by sufficient friction of the powders in the bowl, obtaining a thin and homogeneous film around the drug particles.

A SIMPLE PROCESS

For this new taste-masking process, Gattefossé used:

- A conventional high shear coater, without an external heating or cooling system
- A simple binary formulation of 80% API and 20% Precirol® ATO 5.

The high shear coater is equipped with an impeller and a chopper. The impeller drives the powders in the bowl into motion and, at high speed, generates inter-particle friction, thus producing heat. This heat then partially melts the Precirol® ATO 5, which covers the drug particles. During the process, the chopper prevents agglomeration of the particles.

There are four steps in this process:

1. The binary mixture of 80% API and 20% Precirol® ATO 5 is homogenised at low impeller speed (50 rpm) for three minutes at ambient temperature.
2. The impeller speed is increased to 900 rpm, generating friction and heat. When the process temperature reaches 45°C, impeller speed is reduced to 450 rpm and the chopper is started (500 rpm).
3. Once the process temperature reaches 48°C, effective particle coating with the partially molten lipid begins. Coating lasts 3 minutes.

HSC conditions	FBC conditions
Binary formulation 80% KCl/20% Precirol® ATO 5	Binary formulation 80% KCl/20% Precirol® ATO 5
High shear blender (Diosna P1), 1 L bowl	Top-spray fluid-bed coater (GPCG 1.1, Glatt,)
Mixing of drug and Precirol® ATO 5 at 50 rpm for 3 min.	Fluidisation of the drug powder for 10 min until the product temperature reaches 42°C.
Generation of friction heat with high impeller speed (900 rpm) until the product temperature reaches 45°C.	Precirol® ATO 5 is melted, maintained at 100°C and sprayed
Coating for 3 min at 48°C; impeller speed: 450 rpm; chopper speed: 500 rpm.	Spray rate: 10 g/min
	Atomisation air: 100°C
	Atomisation pressure: 2.5 bar
	Air flow rate: 18 m ³ /h
	Spray nozzle diameter: 0.8 mm; lowest position

Table 1: HSC and FBC process conditions for KCl coating.

4. The process is subsequently cooled down by simply reducing the impeller speed to 50 rpm, to reduce friction, and chopper speed to 100 rpm, to prevent pack formation. Consequently, the temperature decreases leading to the recrystallisation of the lipid on the surface of the drug particles. At 35°C, Precirol® ATO 5 is fully recrystallised in a solid and homogenous film. The coated particles are then removed for further characterisation and processing into finished dosage forms.

The ideal coating temperature is 48°C. At this temperature about 15% of Precirol® ATO 5 is in a molten state. If the temperature exceeds 48°C, caking or granulation of particles may occur due to a higher fraction of molten lipid excipient, leading to granules.

AN EFFICIENT PROCESS

To demonstrate the efficiency of high shear coating (HSC) versus fluid bed coating (FBC), Gattefossé used KCl as a model drug.

KCl has a strong bitter and salty taste. The process conditions are described in Table 1.

Scanning electron microscope (SEM) pictures of pure versus coated KCl particles (Figure 2) show effective coating with both HSC and FBC techniques. Before coating the particles exhibit cubic structures with sharp edges. After HSC, particles have rounded edges due to the lipid coating. With FBC, the coating is less smooth than with the high shear process.

To demonstrate that high shear coating is masking the taste of the drug effectively, Gattefossé used two assays: a dissolution test and a human panel assessment.

The taste perception threshold for KCl is 0.03 M,⁵ corresponding to 2.2 mg/mL. Drug dissolution exceeding this limit is indicative of KCl's bad taste being detectable, i.e. an ineffective taste-masking process. The drug dissolution was assessed for five minutes in 3 mL at 37°C. Both HSC and FBC were shown to be efficient taste-masking processes since the released drug was well below the taste detection threshold (Figure 3).

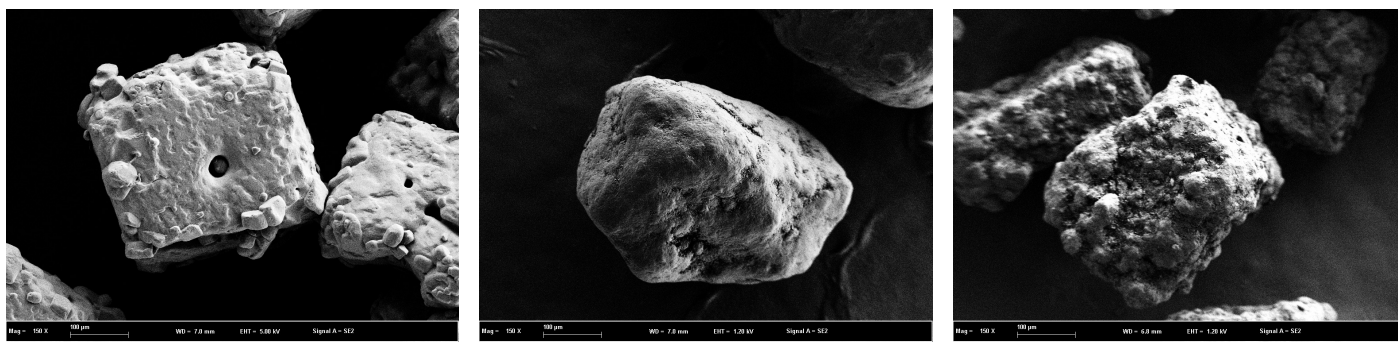


Figure 2: SEM pictures of uncoated and coated KCl particles (magnification: 150). Left: Uncoated KCl; Middle: HSC KCl particles; Right: FBC KCl particles.

“For drugs generating high friction, the impeller speed must be reduced from 900 to 450 rpm when the temperature reaches 42°C (instead of 45°C). This prevents exceeding the ideal coating temperature of 48°C.”

A human taste panel evaluated the uncoated and coated KCl particles using a standardised procedure. The different attributes and their definitions used for the sensory evaluation are listed in Table 2. Each attribute was scored on a scale from 0 (best) to 10 (worst).

The assessors placed the test product on the middle of their tongues. Initial impact was assessed immediately. For the next 20 seconds, assessors ranked the taste, flavour and mouthfeel. After rinse off, aftertaste and afterfeel were scored.⁶

Both processes were demonstrated to be efficient methods for taste masking. They dramatically reduced the unpleasant initial impact, the salty and bitter taste and generally had a positive impact on mouthfeel and aftertaste (Figure 4).

The results of the human taste panel corroborate with drug dissolution and confirm that both processes are efficient for taste-masking KCl.

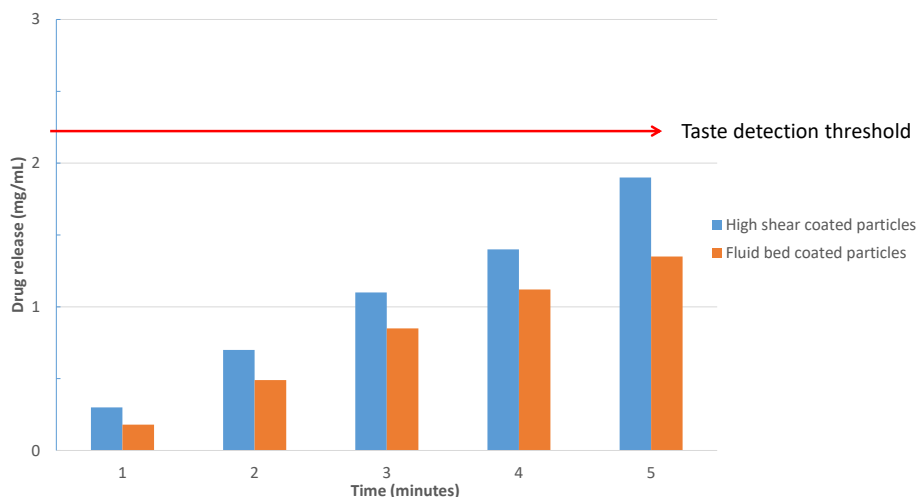


Figure 3: Drug release from coated KCl particles below the taste detection threshold.

Attribute	Modality	Definition
Initial impact	Initial taste, flavour and mouthfeel	The combined intensities for all perceived tastes/flavours/mouthfeels
Salty	Taste/aftertaste	The basic bitter taste associated with NaCl
Bitter	Taste/aftertaste	The basic bitter taste associated with caffeine
Tongue numbing	Afterfeel	A feeling of decreased or loss of sensation on the tongue
Gritty	Mouthfeel	Amount of gritty/grainy particles in the mouth
Tingling	Mouthfeel	A tingling and burning sensation on the tongue and mouth
Astringent	Mouthfeel	A drying, puckering and shrinking sensation in the oral cavity causing contraction of body tissues.

Table 2: Descriptive vocabulary and definitions used by the assessors.

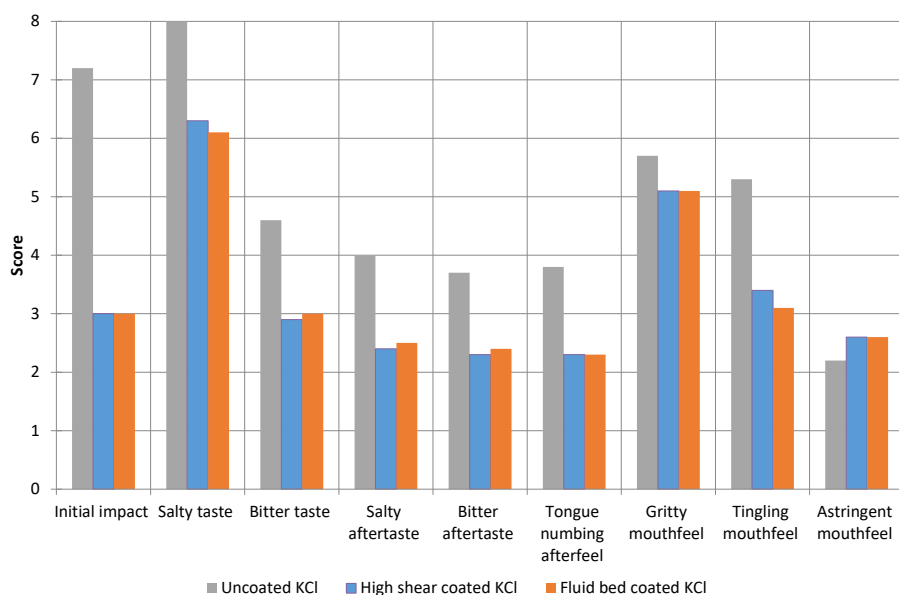


Figure 4: Human taste panel assessment.

A VERSATILE PROCESS

To assess the versatility of the HSC taste-masking process, different APIs were coated (Figure 5). Although the particles were very different in crystalline shape, melting point, mean diameter, particle size distribution and density, they were successfully coated with this process.

It was observed that the generation of friction heat depends on the drug’s physical properties (density, size, shape). Particles with high density and large contact surface area generate more friction heat than particles with low density and small contact surface area.

For drugs generating high friction, the impeller speed must be reduced from 900 to 450 rpm when the temperature reaches 42°C (instead of 45°C). This prevents exceeding the ideal coating

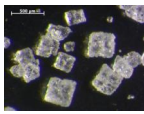
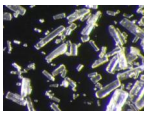
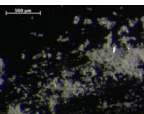
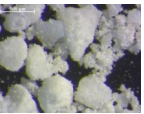
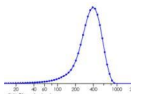
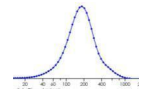
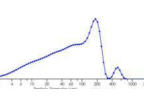
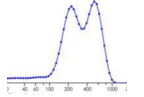
Drug	KCl	Isoniazid	Paracetamol	Ranitidine HCl
Crystalline structure				
Melting point (°C)	770	171	169	140
Mean diameter (µm)	370±150	205±130	100±100	330±220
Particle size distribution				
Density (g/mL)	2.0	0.7	0.3	0.6
Time to reach 42–45°C (min)	25	11	48	21

Figure 5: Properties of the different drugs used for taste masking.

temperature of 48°C. Granulation before initiating the HSC process is recommended for particles with low density and small contact surface to reduce the time required to reach 42–45°C. This was the case with the paracetamol grade used.

SUMMARY

Taste-masking with the HSC process presents many advantages over other techniques due to the following factors:

- Use of conventional equipment
- Absence of organic solvents or water in the formulation and during the process
- Low temperature
- Limited number of process parameters to control.

In conclusion, it is a very simple process with a proven efficiency in different model drugs.

ABOUT THE COMPANY

Gattefossé is a leading provider of lipid excipients and formulation solutions to healthcare industries worldwide, with an in-depth knowledge of lipid excipient physicochemical and functional properties. The company has an international network of technical representatives and Technical Centers of Excellence in the US, France, India and China. Gattefossé provides bespoke technical and regulatory support to accelerate drug development.

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ABOUT THE AUTHORS

Cécile Moran is a food engineer with a long experience in communication in the areas of food, pharmaceutical and cosmetic ingredients. At Gattefossé, she is in charge of print and digital communication for pharmaceuticals.

Yvonne Rosiaux obtained her PhD in pharmaceutical technology in 2011 at the University of Lille, France. At Gattefossé her role is to pilot the application laboratory programme in solid oral dosage forms, which covers solubility and bioavailability enhancement, modified release and taste-masking, among others. Her team investigates the performance of lipid excipients in processes such as hot melt extrusion, melt coating, melt granulation etc.