A Quality by Design Approach for an Immediate Release Hot Melt Coating (HMC) Formulation with Taste Masking Properties

Raphael Janousek, M.Sc., Project Manager; Dr. Mahmud Yunis, Technical Director; BIOGRUND GmbH, Neukirchner Str. 5, 65510 Huenstetten, Germany

Introduction

The reduction of process time is the key driver for cost effective manufacturing of novel pharmaceutical or nutraceutical products. In the past years, R&D specialists started to look for alternative ways to protect their active pharmaceutical ingredients (APIs) from moisture or ways to alter the properties of the dosage form. Besides the immense growth of different film coating formulations like AquaPolish®, formulators have started to apply novel technologies like hot melt coating (HMC) to obtain the desired results [1].

A quality by design approach using HMC allows modification of the dissolution profile of APIs with additional moisture protection or taste masking properties.

In this white paper, we will provide useful information on the general coating process with HMC, demonstrate the advantages of HMC and show the results of a case study for a quality by design approach of a HMC formulation for immediate release with taste masking properties.

HMC Process

HMC is a process of applying fatty or waxy components onto solid particles and it is applied using fluid bed technology. Traditionally, a film coating suspension is pumped through a nozzle and enters the fluid bed reactor, where particles or powders are held in a fluidized state using inlet air, whereas HMC uses melted waxes or fats instead of a coating suspension. The main difference to a film coating application using fluidized bed technology is the obligation to melt the waxes/fats and sustain the melting throughout the coating delivery into the reactor (see Figure 1) [2,3]. This is achieved through a heated container and heated pipes and feeding pump. The applied temperature depends on the used coating formulation and is sustained at temperatures of max 10-15 °C above the melting temperature of the formulation, in order to avoid unnecessary heat stress to the API.

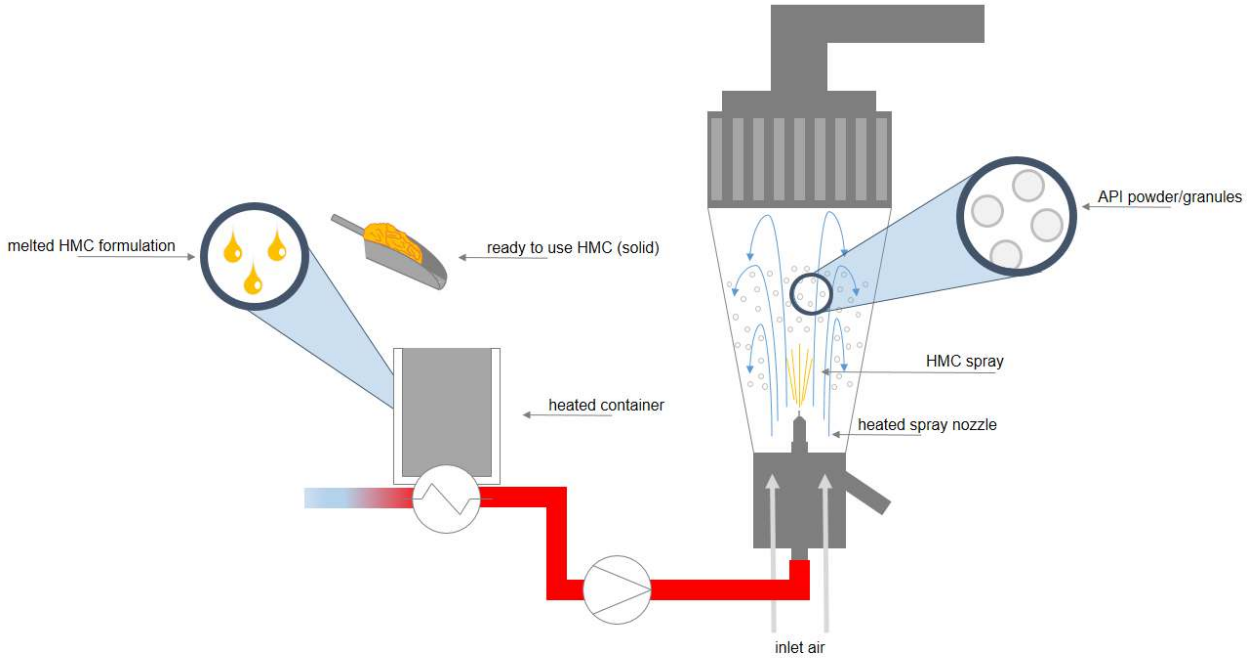

Figure 1: General Process of HMC using fluidized bed technology

BonuWax®

The ready-to-use excipient premix BonuWax® is a combination of waxes and fats for HMC applications (see Figure 2). BonuWax® is applied via fluid bed coating technology and can be sprayed at 100% solid content, yielding in high productivity. HMC using BonuWax® can be used for coating of mini tablets, granules or powders for pharmaceutical and nutraceutical products. Individual ingredients are carefully selected and combined for a tailor made solution that is designed to achieve the desired properties of the final coating. This allows the combination of multiple excipients and their individual advantages.

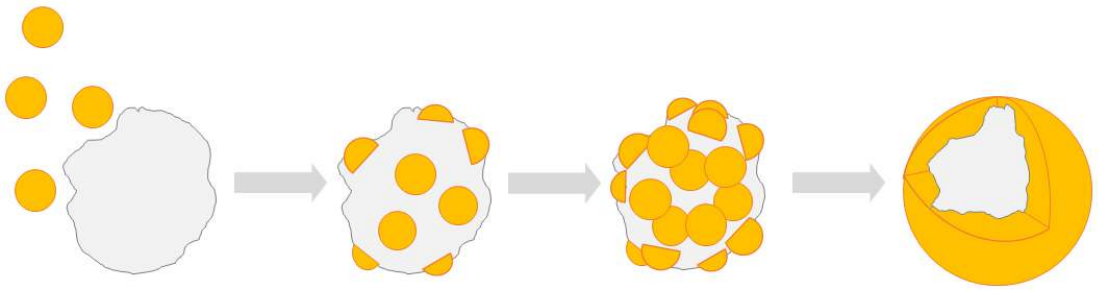

Figure 2: Stepwise formation of a HMC onto solid particles using BonuWax®

Advantages of BonuWax® for HMC

Moisture barrier

The protection of APIs from moisture is an integral part of modern coating formulations that can be achieved through the application of lipophilic excipients. While such lipophilic compounds must be added to common film coating formulation in order to generate a moisture barrier, the waxy or fatty nature of the main HMC components inherently serves the same purpose without any need for further additives [4]. In addition, HMC poses another main advantage for moisture sensitive APIs. As HMC formulations are melted in order to enable a continuous spray and thus, the process is solvent free (both, water and organic), no additional moisture is added to the process. Hence, moisture sensitive APIs can be encapsulated with a minimized risk of water absorption.

Taste masking

As the mode of action is the main driver for drug design, unpleasant or bitter taste of APIs might be accompanying effects. In order to enhance patient compliance, taste-masking formulations are required [5]. Taste masking properties of solid oral dosage forms can be achieved through the application of coatings that entail sweeteners, flavoring or novel excipients. However, chewable dosage forms might be required, to increase compliance of patients that have difficulties swallowing or to speed-up resorption of APIs.

This can be achieved by creating a hydrophobic coating layer such as HMC. Consequently, the API will not directly be released in the patient's mouth after oral application, which will hinder the perception of an unpleasant taste.

Fast release vs. modified release

Depending on the used waxes and fats, the dissolution profile of APIs can be altered using the right HMC formulation [1]. Although the general lipophilicity of waxes and fats is rather related to a slow and sustained release, quality by design formulations can also yield to a short lag phase, followed by immediate release of the API. Therefore, taste-masking properties will not be sacrificed for a fast release of active compounds.

Direct compression

The use of BonuWax® for powders can have several advantages. Besides the use of HMC for powders or granules in dosage forms like Sachets, HMC with BonuWax® also allows direct compression of the final granules with simultaneous modification of the general properties. Hence, BonuWax® can be designed in order to enable immediate release or any form of modified release, taste masking or moisture sealing without additional film coating of the produced tablets.

Fast Process

HMC using BonuWax® combines multiple advantages that directly apply to reduced processing time and hence, increased productivity and lower costs. Since HMC is a solvent free technology, BonuWax® can be sprayed at 100% solid content, leading to a fast formation of the coating layer and an overall faster process. Thus, process-times can be as low as 30-60 min, reaching up to 50% weight gain (wg). Due to the application of HMC without any solvent, there is also no risk of too much moisture in the process. Furthermore, solidification of the coating is instantly achieved after cooling, which circumvents long drying times that can be observed for some traditional film coatings or sugar coatings [2].

Clean-label solutions

The selection of suitable raw materials allows the formulation of ready-to-use HMC that is suitable for nutraceutical products such as some BonuWax® types. Moreover, application of ingredients like beeswax or carnauba wax can also support clean-label approaches without sacrificing the advantages of HMC.

Case study of BonuWax® for HMC with taste masking and immediate release

A total of eight different formulations using twelve individual raw materials were developed and sprayed at 20% and 50% wg onto ibuprofen granules using fluidized bed technology (see Figure 4). The granules were tested for content, actual wg, particle size distribution, shape, taste masking and dissolution.

HMC was applied using a Romaco Innojet (Steinen, Germany) Ventilus V 2.5 with a Romaco Innojet hot melt System IHD-2.5 (see Figure 3). 300 g of granulized ibuprofen (Ibuprofen DC85, BASF, Ludwigshafen am Rhein, Germany) were presented in the fluidized bed reactor and coated until 50% theoretical wg were reached. Additional samples were withdrawn at 20% wg.

The quality of the obtained granules was evaluated regarding the dissolution profiles and a double blind tasting, considering general texture/mouth feel, taste, and time of the subjective lag phase of the taste masking effect. Participants were asked to rate the coating regarding taste masking on a scale from 1-5 (1 = excellent; 5 = poor).

Figure 3: Romaco Innojet Ventilus V 2.5 (right) with a Romaco Innojet hot melt System IHD-2.5 (left)

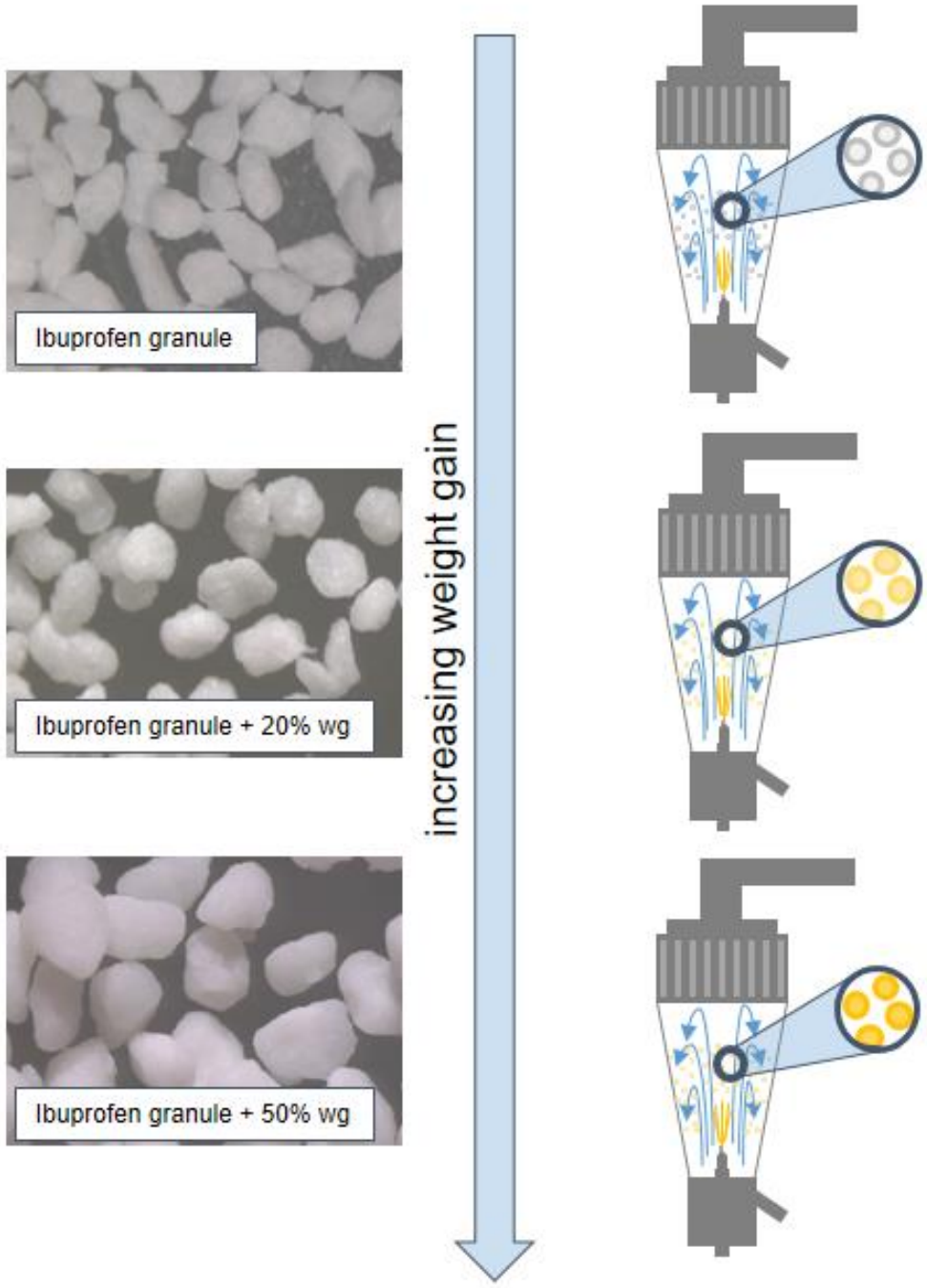

Figure 4: Flow chart of gradual application of HMC onto Ibuprofen granules

The dissolution profiles of Ibuprofen granules with 20% and 50% HMC were compared to the Ibuprofen granules without coating. All formulations allowed dissolution of < 85% API after 45 min, hence making all formulations suitable for immediate release applications. Four coating formulations showed excellent modifications of the dissolution profile in the first 5 min, which – in combination with the average dwell time in the mouth – can be translates to the probability of good taste masking properties. However, subjective evaluations during the tasting identified the best candidate for taste masking with an average

score of 1.3 at 50% wg. Figure 5 shows the dissolution profile of the API coated with this HMC formulation. While 20% wg did not lead to a significant lag phase in the first 5 min, application of a higher wg allowed a nice lag phase, followed by a just slightly shallower slope for the dissolution compared to uncoated Ibuprofen. However, subjective evaluation of the taste masking properties at 20% wg still yielded at an average score of 2.6, demonstrating the general taste masking suitability of this formulation.

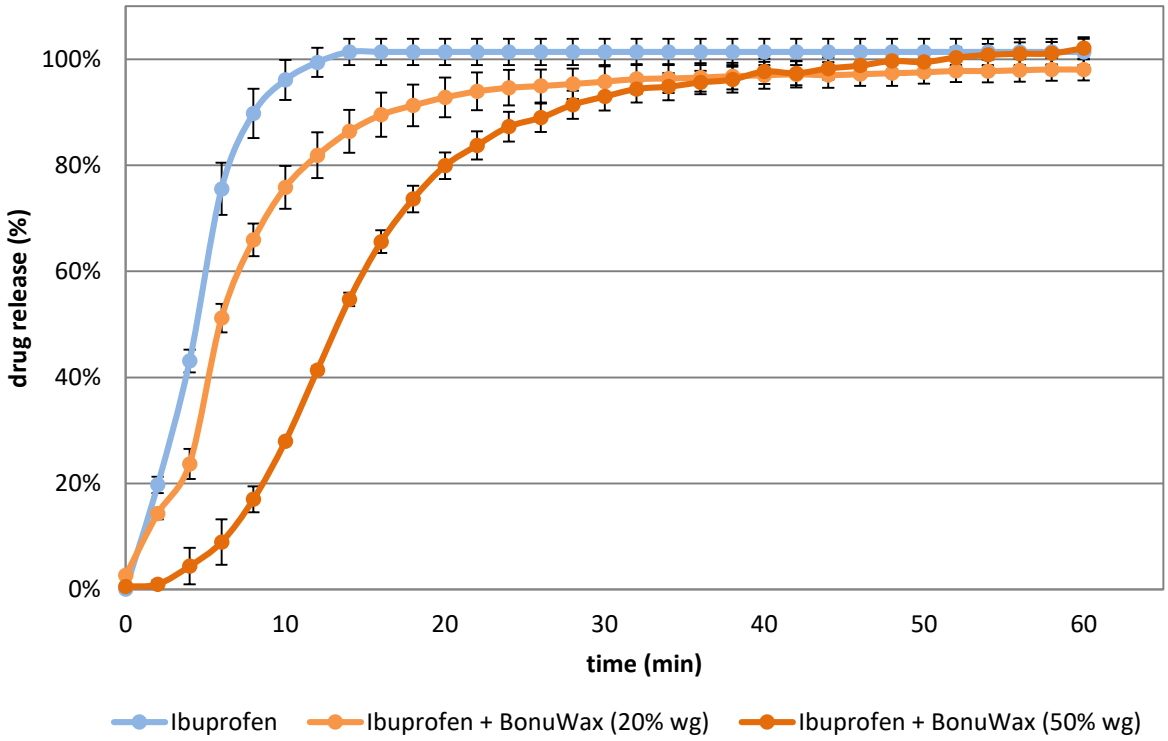

Figure 5: Dissolution profile of uncoated ibuprofen granules (blue), Ibuprofen granules with 20% wg HMC (light orange) and Ibuprofen granules with 50% wg HMC (dark orange)

Conclusion

The presented data shows the importance of a quality by design approach to identify the best formulation for a given task. In this study, we identified several HMC formulations that enable the alternation of the API dissolution within the first 5 min, without creating a sustained release. However, actual tasting of the formulations enabled an identification of the best fit for purpose formulation amongst these four formulations.

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