

Soft Gel Enteric Coating Using Methacrylic Acid - Ethyl Acrylate Copolymer

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PURPOSE

Unlike the conventional tablet enteric coating, soft gel enteric coating always presents a significant challenge due to the physicochemical properties of the gelatin shell. The bed temperature of the coating pan should be low due to the low melting point of the gelatin, while the water-soluble nature of the gelatin shell makes soft gels easy to agglomerate during low temperature pan coating. The enteric polymer selection and the plasticizer amount are crucial to the success of the enteric soft gel coating. An anti-tacking agent, such as GMS or talc is usually recommended to mix with the plasticized enteric polymer before spraying. Previous studies¹ demonstrated Kollicoat[®] MAE 30DP, an aqueous dispersion of methacrylic acid and ethyl acrylate copolymer, is an excellent polymer for soft gel enteric coating.

Kollicoat[®] MAE 100-55 is a newly developed powder form of methacrylic acid and ethyl acrylate copolymer². The current study investigated the enteric film properties of Kollicoat[®] MAE 100-55 during soft gel coating, compared to those coated with Kollicoat[®] MAE 30DP without the addition of an anti-tacking agent.

METHODS

Neutralization of Kollicoat[®] MAE 100-55 was conducted by adding 6 mol % of 1N NaOH slowly into the Kollicoat[®] MAE100-55 powder suspension and mixing for 30 minutes. The plasticizer Triethyl citrate (TEC) (15% based on polymer) was added to the suspension and mixed for two hours to increase the flexibility of the film. Kollicoat[®] MAE 30DP was used directly by mixing with the same percentage of TEC.

To facilitate the comparison, the polymer content and the total solid content of the final coating suspension remained the same for both formulations.

The fish oil soft gel capsules (size 20 oval) were purchased from NBTY. An O'Hara LabCoat System was used for the soft gel enteric coating. A comparative study was conducted under the same process parameters (Table 1) to coat the same lot of fish oil soft gel capsules using three different lots of Kollicoat[®] MAE100-55 and one lot of Kollicoat[®] MAE 30DP.

Table 1 Coating parameters for O'Hara 10.5" pan

Parameter	Data
Batch size	700 gram of fish oil soft gel capsules
Coating Pan Diameter	10.5 inches
Inlet Air Volume	70 CFM
Inlet Air Temperature	45 °C
Exhaust Temperature	30 °C
Atomized Air Pressure	16 psi
Pattern air pressure	15 psi
Spray Rate	4 - 6 g/min
Pan Speed	18 RPM
Coating Weight Gain	5%, 10% and 15%

After the targeted coating weight gain was reached, a post waxing procedure was conducted by dispersing the melted carnauba wax slowly onto the enteric coated soft gels bed while tumbling.

A modified USP disintegration method was used to assess the effectiveness of enteric film coating. To evaluate the integrity of the film coating, the coated fish oil soft gel capsules were tested in triplicate under 37 °C in 0.1N HCl medium for one hour. The soft gels were then removed from the tester and blotted dry before weighing. The acid uptake was measured by the weight difference before and after the disintegration test. The disintegration time in pH 6.8 phosphate buffer was also measured in triplicate, and the average time was recorded as the disintegration time.

The enteric coated fish oil soft gels (20 capsules) were placed in an open dish condition under high humidity (room temperature / 75%RH) for one week to study the degree of agglomeration. The appearance and agglomeration was examined.

RESULT(S)

Three lots of Kollicoat[®] MAE 100-55 were evaluated. Coating processes were very smooth with good uniformity. All showed the same coating properties. The seams were well coated. No bubbles or stripes were observed in the films, indicating a good adhesion between the enteric films and the soft gel surfaces.

Upon controlling the process conditions and polymer /plasticizer ratio, no soft gels had agglomerated or had stuck-on-the pan, even though an anti-tacking agent was not used during the enteric coating. There was also no observed tubing or nozzle logging during the coating process.

The coating process for Kollicoat[®]MAE 30DP was very similar to Kollicoat[®] MAE100-55. From the coating process point of view, no difference was observed when using these two dispersions for soft gel coatings.

The average acid liquid uptake during one hour disintegration test in 0.1N HCl showed very similar results among those coated with three lots of Kollicoat[®] MAE100-55, as well as those coated for Kollicoat[®] MAE 30DP. The liquid uptake decreased as the coating level increased. The maximum acid uptake for all coated capsules is less than 1.5%, which is very good for large soft gels (Figure 1).

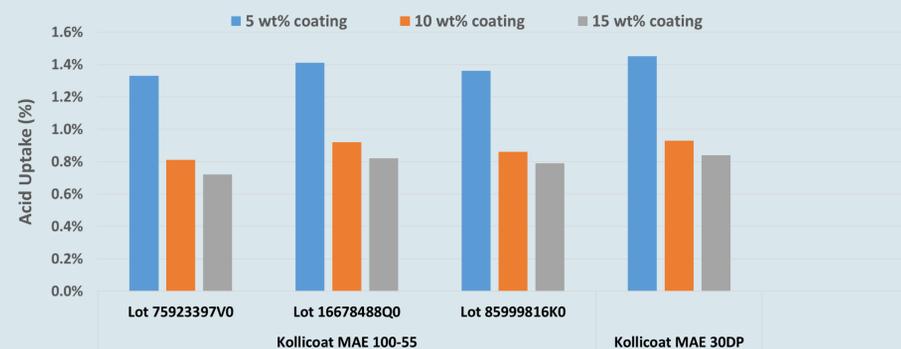


Figure 1 Acid uptakes in fish oil soft gels after disintegration in 0.1N HCl

The disintegration time for uncoated soft gels in pH 6.8 phosphate buffer is about 10 minutes. All the coated samples showed some delay before total disintegration in buffer.

The higher the coating level, the longer the disintegration time (Figure 2). The soft gels with the highest coating level disintegrated in approximately 17 minutes.

The agglomeration test samples under 75% RH were removed from the desiccator after one week. The dish was tilted at a 30-degree angle to check the movement of the soft gels. All the capsules flowed individually out of the dish. No agglomeration and appearance change was observed, indicating a stable short term stability. The post waxing process demonstrated a good approach for increasing storage stability.

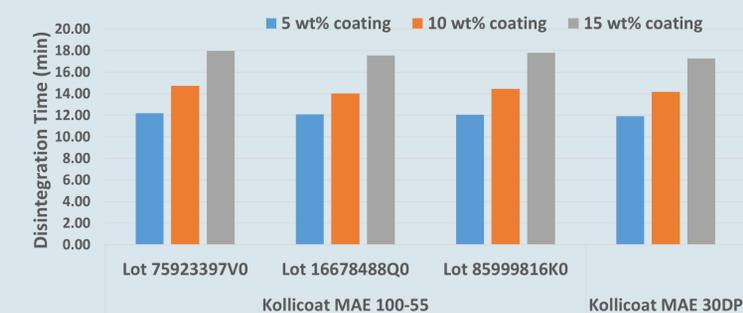


Figure 2. The disintegration time in pH 6.8 phosphate buffer

CONCLUSION(S)

The current study showed Kollicoat[®] MAE100-55 is an excellent polymer for soft gel enteric coating. The redispersion of Kollicoat[®] MAE100-55 is a simple and quick procedure without any dust generation. 5% coating level is sufficient to provide an effective enteric coating, which had a low acid uptake, and would not dissolve in 0.1N HCl medium. The film coating properties of Kollicoat[®] MAE100-55, including the film adhesion, uniformity, tackiness, acid uptake, disintegration time, and short term high humidity stability, was equivalent to Kollicoat[®] MAE 30DP. It was shown that an anti-tacking agent, either GMS or talc, was not required under the process conditions employed.

REFERENCE

1. K.Zhuang, Evaluation of lipophilic monoglycerides in enteric coating to provide further moisture protection for soft gelatin capsules, AAPS Poster, 2012
2. Kollicoat MAE 100-55 —A complete match — just better, BASF Product Launch Presentation / Communication, 2016