Evaluation of Lipophilic Monoglycerides in Enteric Coating to Provide Further Moisture Protection for Soft Gelatin Capsules

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Introduction

Soft gelatin capsules coated with Methacrylic acid copolymer have a tendency to agglomerate during storage, especially in a humid environment. Reducing the moisture absorbed by the coated capsules can eliminate the agglomeration tendency[1]. It was shown that the addition of Glycerol Monostearate (GMS) to a Methacrylic coating could further reduce the moisture absorption by the coated soft gelatin capsules[2]. Beside GMS, there are many emulsifiers commonly used in food and pharmaceutical industries, such as the monoglycerides that can be evaluated for the same purpose. The object of this study is to evaluate whether other lipophilic monoglycerides commonly used in food can be used as an alternative to GMS in a Methacrylic acid copolymer coating dispersion (Kollicoat® MAE 30DP) to provide further moisture protection for soft gelatin capsules.

Objectives

- To evaluate lipophilic monoglycerides in Kollicoat® MAE 30DP coating dispersion for their function as moisture barrier.
- To develop a suitable process for incorporating the lipophilic monoglycerides in Kollicoat® MAE 30DP.
- To optimize the coating formulation to achieve the maximum level of moisture protection.

Materials

- Kollicoat® MAE 30DP, BASF (Florham Park, NJ)
- Fish oil 1000mg capsules, Capsulework (Ronkonkama, NY)
- Triethyl Citrate (TEC), Vertellus (Greensborough, NC)
- Acetylated Monoglycerides (AMG), Riken Vitamin Co.
- Glyceryl Monooleate (GMO), BASF (Florham Park, NJ)
- Glyceryl Monostearate (GMS), (Norristown, PA)
- Oleic acid, BASF (Florham Park, NJ)
- Other ingredients used as received

Methods

Soft gelatin capsules were coated in a Thomas Accela-coater equipped with a 15" perforate pan. The coating condition is shown in Table 1. Disintegration test in simulated gastric fluid at 37°C for 1 hour was used to access the integrity of the film. The coated capsules were placed in an open dish over saturated NaCl salt solution (75% relative humidity at room temperature, RT/75%RH) for one week. Moisture pick up by the capsules was accessed by drying the emptied shells in a 40° C oven for 4 days.

Inlet air volume	150 CFM
Inlet air Temperature	35 - 40°C
Exhaust air temperature	25 - 26°C
Actual bed temperature (measured by a infrared gun)	23 - 24°C
Pan speed	19 rpm
Spray rate	8 g/min
Atomize air	30 PS

Table 1. Process parameters for coating of soft gelatin capsules with Kollicoat® MAE 30DP

Results and Discussion

Incorporation of the lipophilic monoglycerides into the aqueous Kollicoat® MAE 30DP

To incorporate the lipophilic monoglycerides into an aqueous coating dispersion, the oily monoglycerides first need to be converted to emulsions. The emulsion was then added to Kollicoat® MAE 30DP to make up the final coating dispersion. Polysorbate 80 is used as the emulsifier for this purpose. The optimum range for Polysorbate 80 is from 25% to 100% of the monoglyceride weight, depending on the types of monoglycerides. Table 1 shows the formulation for initial trials. 5% lipophilic monoglyceride (based on the dry polymer weight of Kollicoat® MAE 30DP) was added to the formulation. GMS is solid wax compared to other liquid monoglycerides. It cannot be incorporated into the coating dispersion with simple mixing. Figure 1 shows the procedure for preparing the coating dispersion with GMS.

	W/O monoglycerides [%]	With AMG [%]	With GMS [%]	With GMO [%]
Kollicoat® MAE 30DP	55.50	55.50	55.50	55.50
Triethyl Citrate	2.50	2.50	2.50	2.50
AMG	—	0.83	—	—
GMS	—	—	0.83	—
GMO	—	—	—	0.83
Polysorbate 80	—	0.83	0.83	0.21
Water	42.00	40.34	40.34	40.96
Total	100.00	100.00	100.00	100.00

Table 2. Kollicoat® MAE 30DP coating formulations with different monoglycerides for fish oil soft gelatin capsules

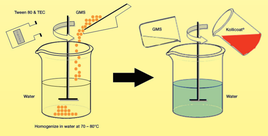

Figure 1. Preparation of Kollicoat® MAE 30DP coating dispersion with GMS

Moisture barrier effect of Kollicoat® MAE 30DP containing the monoglycerides

Soft gelatin capsules are known to absorb moisture during storage. This may cause the capsules to agglomerate and compromise their stability during storage. A moisture protective coating can provide a better stability for these capsules.

Uncoated fish oil capsules can absorb moisture up to 24% of its shell weight when stored in high humidity conditions (room temperature, 75% relative humidity). The capsule shells stored at ambient conditions normally only contain 6 – 7% moisture. When the capsules are coated with Kollicoat® MAE 30DP, the moisture absorption tendency is greatly reduced. GMS has been used to replace talc as the anti-tack agent for Methacrylic coating dispersions. It was previously shown that fish oil capsules coated with Kollicoat® Smartseal 30D containing GMS can further reduce the moisture absorption[3]. The same effect of GMS was tested with Kollicoat® MAE 30DP. Figure 2 shows the moisture uptake by the capsules coated with Kollicoat® MAE 30DP with and without GMS. It is clear that, due to its lipophilic nature, GMS can help further reduce the moisture absorption by the soft gelatin capsules. This will help enhance the stability of coated capsules during storage. The data also show that the higher the level of coating, the better the moisture barrier effect.

GMS is hard to process into the coating dispersion. A similar monoglyceride in liquid form would be much easier to incorporate into the coating dispersion. GMO and AMG were then tested to see whether they could provide the same benefit. Figure 3 shows the moisture uptake by the capsules coated in these formulations. The results show that both formulations reduced the moisture uptake, but GMO is a better moisture barrier that AMG.

Oleic acid was also tested for moisture barrier function. However, at the same 5% level, Oleic acid was not effective. When the formulation was optimized with 8% Oleic acid, the moisture reduction effect was also optimized. Table 3 summarizes the formulations for various Oleic acid amounts. Figure 4 shows the moisture uptake data.

	With 5% Oleic acid [%]	With 8% Oleic acid [%]
Kollicoat® MAE 30DP	55.50	55.50
Triethyl Citrate	2.50	2.50
Oleic acid	0.83	1.33
Polysorbate 80	0.83	0.32
Water	40.34	40.35
Total	100.00	100.00

Table 2. Kollicoat® MAE 30DP coating formulations with different levels of Oleic Acid for fish oil soft gelatin capsules

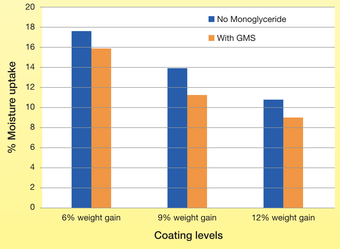

Figure 2. Moisture uptake by fish oil capsules coated with Kollicoat® MAE 30DP with and without GMS

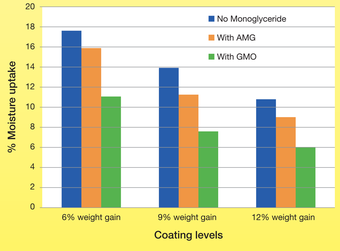

Figure 3. Moisture uptake by fish oil capsules coated with Kollicoat® MAE 30DP and monoglycerides

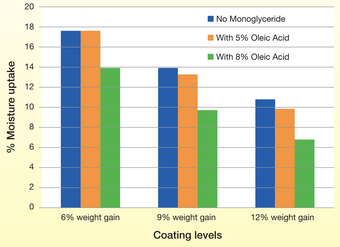

Figure 4. Moisture uptake by fish oil capsules coated with Kollicoat® MAE 30DP and various amounts of Oleic acid

Conclusions

- An aqueous coating system based on Methacrylate acid copolymer, Kollicoat® MAE 30DP can be used for moisture barrier coating.
- Monoglycerides, such as Glycerol Monostearate, normally used as an anti-tack agent for Kollicoat® MAE 30DP, can enhance the moisture barrier function of the coating.
- Other monoglycerides, such as Glycerol Monooleate and Acetylated monoglycerides has the same effect as Glycerol Monostearate. Furthermore, these monoglycerides are easier to incorporate into the coating dispersion than the solid GMS.
- A coating formulation containing Oleic acid also provides moisture barrier function.
- Optimum barrier effect was achieved when the coating dispersion was optimized with the amount of lipophilic monoglycerides added.
- Higher coating levels further reduce moisture absorption.

References

1. Zhuang, K., Onyiuke, C., Quadir, A., 2008 AAPS Poster.
2. Zhuang, K., 2010 AAPS poster
3. Ibid

AAPS Annual Meeting, Chicago, 2012