Suitability of a new aqueous polymer dispersion for moisture barrier coating of soft gelatin capsules

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Introduction

A new aqueous Methacrylate dispersion, Kollicoat® Smartseal 30D was developed for its moisture barrier function. This polymer dispersion is designed to provide a protective coating to prevent moisture absorption by the coated dosage form. Commercially available soft gelatin capsules are known to absorb moisture during storage. The absorbed moisture may compromise the stability of the encapsulated active pharmaceutical ingredient (API). It is desirable to coat the capsules with a moisture protective film. The purpose of this study was to evaluate the suitability of Kollicoat® Smartseal 30D as a moisture protective coating for soft gelatin capsules

Objectives

- To develop a formulation for Kollicoat® Smartseal 30D suitable for coating soft gelatin capsules
- To develop a suitable process for coating soft gelatin capsules with Kollicoat® Smartseal 30D
- To evaluate the moisture protective property of the coating on the soft gelatin capsules.

Materials

- Kollicoat® Smartseal 30D 30% aqueous dispersion, BASF (Florham Park, NJ)
- Fish oil 1000mg capsules, Capsulework (Ronkonkama, NY)
- Tributyl Citrate (TBC) and Tirethyl Citrate (TEC), Vertellus (Greensborough, NC)
- Butylated hydroxytoluene, MP
- Plasacryl PF, Emerson Resources (Norristown, PA)
- Other ingredients used as received

Methods

Soft gelatin capsules were coated in a Thomas Accela-coater equipped with a 15" perforate pan. Disintegration test in pH 6.8 buffer 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.

Results and Discussion

Formulation development for Kollicoat® Smartseal 30D

3 plasticizers were evaluated in the coating dispersion. Table 1 shows the formulae of the coating dispersions.

	%	%	%
Kollicoat® Smartseal 30D	43.30	43.30	43.30
Triethyl Citrate	2.00	—	—
Triacetin	—	2.00	—
Tributyl Citrate	—	—	2.00
Butylated Hydroxy Toluene (BHT)	0.13	0.13	0.13
Water	54.57	54.57	54.57
Total	100.00	100.00	100.00

Table 1 Coating formulations with different plasticizers for fish oil soft gelatin capsules

Kollicoat® Smartseal 30D is a brittle material with a Tg of 57°. A Plasticizer is required for a successful coating otherwise the resulting film is very brittle and may have cracks that can compromise the moisture protection function. Since the polymer is not soluble in pH 6.8 buffer, disintegration in pH 6.8 buffer was used as a way to test the integrity of the film. An intact capsule after the disintegration test indicates that there is no crack in the film. Figure 1 shows the results of the disintegration tests of the capsules coated with dispersions with 3 different plasticizers. It is apparent that the more lipophilic TBC is a better plasticizer for this new polymer.

The polymer though is very soluble in acidic media. Figure 2 shows the disintegration tests in 0.1N HCl of these coated capsules. All 3 capsules showed similarly fast disintegration in 0.1N HCl.

The plasticity of the film increases with the amount of plasticizer used. This was tested with increasing amount of TEC added to the coating dispersions. The results of disintegration tests of the capsules coated with increasing amounts of TEC are shown in figure 3. By increasing the plasticizer amount a more robust film was achieved.

TBC was chosen as the ideal plasticizer and was used for further studies.

Coating process development for Kollicoat® Smartseal 30D

Soft gelatin capsules provide a unique challenge in coating. Soft gelatin capsules usually soften around 40°C, so it is desirable to keep the product temperature below 40°C.

The 15% TBC formulation was used to optimize the coating conditions. The capsules were coated at 3 different process temperatures and the conditions are listed in Table 2. At 30°C some sticking of the capsules to each other and to the coating pan was observed. This led to the film peeling off from the capsules. At 60°C, the capsules started to deform. (See figure 4) The ideal process temperature was 45°C, corresponding to a product temperature around 28 to 31°C.

Inlet Air volume (CFM)	150	150	150
Inlet air Temperature (°C)	30	45	60
Exhaust air temperature (°C)	22-24	30-33	41-43
Product temperature	18-20	28-31	41-43
Pan speed (rpm)	17	17	17
Spray rate (g/min)	8	8	8
Atomize air (PSI)	35	35	35

Table 2 Process parameters for coating fish oil soft gelatin capsules with Kollicoat® Smartseal 30D

Talc or a formulated suspension of Glyceral Monostearate (Plasacryl PF) is commonly used in coating formulations as an anti-tack agent. Talc and Plasacryl were used in combination with Kollicoat® Smartseal 30D to reduce the sticking tendency at lower product temperatures. The formulae are shown in table 3. With the aid of the anti-tacking agent, process temperatures < 45°C could be reached, and less sticking tendency was observed. Hence it was desirable to include an anti-tacking agent in the formulation.

	%	%	%
Kollicoat® Smartseal 30D	43.30	33.30	33.30
Tributyl Citrate	2.00	1.50	1.50
Talc	—	2.50	—
Plasacryl PF	—	—	4.00
Butylated Hydroxy Toluene (BHT)	0.13	0.10	0.10
Water	54.57	62.60	61.10
Total	100.00	100.00	100.00

Table 3 Coating formulations with anti-tack agent for fish oil soft gelatin capsules

Moisture barrier effect of Kollicoat® Smartseal 30D

Soft gelatin capsules are known to absorb moisture during storage. This may compromise the active ingredients that are moisture sensitive in the capsules. 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® Smartseal 30D, the moisture absorption tendency is reduced even at a 4% coating level. Figure 5 shows the moisture protection effect of the coating with 3 different plasticizers. It is surprising that the coatings with the less effective plasticizers provided moisture protection to the same extent as TBC. The small cracks in the coating did not affect its barrier function.

Higher coating levels also helped to reduce the moisture uptake by the capsules. At 7% coating level, further moisture reduction is achieved. Figure 6 shows the percent reduction of moisture uptake at different coating levels compared to uncoated capsules.

Pigments and anti-tacking agents can also retard water vapor permeation. So it is not surprising that talc can further reduce the moisture uptake. Plasacryl, being a lipophylic agent, can also reduce the moisture uptake. Figure 7 shows the percent reduction of moisture uptake by coatings with different anti-tack agents. It is clear that not only does talc or Plasacryl provide aid to the coating process, but they enhance the moisture protection effect as well. It is desirable to include these agents in the coating formulation for Kollicoat® Smartseal 30D.

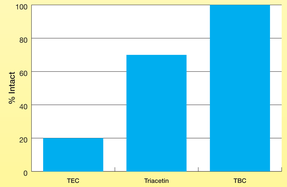


Figure 1 Disintegration tests in pH 6.8 buffer as an indication of film integrity – Effect of various plasticizers

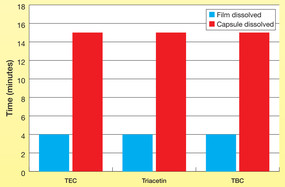


Figure 2 Disintegration time of Kollicoat® Smartseal 30D coated capsules in 0.1N HCl

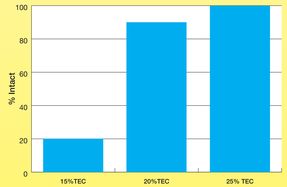


Figure 3 Disintegration tests in pH 6.8 buffer as an indication of film integrity – Effect of plasticizer levels

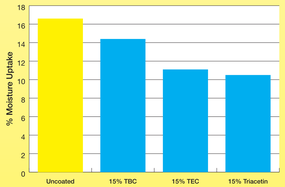
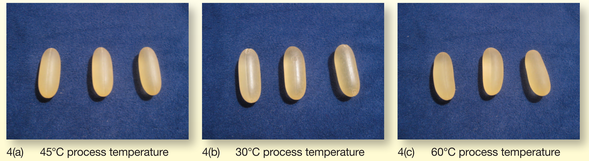


Figure 5 Moisture uptake by uncoated capsules and capsules coated with Kollicoat® Smartseal 30D



4(a) 45°C process temperature 4(b) 30°C process temperature 4(c) 60°C process temperature

Figure 4 Capsules coated at various inlet air temperatures

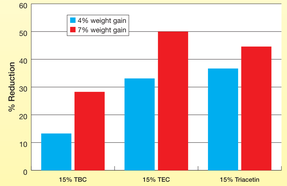


Figure 6 Reduction in moisture uptake by capsules coated with Kollicoat® Smartseal 30D – Effect of coating levels

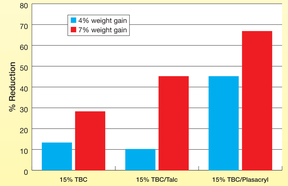


Figure 7 Reduction in moisture uptake by capsules coated with Kollicoat® Smartseal 30D – Effect of anti-tack agent

Conclusion

- A new aqueous coating system based on Methacrylate polymer, Kollicoat® Smartseal 30D was developed for moisture barrier coating.
- A lipophilic plasticizer, Tributyl Citrate, is most suited for the coating dispersion. Triethyl Citrate or Triacetin can also be used, but at 25% level (based on dry polymer weight) vs. 15% for TBC.
- To coat soft gelatin capsules, a product temperature of 28-31°C is ideal for this new coating system.
- The coating is very effective in reducing moisture uptake by soft gelatin capsules stored in high humidity conditions. Up to 60% reduction in moisture absorption was achieved when compared with uncoated capsules.
- Higher coating levels further reduce moisture absorption.
- Best moisture protection was achieved through a formulation containing a lipophilic anti-tack agent, Glyceryl Monostearate.