Evaluation of Formulated Ethylcellulose Aqueous Dispersions to Develop Controlled Release Multiparticulate Formulation of Freely Soluble Drug, Propranolol Hydrochloride

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Purpose

In this study, the controlled release multiparticulate formulation of a freely soluble model drug, propranolol HCl, was evaluated using a fully formulated coating Surelease®, Ethylcellulose Dispersion and Aquacoat® ECD, an ethylcellulose dispersion that allows for the addition of desired type and quantity of a plasticizer.

Methods

Propranolol hydrochloride was layered onto sugar spheres (850 – 1000 µm) (Suglets®, PF011 Colorcon, USA) using an HPMC-based Opadry® (Colorcon, USA) as binder with 70:30 w/w drug/binder ratio in Bosch Hüttlin Unilab. The multiparticulates (MP) were then barrier membrane coated either with Surelease (Colorcon, USA) or with Aquacoat ECD-30 (Colorcon, USA) in a fluid bed coater equipped with Wurster configuration (Glatt GPCG-2). Before coating, a water soluble plasticizer, triethyl citrate (TEC, Vertellus, USA) at 24 % w/w with respect to polymer, was added to Aquacoat ECD. Ethylcellulose aqueous dispersions were coated to a 10 % w/w theoretical weight gain (WG). A top-coat (using the same Opadry) at a 1% w/w WG was applied over the barrier membrane coatings. Each batch of coated MPs was split into three equal parts, then two parts were subjected to post coating curing for 2 hours and 24 h in a 60ºC oven. The drug release from MPs was characterized at 289 nm wavelength using USP Apparatus II (paddles), 1000 mL DI water at 37ºC. The dissolution results generated were compared using the f_2 factor.[1] An f_2 value between 50 and 100 indicates that the two dissolution profiles are similar. The morphology of the barrier membranes was examined using SEM (Phenom XL, Thermo Fisher Scientific, USA).

Table 1: Batch Preparation Overview

Formulation Stages	Component	Solids (%w/w)	Weight Gain (%w/w)
Drug layering	Propranolol HCl Opadry	15	7
Barrier membrane coating	Surelease	15	10
	Aquacoat ECD-30 24% w/w TEC	15	10
Top-coat	Opadry	10	1

Table 2: Suglets Coating Parameters

Process Parameter	Drug Layering	Ethylcellulose Coating
Equipment	**Huttlin Fluid Bed**	**Glatt CPCG-2**
Batch size (kg)	4 – 6 kg	2.0
Inlet temperature (°C)	57 - 58	53 - 65
Product temperature (°C)	45 - 50	41 - 46
Outlet temperature (°C)	41 - 46	38 - 44
Atomizing air (bar)	1.5	2.0
Air volume (CMH) / (m^3/hr)	325	120 - 130
Nozzle size (mm)	1.2	1.2
Fluid delivery rate (g/min)	12 - 24	10 – 14

Results: Dissolution

Stable drug release performance, independent of curing duration, was observed for the Surelease coated multiparticulate systems.

Aquacoat ECD coated multiparticulates required a minimum of two hours of curing to ensure full coalescence of the film and consistent slow drug release.

Figure 1. Drug Release from Propranolol HCl MR MP, Coated with Fully Formulated Ethylcellulose Dispersion (Surelease); Effect of Curing Duration

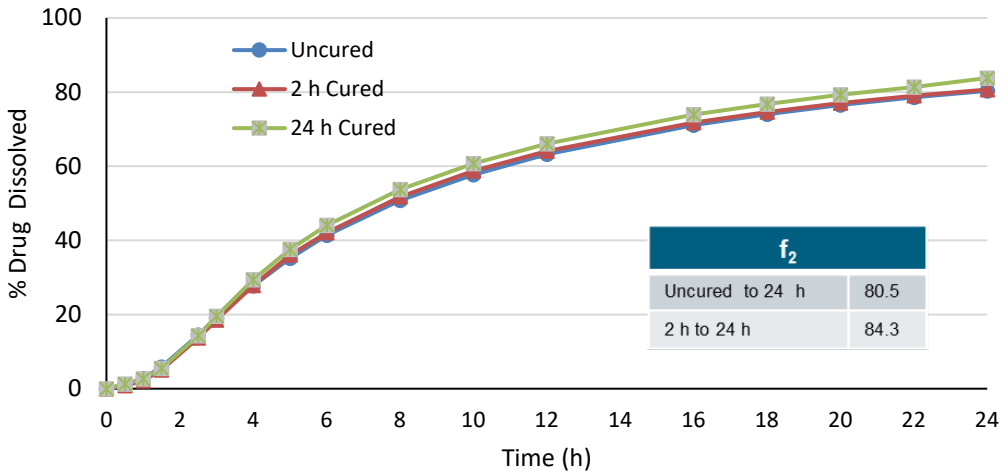
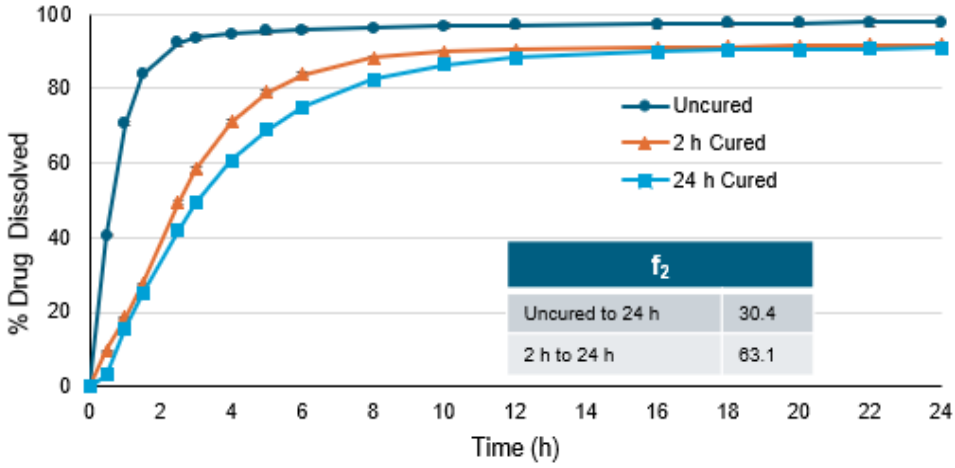
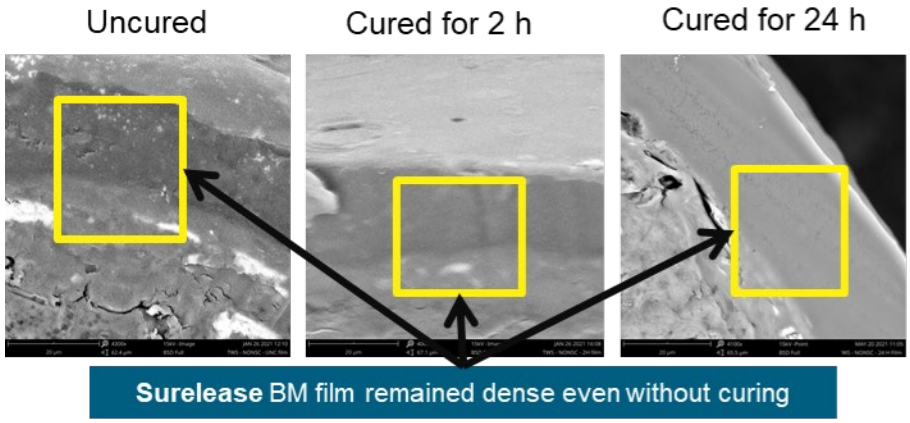
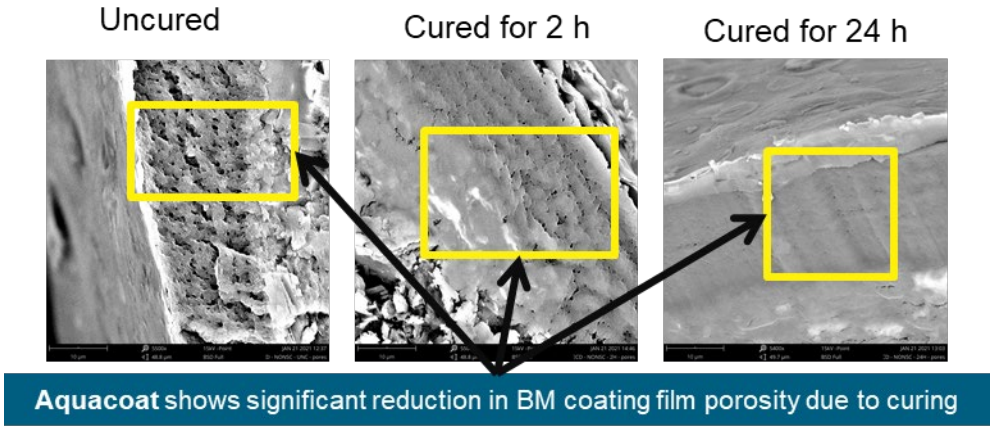


Figure 2. Drug Release from Propranolol HCl MR MPs Coated with Partially Formulated Ethylcellulose Dispersion (Aquacoat); Effect of Curing Duration



Results: SEM Images





Conclusions

Ethylcellulose aqueous dispersions were successfully coated to achieve controlled release for propranolol HCl multiparticulates. Consistent drug release was achieved for ethylcellulose aqueous dispersions. The results showed the importance of curing and processing parameters required for developing controlled release MP systems.

References

1. Moore, J. W. and H. H. Flanner, 1996, "Mathematical Comparison of Dissolution Profiles," Pharmaceutical Technology, 20 (6):64-74.

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