MODIFIED RELEASE

SURETERIC®

AQUEOUS ENTERIC COATING SYSTEM

Technical Data Sheet

Performance Characteristics

A Comparison of the Performance Characteristics of Delayed-Release Film Coating Systems

Objectives

- To compare the performance characteristics of aqueous delayed-release coating dispersions with those obtained from organic, solvent based polymer solutions.
- To assess the quantity of coating required to achieve enteric protection.
- To examine the effects of aging on delayed-release performance.
- To develop a test method that augments and is more discriminating than the current E.P. enteric disintegration method.

Introduction

Delayed-release film-coated products are some of the most complex coated dosage forms to develop. Challenges arise from the requirements that :

- The applied coating should either prevent drug release or the ingress of gastric fluids under specified conditions of pH and also promote rapid release of the drug in the higher pH regions of the jejunum, duodenum etc[(1)].
- Good mechanical film properties are required to ensure integrity of the coating[(2)]
- Performance should remain unchanged with time[(3)].
- Workers and the environment must be protected from the potential hazards of organic solvents
- There is pressure to increase savings in raw material costs.

When designing any functional coating there are a number of important factors that need to be considered and attention to these details at the earliest stages of product development can save considerable amounts of time and money when the project reaches production scale up and manufacture. The following list emphasises some of these variables.

- The quality of the substrate
- The nature of the substrate ingredients
- The pKa of a particular delayed release polymer
- The quantity of coating material applied
- Processing parameters
- The effects of mechanical stress on film integrity

Polymers Examined

Five coating systems were examined:

- Hydroxypropylmethylcellulose Phthalate (HP-55, Shin-Etsu)*
- Aquateric® (FMC)
- Eudragit® L30D-55 (Degussa)
- Eudragit L100-55 (Degussa)
- Sureteric® (Colorcon).

*As a reference, the HP-55 system was applied as a polymer solution in organic solvents (a 2:1 mixture of isopropyl alcohol and water). The remaining systems were prepared as aqueous dispersions according to the respective manufacturer's literature.

Methodology

Each coating system was applied to10mm diameter, 330mg placebo tablets without a breakline or logo. A sub-coat was applied using Opadry® Y-1-7000 (Colorcon) to a 3% weight gain to ensure a reproducible substrate for each system. Coating was performed in a Manesty Model 10 Accela-Cota with a Schlick 930 spray gun, charged with 10kg of placebo tablets. A 12% weight gain of each coating material was applied for each coating system evaluated, and tablet samples were removed at 4, 6, 8, 10 & 12 % weight gains.

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The coating conditions used are shown in Table 1.

Table 1-A

Process Parameters	**Aquateric**	**HPMCP**
Inlet air temperature, ^{o}C	58	42
Exhaust air temperature, ^{o}C	42	34
Tablet bed temperature, ^{o}C	35	29
Atomising air pressure, psi	35	20
Pan speed, rpm	14	14
Dispersion solids content, %	15	10
Spray rate, g/min	49	60

Table 1-B

Process Parameters	**L30D-55**	**L100-55**
Inlet air temperature, ^{o}C	52	52
Exhaust air temperature, ^{o}C	39	39
Tablet bed temperature, ^{o}C	35	35
Atomising air pressure, psi	35	35
Pan speed, rpm	14	14
Dispersion solids content, %	15	15
Spray rate, g/min	50	50

Table 1-C

Process Parameters	**Sureteric**
Inlet air temperature, ^{o}C	54
Exhaust air temperature, ^{o}C	41
Tablet bed temperature, ^{o}C	34
Atomising air pressure, psi	35
Pan speed, rpm	14
Dispersion solids content, %	15
Spray rate, g/min	50
Coating time, min	160

Tablet samples at each weight gain were individually weighed (n=6) and reciprocated for 2 hours in 0.1N HCl in a USP compliant disintegration apparatus. At the end of this time interval the tablets were removed from the disintegration bath for visual inspection of any defects (bloating or swelling). In addition any excess surface moisture was gently dabbed dry using tissue paper, and the tablets individually reweighed. The percent acid uptake for a tablet was calculated according to Equation 1.

Equation 1

$$\text{Percent Acid Uptake} = (T_f - T_i)/T_i \times 100$$

T_f = Tablet weight final (mg)

The data shown in Table 2 shows the acid uptake values recorded after exposing the coated tablets for two hours in 0.1N hydrochloric acid. Values less than 10% acid uptake typically correspond to suitable performance during dissolution testing.

Table 2

	Acid uptake (%w/w) at stated quantity of coating applied				
Coating level	**4%**	**6%**	**8%**	**10%**	**12%**
Aquateric	>100	>100	>100	>100	2.2
HPMCP	8.7	6.0	2.9	2.8	2.5
L30D-55	27.6	6.6	4.0	3.7	3.8
L100-55	9.6	6.6	6.6	5.1	2.9
Sureteric	15.8	4.8	4.1	3.3	3.0

Tablet samples at each weight gain were rotated 100 times in a Roche friabilator and analyzed for percent acid uptake. This method is utilized to understand the impact of physical stress on the robustness of a delayed release dosage form. The data in Table 3 shows the acid uptake values of samples taken from the same coating runs after 100 rotations in the Roche Friabilator.

Table 3

	Acid uptake (%w/w) at stated quantity of coating applied				
Coating level	**4%**	**6%**	**8%**	**10%**	**12%**
Aquateric	>100	>100	>100	>100	>100
HPMCP	15.8	2.4	3.1	2.8	1.9
L30D-55	17.7	6.4	5.6	3.5	2.7
L100-55	15.2	2.4	3.1	2.8	1.9
Sureteric	11.1	7.7	5.5	5.0	4.7

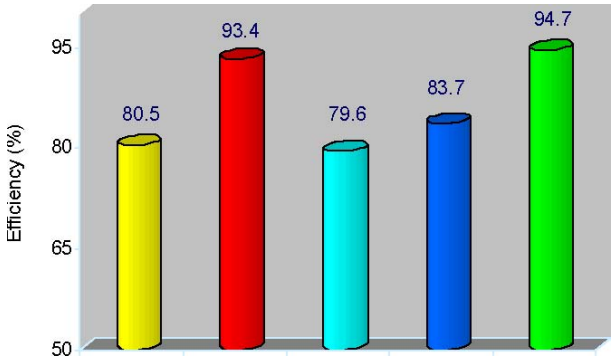
Tablet samples from each weight gain were packaged and stored for months at 25ºC, 40%RH. The data in Table 4 shows the acid uptake values for the samples after storage for 24 months at 25ºC, 40%RH.

Table 4

	Acid uptake (%w/w) at stated quantity of coating applied Time point 24 months				
Coating level	**4%**	**6%**	**8%**	**10%**	**12%**
Aquateric	>100	>100	>100	>100	6.6
HPMCP	17.2	3.0	2.8	2.2	2.1
L30D-55	7.9	7.0	4.0	4.1	3.8
L100-55	22.1	13.9	6.0	5.5	3.2
Sureteric	14.9	6.0	4.8	4.6	4.5

Process Efficiency

Determination of coating process efficiency is critical when the applied film coating has a specific functionality, as is the case with an enteric coating. Coating processes should always be optimised so that material losses are kept to a minimum. Although one should not expect to achieve 100% efficiency, the result should be reproducible, especially if product performance is in any way sensitive to changes in the amount of coating applied. In all cases, process efficiencies can be expected to be proportionally higher in commercial scale equipment than those seen in this laboratory study. While it is recognised that the coating process has not been fully optimised to suit each particular coating system, it is evident in some cases that the coating process efficiencies obtained would have been unacceptable as the basis for further scale-up trials to take place.



Conclusions

Although limited in scope, this preliminary evaluation of the performance of several delayed release systems suggests that it is possible to achieve acceptable enteric protection from water borne formulations with percent acid uptake results that are comparable to those obtained from organic solvents. Effective enteric protection is, however, contingent on the level of coating applied, and clearly not all coating systems are equivalent in this respect, especially if the results shown in this study are typical of what can generally be achieved. The use of the <10% acid uptake limit provided a method of testing that was more revealing than the E.P enteric disintegration test and one that was beneficial in the assessment of the minimum enteric coating material requirement. These data in combination with known coating process efficiencies should provide some confidence in developing an economic and reproducible process that can be taken on to the scale-up process.

All of the samples tested showed reduced acid resistance after stressing in the Roche friabilator. It is therefore important that adequate care is taken during unloading of the coating pan and when subjecting finished tablets to the effects of vigorous packaging equipment to avoid possible product failure. The acid uptake of both the organic solvent and water based systems showed only small changes with time after storage at 25ºC, 40% RH for 24 months and there were no changes to the enteric pass performance by the EP enteric disintegration test method.

References

(1) S.C. Porter & K. Ridgeway, The permeability of enteric coatings and dissolution rates of coated tablets, J. Pharm. Pharmacol. 34, 5 (1982)
(2) R. C. Rowe, Molecular weight studies on Hydroxypropylmethycellulose phthalate (HP55), acta pharm. Technol. 28(2), 127 (1982)
(3) Chang, R-K, Pharm Tech, pp 62-70 (October 1990)

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