The Influence of a pH Dependent Pore Former on Acid Protection from Tablets Coated with an Aqueous Ethylcellulose Barrier Membrane

INTRODUCTION

Ethylcellulose (EC) is commonly used in the pharmaceutical and nutritional industries for extended release applications. EC is a swellable, water-insoluble pH independent polymer which forms a non-eroding diffusional barrier[1]. Polymethacrylates, cellulose phthalates and poly vinyl acetate phthalates are widely used in delayed release applications in the pharmaceutical industry, but are not GRAS materials and therefore, not approved for food and nutritional use. Nutrateric®,nutritional enteric coating system, may be a viable alternative, utilizing an aqueous ethylcellulose dispersion (Surelease®, GRAS) and NS Enteric® nutritional enteric component, a dry powder additive containing sodium alginate (GRAS). The sodium alginate functions as a pore former within the EC film to provide delayed release functionality. The purpose of this study was to determine the coating level of Nutrateric on aspirin and caffeine tablets, required to withstand 0.1N HCl for two hours, but disintegrate in 0.05M phosphate buffer pH 6.8.

METHODOLOGY

Materials:

Aspirin tablets were obtained from LNK International Inc. (NY, USA). Caffeine (Spectrum Chemical Manufacturing Corp., NJ, USA) was blended with microcrystalline cellulose (Emcocel 90M, JRS), partially pregelatinized starch (Starch 1500®, Colorcon), colloidal silicon dioxide (Cab-O-Sil M5, Cabot), and stearic acid (Oleotec) and directly compressed on a Piccola 10 station rotary tablet press (Colorcon, USA). Ethylcellulose (Surelease E-7-19040, Colorcon, USA) and NS Enteric Clear 29Z19241 (Colorcon, USA) were used at the recommended (Colorcon) ratio of 85/15% (w/w): Surelease/NS Enteric.

Preparation and Characterization:

The coating dispersion was prepared by dispersing the NS Enteric in water and mixing for 60 minutes. Surelease was added and mixed slowly for an additional 10 minutes, achieving a uniform dispersion of Surelease (85%) and NS Enteric (15%). The solids content of the final dispersion was 10% (w/w). The dispersion was slowly stirred during spraying.

The coating dispersion was characterized by measuring the pH (Beckman 240 pH/Temp Meter), viscosity (Brookfield Model DV-II+ Viscometer with RV spindle set, spindle #1), and particle size (Coulter LS Particle Size Analyzer).

Tablets were coated, without a seal-coat, according to the coating conditions shown in Table 1. Table 2 shows the theoretical weight gains and corresponding coating levels.

Table 1. Coating Conditions

Coating Parameter	Thomas Compu-Lab 15" pan
Tablet Charge	1
Inlet Air Temperature (°C)	70-74
Drying Air Volume (cfm)	180
Tablet Bed Temperature (°C)	43-46
Exhaust Air Temperature(°C)	52-55
Atomization Air Pressure (psi)	30
Pattern Air Pressure (psi)	30
Spray rate (g/min.)	15
Pan Speed (rpm)	18

Table 2. Theoretical Coating Weight Gains and Coating Levels

Weight Gain (% w/w)		Coating Levels
Aspirin	Caffeine	
1.5	1.3	1.6
3.0	2.7	3.3
4.4	3.9	4.9
5.9	5.3	6.7
7.4	6.6	8.4
9.0	8.0	10.2

The physical characteristics of the tablets including weight, thickness, hardness, diameter, and friability were measured using an Erweka Multicheck and Vanderkamp Friability Tester.

Sample Analysis:

Disintegration testing was performed in an Erweka ZT-44 disintegration apparatus. The disintegration time of the uncoated and coated cores (n=6) in 900ml of 0.1N HCl and 0.05M potassium phosphate buffer (pH 6.8) was recorded.

RESULTS AND DISCUSSIONS

Coating Dispersion and Tablet Characterization:

Table 3 shows the pH, viscosity, and particle size characteristics of the dispersions used in the study.

Table 3. Coating Dispersion Characteristics

Dispersions	pH	Viscosity (cP)	Particle Size D_{90}(µm)
Surelease (24.6% solids)	10.5	1776	0.195
NS Enteric (2.3% solids)	8.2	264	154
85/15:Surelease/NS Enteric (10% solids)	10.2	776	0.272

The aspirin and caffeine cores differed in weight, thickness, hardness, and diameter (Table 4). The amount of Nutrateric applied to the tablets was adjusted to account for the differences in surface area between the two cores (Table 2). Both formulations contained insoluble filler (microcrystalline cellulose).

Table 4. Tablet Characteristics (n=20)

Uncoated Cores (surface area)	Weight (mg)	Thickness (mm)	Hardness (kp)	Diameter (mm)	Friability (%)
Aspirin (3.37cm^2)	380.2 ± 3.0	4.8 ± 0.03	6.4 ± 0.6	10.6 ± 0.02	0.7
Caffeine (3.94cm^2)	500.8 ± 4.7	5.5 ± 0.04	17.5 ± 1.3	11.3 ± 0.02	0.4

Disintegration Results:

The uncoated cores disintegrated in the acid and buffer phases in ≤ one minute, as expected. The coated aspirin tablets remained intact for two hours in the acid phase, regardless of coating level, and dissolved in the buffer phase in 2-7 minutes. The coated caffeine tablets disintegrated in the acid phase (30 minutes) at lower coating levels (<6.7mg/cm2), but remained intact at higher coating levels (≥6.7mg/cm^2). All coating levels disintegrated in the buffer phase in 2-9 minutes (Table 5).

Table 5. Disintegration Time, n=6

Tablet Formulations	0.1N HCl	Phosphate Buffer pH 6.8
Uncoated Aspirin	<1.00 min.	1.00 min.
Uncoated Caffeine	<1.00 min.	1.00 min.
Coated Aspirin	All Intact 120 min.	2-7 min.
Coated Caffeine	30 min. <6.7mg/cm^2) Intact 120 min. (≥6.7mg/cm^2)	2-9 min.

CONCLUSION

Acidic aspirin cores required less coating (1.6 mg/cm^2) than alkaline caffeine cores (6.7 mg/cm^2) to obtain the same level of protection in 0.1N HCl, as expected. The coating levels corresponded to lower weight gains (1.5 and 5.3% (w/w), respectively), indicating shorter processing times, compared to traditional enteric polymers (typically 8-12% weight gain). Resistance to 0.1N HCl (two hours) and disintegration in phosphate buffer pH 6.8 (2-9 minutes) was achieved by inclusion of a pH dependent pore former in a permeable ethylcellulose film. Nutrateric is a viable alternative to enteric polymers to achieve a delayed release dosage form for pharmaceutical products.

REFERENCES

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This ADS has been adapted from the following CRS poster: Young C, Dietzsch C, Fegely K, Rajabi-Siahboomi A. The Influence of a pH Dependent Pore Former on Acid Protection from Tablets Coated with an Aqueous Ethylcellulose Barrier Membrane. Poster presented at: Controlled Release Society, Annual Meeting, July 2006.

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