Performance Comparison of Two Delayed Release Coating Systems for Dietary Supplements

ABSTRACT SUMMARY

Two delayed release (DR) coating systems were compared on garlic tablets. The first, an aqueous ethylcellulose dispersion and pH dependent pore-former-based coating, successfully resisted simulated gastric fluid (SGF) then disintegrated in simulated intestinal fluid (SIF) at initial testing and after accelerated storage. The second, a shellac-based coating, cracked at initial testing, discolored and completely disintegrated in SGF after accelerated storage.

INTRODUCTION

DR coatings are a convenient and effective way to improve consumer appeal for dietary, nutritional and herbal products by reducing unpleasant tastes and odors caused by release in the stomach. The purpose of this study was to evaluate the performance of two DR coating systems on garlic tablets. Both coating systems have regulatory approval for use in dietary supplement applications.

EXPERIMENTAL METHODS

Materials:

Garlic tablets (Hampshire Labs, 250 mg tablet weight, 10 kp crushing strength, and 0.3% friability) were used as the substrate for DR coating. An Opadry®, complete film coating system (Colorcon,03K19229), was first applied (3% weight gain at 10% solids) as a seal-coat to all of the garlic tablets to improve tablet mechanical strength prior to DR coating. Next, the cores were coated with either Nutrateric®, nutritional enteric coating system (Colorcon), or AquariusEN pHolar coating system (Aqualon), according to their respective manufacturer's guidelines.[1,2,3] Nutrateric consists of Surelease®, aqueous ethylcellulose dispersion (E-7-19040), and NS Enteric®, nutritional enteric component (29Z18633). Ethylcellulose (EC) is a water-insoluble, pH independent polymer that forms a non-eroding diffusional barrier. The NS Enteric additive functions as a pH dependent pore-former within the EC film to provide DR functionality. In contrast, Aquarius EN (SCG18160) is a fully formulated dry powder blend comprised of shellac and sodium alginate. Shellac is a naturally occurring resin secreted by the insect Kerria lacca. Shellac is insoluble in acidic conditions and soluble at higher pH.

Dispersion Preparations:

NS Enteric was dispersed in room temperature DI water (26°C) under low shear and mixed for 60 minutes. Surelease was added to the NS Enteric and mixed slowly for an additional 15 minutes. Aquarius was dispersed in hot DI water (60°C) under low shear and mixed for 60 minutes. Particle size (Beckman Coulter LS230), viscosity (Brookfield DVII,RVA spindle set, spindle #2,), and pH (Symphony SP70P VWR pH meter) were determined on the Nutrateric and Aquarius dispersions. Dispersion quantities are listed in Table 1.

Table 1. Dispersion Compositions

Formulation	Nutrateric White	Aquarius White
Batch size (kg)	3	3
Weight gain (%)	6	6
Final solids conc. (%)	10	20
Product (g)	66.2 NS Enteric 455.0 Surelease	180.0
DI water (g)	1278.8	720.0
DI water temp. (°C)	26	60
Total dispersion (g)	1800	900
Composition (w/w)	63.2% Surelease 36.8% NS Enteric	100% Aquarius

Cast Film Preparations:

Films were cast 24 hours after dispersion preparation (Table 1). Nutrateric and Aquarius formulations were cast and dried on an MFT Thermostair using a 45-46°C gradient and a Gardner knife to target a dry film thickness of 0.1 mm. Films were removed from the substrate and equilibrated at controlled atmospheric conditions (20°C/55%RH) for 24 hours prior to testing. Tensile strength and modulus of elasticity were determined using an Instron Mini 44 Materials Analyzer (n=10). Moisture vapor transmission rate was measured using a WPA 100 Water Permeability Analyzer (n=2).

Tablet Film Coating:

Garlic tablets were coated to 6% theoretical weight gain (WG) in an O'Hara Labcoat I fully perforated 15 inch pan. The coating dispersions were mixed continuously during coating. Waxy and non-waxy flat face tablets were also coated for adhesion testing (Instron Mini 44 Materials Analyzer, n=10). Coating parameters are listed in Table 2.

Table 2. Coating Parameters

O'Hara Labcoat I 15 inch Pan	Nutrateric	Aquarius
Batch size (kg)	3	3
Inlet temperature (°C)	55	50
Exhaust temperature (°C)	45	42
Product temperature (°C)	45	41
Spray rate (g/min)	15	12
Atomizing air pressure (psi)	20	30
Pattern air pressure (psi)	25	30
Air volume (cfm)	170	175
Pan speed (rpm)	18	18
Mixing time prior to coating (min)	75	60
Total coating time (min)	120	75

Disintegration Testing:

DR disintegration (DT) testing was performed according to USP 32-NF 27, <2040> Disintegration and Dissolution of Dietary Supplements, Delayed Release Tablets. SGF and SIF were prepared according to the USP.

Stability Testing:

Garlic tablets coated to 3, 4, and 6% WG with Nutrateric or Aquarius coatings were placed in HDPE induction sealed 100 cc bottles for six months at accelerated conditions (30°C/65%RH and 40°C/75%RH). DR disintegration testing was performed at one month.

RESULTS AND DISCUSSION

Dispersion Properties:

Nutrateric had a higher pH and viscosity (at lower solids concentration), but significantly smaller particle size compared to Aquarius. Dispersion properties are shown in Table 3.

Table 3. Dispersion Properties

Dispersion Properties at 25ºC	Nutrateric White 10% Solids	Aquarius White 20% Solids
pH	10.10	8.18
Viscosity (cP)	880	690
Particle size, D_{50} (µm)	0.975	163.8

Film Properties:

Nutrateric films appeared smooth, glossy and uniform. Aquarius films were uniform although rough and irregular due to insoluble dispersed particles. Nutrateric films were stronger and more flexible, however compared to Aquarius films, adhered less to waxy cores. Both films adhered similarly to non-waxy cores. Nutrateric films had lower MVTR compared to Aquarius films, although poor cast film quality observed with Aquarius films could have contributed to the higher transmission rates and standard deviations. Results are summarized in Table 4.

Table 4. Film Properties

Film Coating Formulas	Tensile Strength MPa (SD)	Modulus of Elasticity MPa (SD)	Adhesion kPa (SD)		MVTR g H_2O/day/ 100 sq in (SD)
			Waxy	Non Waxy	
Nutrateric	3.5 (0.8)	312.8 (67.5)	134.1 (30.8)	161.4 (28.3)	26.8 (0.4)
Aquarius	1.5 (0.8)	545.0 (145.6)	179.8 (29.5)	160.9 (39.4)	74.1 (19.5)

Disintegration Testing:

Uncoated garlic tablets eroded yet did not completely disintegrate after one hour in SGF. Nutrateric coated garlic tablets met USP delayed release tablet criteria after one hour in SGF. That is, the tablets showed no evidence of disintegration, cracking, or softening. Aquarius coated garlic tablets however, did not meet USP criteria because cracks were observed in the Aquarius film coating after one hour in SGF (Figure 1).

In SIF, uncoated garlic tablets completely disintegrated in 1.2 hours. Nutrateric and Aquarius coated tablets, following one hour in SGF, had similar DT times at each coating WG. DT times ranged from 1.0 to 1.8 hours compared to 1.2 hours for uncoated tablets. DT results are listed in Table 5.

Figure 1. Coated Garlic Tablets After One Hour in SGF

Table 5. Delayed Release Disintegration Results

WG (%)	After 1 hour in SGF		DT Time in SIF (hours)*	
	Nutrateri	Aquarius	Nutrateric	Aquarius
2	Pass	Fail, cracked film	1.1	1.0
3	Pass	Fail, cracked film	1.1	1.1
4	Pass	Fail, cracked film	1.3	1.5
5	Pass	Fail, cracked film	1.4	1.7
6	Pass	Fail, cracked film	1.8	1.5

*Uncoated garlic tablets disintegrated in SIF in 1.2 hour

Stability:

After one month of storage at 30°C/65%RH in HDPE induction sealed bottles, no significant difference in SGF or SIF was observed for Nutrateric or Aquarius coated garlic tablets. However, after one month of storage at 40°C/75%RH, garlic tablets coated with Aquarius to 3, 4, and 6% WG appeared off-white and disintegrated in SGF. Nutrateric coated garlic tablets remained white and intact after one hour in SGF at 3, 4, and 6% WG. DT times in SIF for Nutrateric coated garlic tablets were similar to initial DT times. Stability results are summarized in Table 6.

Table 6. DT Results after One Month at 40°C/75%RH

WG (%)	After 1 hour in SGF		DT Time in SIF (hours)	
	Nutrateric	Aquarius	Nutrateric	Aquarius
3	Pass	Fail, disintegrated	1.0	-
4	Pass	Fail, disintegrated	1.0	-
6	Pass	Fail, disintegrated	1.4	-

CONCLUSIONS

Overall, Nutrateric outperformed Aquarius EN. Nutrateric reconstituted easily in cold water and was resistant to SGF. However, Nutrateric disintegrated in SIF, as desired for DR supplements. Aquarius required hot water for reconstitution and was resistant to SGF, but cracked on tablets during testing. After one month at 40°C/75%RH, Nutrateric remained white and resistant to SGF then disintegrated in SIF at each coating WG; whereas, after identical exposure, Aquarius coatings discolored and disintegrated in SGF.

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