Stability and Use Guidelines

ABSTRACT:

The objective of this study was to characterize the physical stability of Nutrateric®, nutritional enteric coating system, and study the effect of time between dispersion preparation and application, on stability of the coated product. Excellent dispersion stability of Nutrateric was demonstrated in this study. Properties including pH, viscosity, and particle size remained unchanged over a period of 72 hours after dispersion preparation. In addition, garlic tablets coated with the Nutrateric dispersion held for up to a 72 hour period exhibited good enteric properties in simulated gastric fluid and disintegrated within 90 minutes when exposed to simulated intestinal fluid.

INTRODUCTION:

Nutrateric is an aqueous enteric coating system designed specifically to meet the regulatory requirements for dietary supplement, nutritional and herbal products in the United States and North American regions. Tablets and capsules can be easily coated using standard processing equipment with reliable and reproducible enteric protection. The Nutrateric coating dispersion is comprised of Surelease®, aqueous ethylcellulose dispersion, supplied as a liquid at 25% solids concentration, and NS Enteric™, nutritional enteric component, supplied as a dry powder. A final dispersion concentration of 10% solids is recommended for film uniformity. The objective of this study was to characterize the physical stability of Nutrateric dispersion and study the effect of time between dispersion preparation and application on stability of the coated product.

METHODS:

Materials & calculation used to prepare Nutrateric dispersion:

The materials used to prepare Nutrateric dispersion are listed in Table 1.

Table 1. Materials Used

Ingredients	%	Kg
Surelease E-7-19010	34.00	0.204
NS Enteric 29Z19241	1.50	0.009
Purified water	64.50	0.387
Total dispersion	-	0.600

The total required solids (kg) were calculated using the quantity of tablets to be coated (kg) and the target coating weight to be 0.06 kg (i.e., 1 kg batch size coated to 6% WG). The quantity of coating solution needed as 10% solids was then determined to be 0.6 kg. Using an 85:15 ratio of Surelease: NS Enteric solids, the

quantity of each product was determined. Since Surelease is supplied as a 25% solids dispersion, the quantity needed based on required solids was calculated. The amount of water was calculated by subtracting the weight of Surelease dispersion and NS Enteric solids from the total coating dispersion weight.

Nutrateric Dispersion Preparation:

The required quantity of water (0.387 kg) was weighed into a mixing vessel and a variable speed low shear mixer was used to generate a vortex. A high efficiency propeller stirrer with blade diameter equivalent to 25% - 30% of the diameter of the mixing vessel was used. The weighed quantity of NS Enteric (0.009 kg) was added to the water in a slow steady stream while maintaining the vigorous vortex. After addition of the required amount of NS Enteric powder, the mixer speed was then reduced and mixing was continued for 60 minutes. The required quantity of Surelease (0.204 kg) was then added to the mixing vessel and mixing was continued for additional 15 minutes. The total solids content was 10% w/w.

The film composition based on solids consisted of 85% Surelease and 15% NS Enteric.

Characterization of Nutrateric Dispersion:

Sedimentation: The stability of Nutrateric dispersion was investigated by monitoring the sedimentation rate of the dispersion over a period of 72 hours. The sedimentation ratio, F, was calculated as the volume of the sediment (ml)/volume of total mixture (ml).

Viscosity: Viscosity of the Nutrateric dispersions were studied using a Brookfield DV-II+ Viscometer (Brookfield Engineering Laboratories, Inc., Middleboro, MA, USA) equipped with LV spindle number 2. The experiments were conducted at constant spindle speed of 20 rpm. Viscosity was measured at a controlled temperature of 20.5 ± 0.5 °C

pH: The pH of the dispersion was measured using a PerpHecT LogRmeter (Model 310, Thermo Orion, US).

LOD: Moisture content of the dispersion was measured by loss on drying (LOD) using an Ohaus moisture balance at a temperature of 100°C.

Particle size: The particle size of the dispersion was determined using a Coulter LS Particle Size Analyzer (Beckman Coulter Inc, Fullerton, CA, USA).

Coating of Garlic Tablets: Nutrateric was coated onto 1kg of garlic tablets in a Thomas Engineering Compu-Lab 15" side-vented coating pan using one Spraying Systems 1/8" VAU nozzle. The garlic tablets were coated with a sub-coat of 3% weight gain solids of Opadry® NS, complete film coating system for nutritional supplements, (70W19143) followed by a 6% weight gain of Nutrateric. The Nutrateric coat was applied to the garlic tablets at 0, 24, 48, and 72 hours after dispersion preparation. The process parameters for Nutrateric coating are shown in Table 2.

Table 2. Coating Conditions

Parameter	Value
Product bed temperature	43-46ºC
Atomizing air pressure	30 psi (2.06 Barr)
Pattern air pressure	30 psi (2.06 Barr)
Gun to bed distance	6 inches
Fluid delivery rate	15 g/minute
Pan speed	18 rpm

Enteric Testing/Acid Uptake: Testing of coated dosage forms utilized the six-tablet basket-rack disintegration apparatus, without disks, as described in USP test method 701. The acid uptake after exposure to simulated gastric fluid (SGF, USP) for 60 and 120 minutes was measured as a function of weight change of the tablets. The tablets were then exposed to simulated intestinal fluid (SIF, USP) and the disintegration time (with disks) was recorded.

RESULTS:

Nutrateric Dispersion Stability:

Nutrateric dispersion was prepared as described above and aliquots of the dispersion were tested for pH, viscosity, LOD, and sedimentation behavior. The Nutrateric dispersion properties are listed in Table 3.

Table 3. Nutrateric Dispersion Stability

Time (hours)	pH	Viscosity (cP)	% Solids (100%-LOD)	Sedimentation Ratio (F)
0	10.48	630.0	9.94	0
24	10.34	462.0	10.01	0
48	10.24	556.5	9.83	0
72	10.42	541.0	9.88	0

The pH and viscosity of the Nutrateric dispersion did not significantly change between 0 to 72 hours after preparation. The % solids as measured from the LOD values indicated no change in dispersion concentration from time zero. No sediment or visual separation was noted during the test period. The particle size determination of the Nutrateric dispersion indicated the mean particle size to be 0.334-0.345 µm. No significant changes were noted during the test period with respect to dispersion particle size (Table 4).

*Table 4. Nutrateric Dispersion Particle Size**

	Time between preparation of dispersion and coating (hours)			
	0 hours	24 hours	48 hours	72 hours
Mean (µm)	0.339	0.334	0.345	0.340
Medium (µm)	0.136	0.138	0.137	0.136
D(3,2) (µm)	0.145	0.147	0.145	0.145

*Coulter Measurement

Nutrateric Coating on Garlic Tablets:

The acid uptake after exposure to simulated gastric fluid (SGF, USP) for 60 and 120 minutes was measured as a function of weight change of the tablets. The acid uptake values for the garlic tablets coated with Nutrateric (6% weight gain) are shown in Table 5. Typically, a value of less than 10% acid uptake corresponds to good enteric protection.

Table 5. Acid Uptake Values for Coated Garlic Tablets in Simulated Gastric Fluid

Time (hours)	Acid Uptake (%)	
	60 min	120 min
0	3.4 ± 0.2	5.6 ± 0.3
24	3.2 ± 0.1	5.4 ± 0.3
48	3.1 ± 0.1	5.3 ± 0.2
72	3.3 ± 0.1	5.6 ± 0.2

Although acid uptake values were higher for tablets that were exposed to SGF for 2 hours as compared to tablets exposed to 1 hour, they were less than 10% and corresponded to good enteric protection. No significant differences in acid uptake were observed between Nutrateric dispersions that were coated immediately after preparation or those that were coated 72 hours after dispersion preparation.

The tablets were then exposed to simulated intestinal fluid (SIF, USP) and the disintegration time (with disks) was recorded. The disintegration time in simulated intestinal fluid for the tablets previously exposed to simulated gastric fluid are shown in Table 6.

Table 6: Tablet Disintegration Time in Simulated Intestinal Fluid

Time (hours)	Disintegration Time (min)
0	59.8 ± 7.1
24	59.7 ± 6.4
48	64.0 ± 5.4
72	55.3 ± 6.4

All tablets disintegrated within 90 minutes after exposure to SIF. No significant differences in disintegration were observed between Nutrateric dispersions that were coated immediately after preparation or those that were coated 72 hours after preparation.

CONCLUSIONS:

Excellent dispersion stability of Nutrateric - a new enteric coating formulation that meets the US regulatory requirements for nutritional supplements - was demonstrated in this study. Properties including pH, viscosity, and particle size remained unchanged over a period of 72 hours after dispersion preparation. In addition, garlic tablets coated with the Nutrateric dispersion held for up to a 72 hour period exhibited good enteric properties in simulated gastric fluid and disintegrated within 90 minutes when exposed to simulated intestinal fluid.

This study confirms that Nutrateric product has excellent dispersion stability and can be prepared and used up to 72 hours prior to application. Nutrateric provides for excellent enteric protection and delivers consistent performance as expected from a Colorcon formulated coating system.

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