Application of Powder Layering Technology and Aqueous Enteric Coating of Lansoprazole 15mg Pellets

OBJECTIVES

Lansoprazole delayed release pellets have been shown to have better absorption properties than a delayed release tablet.[1] However, binder solutions for drug layering and extrusion-spheronization excipients are incompatible with lansoprazole.[2] In contrast, dry powder layering technology has been reported to provide a more stable manufacturing method for acid-labile drugs.[3] The objective of this study was to evaluate the performance of lansoprazole powder layered pellets coated with Acryl-EZE®, aqueous acrylic enteric system, 93F19255 in various media.

METHODOLOGY

Powder Layering

Lansoprazole was applied to sugar spheres (840-1000µm) in a centrifugal fluid bed granulator (Glatt, GPCG-1) using dry powder layering technology. The dusting powders (Table 1) were applied individually while spraying a 3% HPC binder solution (approximately 1340g and 660g, respectively). The second dusting powder was applied to the pellets to enhance drug protection. The process parameters used are listed in Table 2.

Aqueous Enteric Coating

The drug layered pellets were dried (40°C) and screened (1190µm) prior to coating in a Strea-1 Aeromatic fluid bed coater (Schlick gun) with Acryl-EZE 93F19255 to a 26% theoretical weight gain. The coating dispersion was prepared under low shear mixing (Table 3), screened (250µm), and applied to the pellets using the processing parameters listed in Table 4.

Dissolution Testing

Dissolution testing was performed in a USP apparatus 2 (VanKel VK7000 dissolution bath) at 75rpm, 37.0±0.5°C. The delayed release dissolution testing (n=6) was performed in 500ml of 0.1N HCl or 0.05M sodium acetate buffer (pH 4.5), followed by phosphate buffer (pH 6.8). Lansoprazole absorbance was measured at 306nm (Agilent 8453 spectrophotometer).

Acid Phase

Six capsules or bead samples (15mg/253mg beads) were placed in 0.1N HCl or acetate buffer (pH 4.5) for 60 minutes. A 25ml aliquot was removed and scanned for the amount of drug released in the acid phase. The specification for the acid phases was not more than 10% drug dissolved after 60 minutes.

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Buffer Phase

25ml of 0.1N HCl was removed from each vessel and 425ml of 0.05M phosphate buffer (pH 6.8) was added to obtain 900ml of pH 6.8 media, or all of the 0.05M acetate buffer was removed and 900ml of 0.05M phosphate buffer (pH 6.8) was added to obtain a final pH of 6.8. Sample aliquots were withdrawn from the dissolution vessels at 5, 10, 15, 30, 45, and 60 minutes and analyzed for the amount of drug dissolved. The specification for the buffer phase was not less than 80% drug dissolved after 60 minutes.

Stability Evaluation

Hand-filled capsules (Capsugel hard gelatin, 15mg/253mg beads) were stored (HDPE bottles) at 30°C/ 60%RH and 40°C/75%RH for 1 month.

Table 1. Lansoprazole Powder Layering Formulation[4]

Step #1: Dusting Powder	Function	Supplier	% w/w
Lansoprazole	Active	Cadila Ahmedabad, India	13.0
Magnesium Carbonate, Heavy	Stabilizer	EDM Chemical NJ, USA	13.0
Sucrose	Filler	Domino Sugar NY, USA	13.0
Corn Starch	Filler	Staley Starch IL, USA	13.0
L-HPC	Disintegrant Binder	Biddle Sawyer NY, USA	13.0
Step #: Dusting Powder			
Sucrose	Filler	Domino Sugar NY, USA	12.2
Corn Starch	Filler	Staley Starch IL, USA	10.4
L-HPC	Disintegrant Binder	Biddle Sawyer NY, USA	10.4
Steps #1 and 2: Binder Solution			
HPC and Water	Binder	Shin Etsu Tokyo, Japan	3.0
Total (solids):	-	-	100

Table 2. Powder Layering Parameters

Parameters	Value
Batch Size (g), 840-100µm nonpareil	2250
Rotor Speed (rpm)	200
Binder Spray Rate (g/min)	20
Powder Addition Rate (g/min)	15
Inlet Air Temperature (C)	55
Outlet Air Temperature (C)	45
Bed Temperature (C)	45
Atomization Air Pressure (bar)	1.5
Air Flap (%)	20
Air Flow (m^3/hr)	68 – 80
Total Processing Time (min)	113

Table 3. Dispersion Preparation

Parameters	Acryl-EZE 93F19255
Dispersion Solids Content (%)	20
Theoretical Weight Gain (%)	26
Powder (g)	130
Deionized Water (g)	520
Total Dispersion (g)	650
Dispersion Mixing Time (min.)	30

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Table 4. Enteric Coating Parameters

Parameters	Value
Batch Size (g). 1190µm Drug Layered Pellets	500
Coating Spray Rate (g/min)	4.5
Inlet Air Temperature (C)	44
Outlet Air Temperature (C)	33
Bed Temperature (C)	32
Atomization Air Pressure (bar)	1.2
Total Processing Time (min)	144

RESULTS

Lansoprazole powder layered pellets prepared in a centrifugal fluid bed granulator, increased in size from 840-1000µm (nonpareils) to 1190-1410µm. No purple/brown discoloration (sign of degradation) was observed. Pellets appeared spherical, dense, had very few fines, and were therefore suitable for aqueous enteric coating.

Figure 1. Drug Layered and Coated Pellets

840-1000µm
Sugar Spheres
(18-20 mesh)

Drug Layered
Pellets 1190µm
(16 mesh)

Enteric Coated Pellets
28% Weight Gain
Acryl-EZE 93F19255

Lansoprazole pellets coated with Acryl-EZE 93F19255 (26% theoretical weight gain) exhibited excellent enteric protection in acidic media (pH 1.2 and 4.5) and rapid drug release in phosphate buffer (pH 6.8). The results showed no drug release in 0.1N HCl, followed by 80% release in phosphate buffer (pH 6.8) in 15 minutes or no drug release in acetate buffer (pH 4.5) after 60 minutes followed by 80% release in 20 minutes in phosphate buffer (pH 6.8).

Figure 2. Lansoprazole Dissolution Profiles

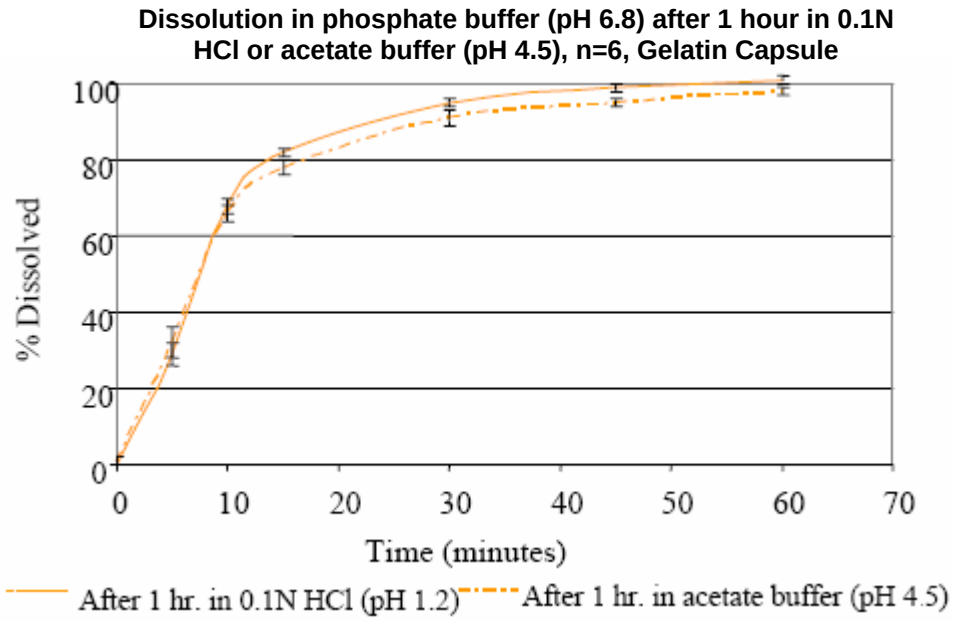

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Table 5. Stability Evaluation

Lansoprazole Pellet Assay	% Label Claim
1 month 30ºC/60%RH with desiccant	97.2
1 month 30ºC/60%RH without desiccant	97.2
1 month 40ºC/75%RH with desiccant	96.0
1 month 40ºC/75%RH without desiccant	96.2

CONCLUSIONS

Dry powder layering technology was used to prepare pellets of an acid-labile drug, lansoprazole (15mg), suitable for aqueous enteric coating. Acryl-EZE 93F19255 provided enteric protection in 0.1N HCl and acetate buffer (pH 4.5) and immediate drug release in phosphate buffer (pH 6.8).

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3. Tabata, T., et al., Drug Development, Industrial Pharmacy, 20 (9), 1661-1672 (1994)
4. United States Patent 5,045,321

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