Pharma Vision: Research and Reviews

Journal home page :https://sites.google.com/a/ves.ac.in/pharmavision/

Formulation and Evaluation of Enteric-Coated Lansoprazole Pellets

Ayre Anita[1]*, Karia Palak[1]

[1]Vivekanand Education Society's College of Pharmacy, Chembur (East), Mumbai - 400074
*Corresponding Author: Ayre Anita [Associate Professor], Vivekanand Education Society's College of Pharmacy, Chembur (East), Mumbai - 400074 Mobile No: *9769174278*, E-mail anita.ayre@ves.ac.in

Article Information

Article history
Received February 22, 2023
Accepted March 1, 2023
Published March 4 2023

Keywords
Pellets, Lansoprazole, suspension layering method, Hypermellose, and Eudragit L30 D55.

Abstract

The objective of the research work was to develop an effective formulation for enteric-coated pellets of lansoprazole. The active ingredients and fillers in bulk pharmaceuticals were compressed into pellets. They are typically intended for oral delivery and have a unit size ranging from around 0.5mm to 1.5mm with a spherical or semi-spherical shape. There are a variety of ways to make pellets, but the most common include compression and drug stacking. The purpose of this research was to create a delayed-release pellet dosage form of lansoprazole, a Benz-imidazole anti-ulcer agent that is one of the most commonly prescribed medications for both mild and severe ulcers. In this investigation, polymers such as Hypermellose and Eudragit L30 D55 were used to create enteric-coated pellets. Suspension layering was used to create the pellets. USP II equipment was used to examine the release of the drug from the enteric-coated pellets in 0.1 N HCL and phosphate buffer at pH 6.8. The cumulative percentage of drug release was calculated.

1. INTRODUCTION:

Acid and secretion from the stomach can be tempered with proton pump inhibitors (PPIs). A proton pump inhibitor (PPI) works by inhibiting the activity of the hydrogen/potassium adenosine triphosphatase (H^+K^+ATPase) of the stomach parietal cell, also known as the "proton pump"[1]. Peptic ulcers are sores in the stomach, duodenum, or oesophagus that allow digestive juices to leak out. Gastric ulcers are those that form in the stomach, duodenal ulcers in the duodenum, and esophageal ulcers in the oesophagus. The stomach's acidic digesting acids can damage the lining of these organs, leading to an ulcer. Millions of people suffer from peptic ulcer disease yearly. The principal effect of proton pump inhibitors (or "PPIs"), as a class of medications, is a significant and long-lasting reduction in gastric acid output. Dyspepsia, Peptic Ulcer Disease (PUD), and Gastroesophageal Reflux Disease (GERD) are just few of the many disorders that these medications are used to treat. Disease of the Larynx (LPR), Esophagus (Breslow's), and Stomach (Stress Gastritis) Prevention. Hypersecretory diseases, such as gastrinomas and various tumours of the stomach lining, are also included. The syndrome of Zollinger-Ellison[5].

The H^+/K^+ATPase, or more commonly the gastric proton pump, is an enzyme system found in the gastric parietal cell that is irreversibly blocked by proton pump inhibitors. Since the proton pump is directly responsible for the secretion of H^+ ions into the gastric lumen, it is a prime target for suppressing acid production from the stomach.

In order to repair acid-related illnesses like gastric ulcers, duodenal ulcers, and reflux oesophagitis, lansoprazole may be used. It's an adjunct in the elimination of Helicobacter pylori and is used to treat acid-related dyspepsia, ulcers, and GERD. The pharmaceutical sector is extremely interested in pellets for many different reasons. Pelletized products are used to increase the safety and effectiveness of bioactive agents, and they also provide greater freedom in dosage form design and development. The primary goal of the current research work was to create a micro pellet

formulation of Lansoprazole that is stable, effective, robust, and has a delayed onset of action [2, 3].

The primary goal of enteric polymers is to delay the release of drugs that are inactivated by stomach contents or that may cause bleeding or nausea due to the irritation of gastric mucosa; because they remain intact in the stomach but dissolve and release the contents once it reaches the small intestine, they are gaining in popularity[4].

2. EXPERIMENTATION:

2.1 Materials:

Lansoprazole API was procured from Cipla Pvt. Ltd., Mumbai. Colloidal silicon dioxide, sugar spheres, light Magnesium carbonate, talc, titanium dioxide polyethylene glycol, and talc were obtained from Molychem Lab., Mumbai. Eudragit L30D55 copolymer methacrylic acid was procured from Evonik, Mumbai.

2.2 Methods:

2.2.1 Preparation of Lansoprazole pellets: Using The first generation of Lansoprazole pellets was created with the help of a Wruster coater and a suspension layering process,. Lansoprazole, sugar spheres, Hypermellose, Magnesium carbonate, Talc, and sterile water were mixed together to make the medication slurry. The pellets' center of gravity was measured. Following this, the pellets were sprayed with a sub-coating. The components of the sub-coating solution were Hypermellose, Magnesium carbonate, and distilled water. There was a record of both the undercoat and overall weight. The pellets containing the necessary amount of medication were removed and coated with a barrier. The pellets were filled with a barrier coat solution including Hypermellose, Talc, Titanium dioxide, and distilled water. The Wruster coater was used to apply an enteric coating to a measured amount of pellets. Pellets were loaded with a compound made of methacrylic acid copolymer (Eudragit L30D55), polyethylene glycol, talc, titanium dioxide, and distilled water. Both the total pellet weight and the enteric coat weight were recorded. Talc and colloidal silicon dioxide were used as lubricants on these drug-loaded and coated pellets.

2.2.2 Physical Appearance:

Visual inspection of pellets was performed during daytime hours.

2.2.3 Loss on drying (LOD):

The procedure recommended by U.S. Pharmacopeial Convention (U.S.P) was followed. About 1 g of the pellet was dried in a vacuum over phosphorus pentoxide at 60ºC for one hour. The formula used for calculation of LOD was:

$$\frac{W_1 - W_2}{W_1 - W_T} \times 100 = \%LOD$$

Where -

W_T = weight of empty bottle and stopper

W_2 = weight of bottle and dried sample

W_1 = weight of bottle and undried sample

2.2.4 Content in Drug loaded, sub - coated and barrier coated pellets:

Pellets were weighed, then transferred to a 250 ml volumetric flask (300 mg Lansoprazole). The pellets were sonicated in 60 ml of 0.1 M NaOH. The solution was diluted up to 100 ml with acetonitrile and mixed thoroughly. 25 ml of the resulting solution was further diluted up to 100 ml. To prepare the test solution, 5 ml of the stock solution to be tested was taken in a 50 ml volumetric flask and volume was made up to 50 ml. Remove the initial 2 ml of the solution and centrifuge the rest for at least 20 minutes at 2500 rpm before filtering the supernatant through a 0.45 nylon filter. (About 30 parts per million concentration)

% content of Lansoprazole for 30 mg drug was calculated using the following formula:

$$\text{\% Content of Lansoprazole for 30 mg strength} = \frac{At \times W\,ref \times 5 \times 250 \times 50 \times M \times P \times 100}{As \times 100 \times 50 \times W\,test \times 5 \times 100 \times 30}$$

A_t: Absorbance of the Lansoprazole from test solution;

A_s: Mean Absorbance of the Lansoprazole from the reference solution;

W_{ref}:: Mass (mg) of standard taken;

W_{test}: Mass (mg) of test substance;

M: Theoretical mass, in mg equivalent to unit dose;

P: Purity of standard on dry basis

2.2.5 Blend uniformity of pellet:

With the use of a funnel, the contents of the filled vial were carefully transferred to a "y" ml volumetric flask. Pellets were sonicated in 24% of the flask's capacity of 0.1M sodium hydroxide until they were entirely destroyed. After cooling the solution, 16% acetonitrile was added to the flask's capacity, the solution was shaken, and about 40% of diluent was added to fill the flask. The solution was stirred on a magnetic stirrer for 15 mins and volume was made up with the diluent. The test solution was prepared again and applied it to 9 more samples. The empty vial was dried for 10 minutes at 105°C, after rinsing it with acetone (around 5 ml to 10 ml). The vial was kept in a desiccator, and weighed after complete drying. Test solution was prepared by diluting 5 ml of the stock up to 50 ml with diluent. A part of solution was centrifuged for at least 20 minutes at 2500 rpm and a portion of the supernatant solution was filtered through 0.45µ nylon filter discarding the first 2 ml.

2.2.6 Dissolution of pellets:

Acid Stage:

For composite sample – Pellets were added into each of the six glass beakers which would amount to around 1 unit of dosage. Pellets were placed into the dissolution apparatus and the test was run under the specified parameters.

For unit dose sample - Full unit dose sample pellets were accurately weighed and transferred to the dissolving vessel. The dissolution profile was executed under the specified circumstances.

Using a pipette covered in nylon fabric, 5 ml of each test solution was removed at the end of the allotted time. The first 2 ml of the filtered solution was discarded.

Buffer Stage:

425 ml of preheated buffer was added to the remaining 475 ml of solution in each jar from the acid stage as soon as possible (within no more than 3 minutes). Temperature was maintained at 37 °C ± 0.5°C Appropriate amount of sodium hydroxide or phosphoric acid was added at the same time, following the instructions for making a blank solution.

Using a pipette whose tip is wrapped in nylon fabric, 10 ml of each test solution was removed at the end of the time period prescribed. The first 2 ml of the filtered solution was thrown away.

3. RESULTS AND DISCUCSSION

3.1 Physical parameters of drug loaded pellets:

Appearance was found to be white to off-white pellets, loss on drying at 60^0C for 30 minutes, and sieve analysis were done. It was found that the lansoprazole pellets met all the ideal characteristics and the acceptance criteria.

3.2 Uniformity of content for drug-loaded pellets:

Acceptance criteria: 90.0 – 110.0 % of the labelled amount with RSD of NMT 5.0%.

The Lansoprazole pellets formulated met the acceptance criteria.

The graphical representation of Uniformity of content results at the Drug loading stage of sugar pellets is described in **Figure 1.**

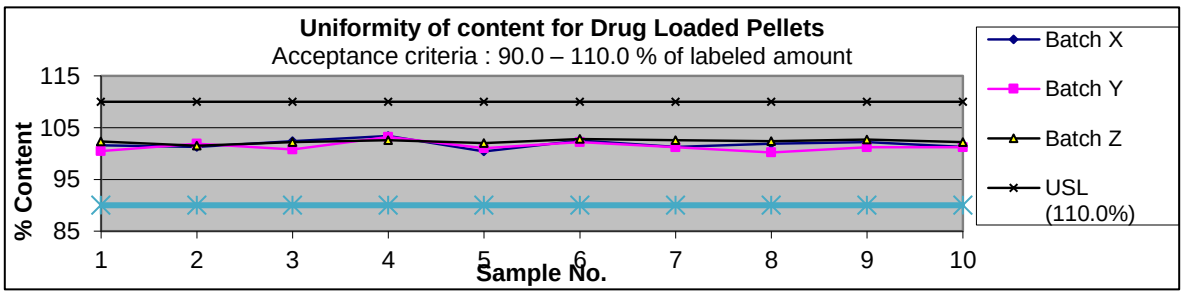

Fig 1: Graphical representation of results of Uniformity of content of Drug loaded pellets

3.3 Physical parameters of Sub-coated and barrier-coated pellets:

Three batches were formulated. The physical parameters like appearance, sieve analysis, loss on drying were tested. It was found that the pellets met the acceptance criteria.

3.4 Evaluation parameters of Enteric-coated pellets:

3.4.1 Physical parameters, Sieve analysis, and content uniformity of Enteric-coated pellets:

The appearance, sieve analysis, and content of lansoprazole results of enteric-coated pellets are described in **Table 1**.

Table 1: Appearance, Sieve analysis, and Content of Lansoprazole of Enteric-coated pellets

Test	Acceptance Criteria	Validation batches results		
		Batch X	Batch Y	Batch Z
Appearance	White to off white pellets	White to off white pellets	White to off white pellets	White to off white pellets
Content of Lansoprazole	95% to 105% of labeled amount	101.6%	101.4%	102.6%
Sieve analysis			---	
% retained on 18 # (1000 µ)	10% to 40% w/w	21.03%	24.4%	26.5%
% retained on 20 # (850 µ)	60% to 90% w/w	77.77%	74.5%	70.5%
Collector	NA	1.20%	1.1%	3.0%

3.4.2 Blend uniformity of Enteric-coated pellets:

Acceptance criteria: 90.0 – 110.0 % of labelled claim (mean of individual results) with RSD of NMT 5.0%. The blend uniformity results for three batches are described in **Table 2**.

The graphical representation of Blend Uniformity results of Enteric-coated pellets stage is given in **Figure 2**.

Table 2: Blend uniformity of Enteric-coated pellets

Sr. No.	% Content		
	Batch X	Batch Y	Batch Z
1	102.2	102.4	102.2
2	102.0	99.8	102.3
3	101.2	102.0	102.0
4	102.6	99.6	103.8
5	100.7	100.5	101.8
6	100.1	101.4	103.0
7	101.9	101.3	101.5
8	100.5	99.6	103.6
9	100.7	100.1	103.1
10	101.3	101.2	102.4
Min	**100.1**	**99.6**	**101.5**
Max	**102.6**	**102.4**	**103.8**
Mean	**101.3**	**100.7**	**102.6**
% RSD	**0.81**	**1.00**	**0.75**

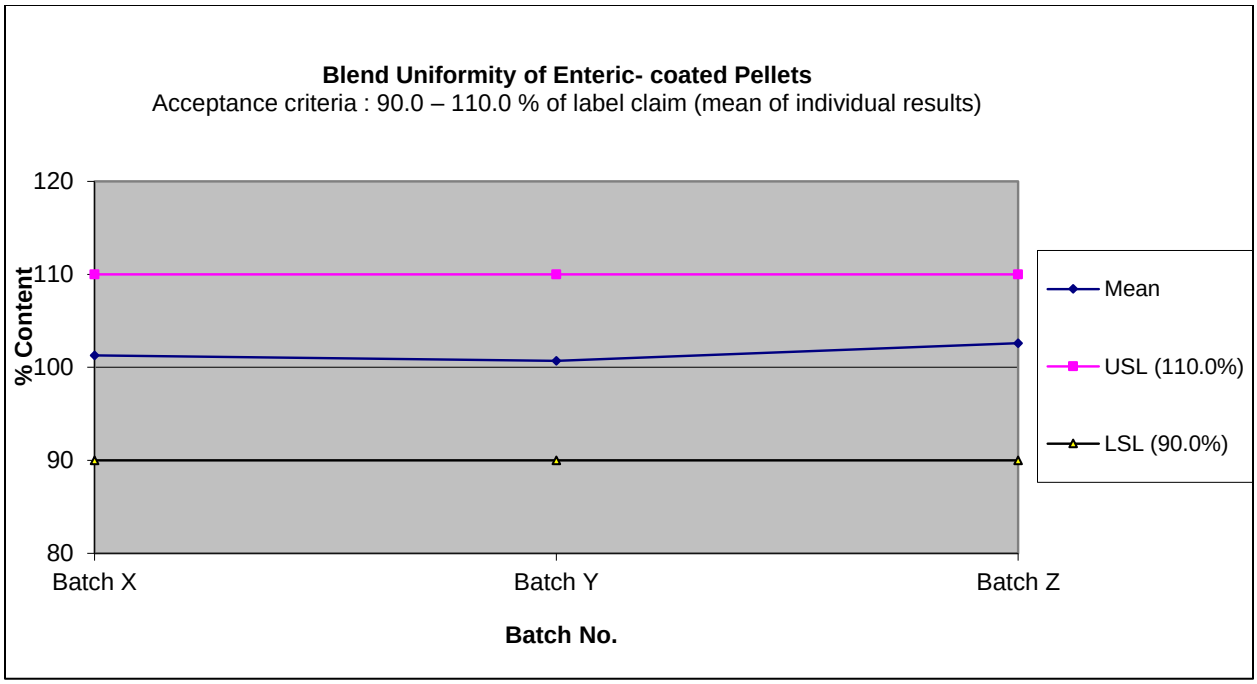

Figure 2: Graphical representation of results of Blend Uniformity of Enteric-coated pellets

3.4.3 Dissolution of Enteric-coated pellets:

Acceptance criteria for dissolution:

A) Acid Stage: NMT 10% of the labelled amount of Lansoprazole is released.

B) Buffer stage (After 60 minutes): NLT 80% (Q) of the labeled amount of Lansoprazole.

The dissolution data of Enteric-coated pellets is given in **Table 3**.

The graphical representation of Dissolution results of Enteric-coated pellets is shown in **Figure 3** for Acid stage and in **Figure 4** for Buffer stage.

Table 3: Dissolution data of Enteric-coated pellets

Sample No.	(%) release of Lansoprazole					
	Batch X		Batch Y		Batch Z	
	Acid Stage	Buffer stage	Acid Stage	Buffer stage	Acid Stage	Buffer stage
1	0	104	0	102	0	99
2	0	105	0	104	0	105
3	0	103	0	103	0	104
4	0	104	0	102	0	105
5	0	103	0	102	0	106
6	0	103	0	103	0	105
Min	**0**	103	**0**	102	**0**	99
Max	**0**	105	**0**	104	**0**	106
Mean	**0**	104	**0**	103	**0**	104

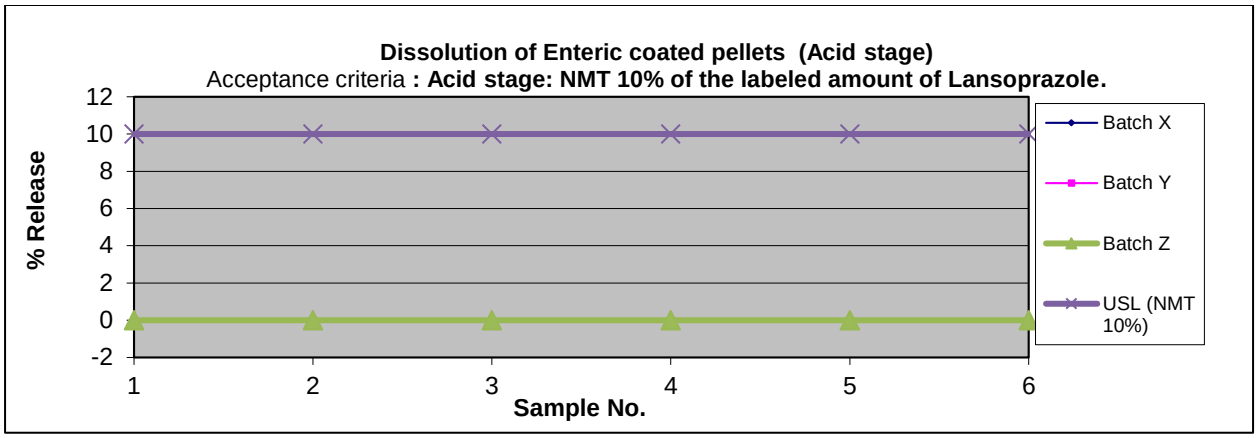

Figure 3: Graphical representation of Dissolution (Acid stage) results of Enteric-coated pellets

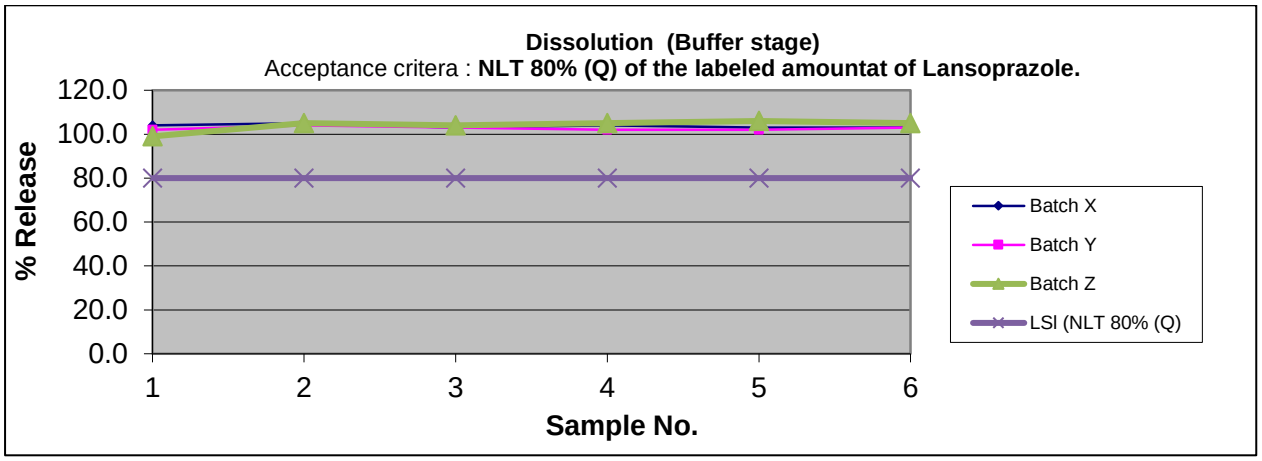

Figure 4: Graphical representation of Dissolution (Buffer stage) results of Enteric-coated pellets

4. CONCLUSION:

Lansoprazole was chosen as the active pharmaceutical ingredient and was developed into an Enteric Coated Pellet form. The developed formulation was found to deliver the appropriate drug release pattern. The technology used for pellet formulation exhibited the best way to incorporate the retarding agents Eudragit L-30D-55 and Hypermellose into a Lansoprazole Enteric Coated Pellet. However further work needs to be done to evaluate the preclinical and clinical efficacy of the formulation.

5. ACKNOWLEDGMENT:

The authors are thankful to Cipla, Vikroli for providing sample of Lansoprazole. The authors also wish to thank Vivekanand Education Society's College of Pharmacy, Principal and management for their constant support and guidance.

6. REFERENCES:

1. Babu, K.; Teja, N. B.; Ramakrishna, B.; Balagangadhar, B.; Kumar, B. V.; Reddy, V. G. Formulation and Evaluation of Double Walled Microspheres of Loaded with Pantoprazole. *Int. J. Res. Pharm. Chem.* **2011**, *1* (4), 770–779.
2. Singh, S. K.; Borkhataria, C. H.; Seth, N. R.; Patel, R. P.; Singh, S.; Parmar, G. R. Formulation and in Vitro Evaluation of Lansoprazole Micropellets. *Int. J. PharmTech Res.* **2009**, *1* (4), 1530–1540.
3. Chakravarthy, K. K.; Younus, M.; Shaik, S.; Pisipati, S. V. V. Formulation and Evaluation of Enteric Coated Pellets of Omeprazole. *Int. J. Drug Dev. Res.* **2012**, *4* (4), 257–264.
4. Lay, J.; Soh, P.; Sarkar, S. Pelletization Techniques. *Encycl. Pharm. Sci. Technol.*

Fourth Ed. **2020**, No. January 2013, 2515–2524.

5. Wilde, M. I.; McTavish, D. Omeprazole: An Update of Its Pharmacology and Therapeutic Use in Acid-Related Disorders. *Drugs* **1994**, *48* (1), 91–132.
6. Kuang, C.; Sun, Y.; Li, B.; Fan, R.; Zhang, J.; Yao, Y.; He, Z. Preparation and Evaluation of Duloxetine Hydrochloride Enteric-Coated Pellets with Different Enteric Polymers. *Asian J. Pharm. Sci.* **2017**, *12* (3), 216–226.
7. Fang, Y.; Wang, G.; Zhang, R.; Liu, Z.; Liu, Z.; Wu, X.; Cao, D. Eudragit L / HPMCAS Blend Enteric-Coated Lansoprazole Pellets : Enhanced Drug Stability and Oral Bioavailability. **2014**, *15* (3).
8. Raval, M. K.; Ramani, R. V; Sheth, N. R. Formulation and Evaluation of Sustained Release Enteric-Coated Pellets of Budesonide for Intestinal Delivery. **2013**, *3* (4), 203–211.
9. Cui, C.; Sun, J.; Wang, X.; Yu, Z.; Shi, Y. Factors Contributing to Drug Release From Enteric-Coated Omeprazole Capsules : An In Vitro and In Vivo Pharmacokinetic Study and IVIVC Evaluation in Beagle Dogs. **2020**, No. 31, 1–13.
10. Srebro, J.; Brniak, W. Formulation of Dosage Forms with Proton Pump Inhibitors : State of the Art, Challenges and Future Perspectives. **2022**.