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Preparation and evaluation of enteric coated tablets of hot melt extruded lansoprazole

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Abstract

The objective of this work was to use hot-melt extrusion (HME) technology to improve the physiochemical properties of lansoprazole (LNS) to prepare stable enteric coated LNS tablets. For the extrusion process, we chose Kollidon® 12 PF (K12) polymeric matrix. Lutrol® F 68 was selected as the plasticizer and magnesium oxide (MgO) as the alkalizer. With or without the alkalizer, LNS at 10% drug load was extruded with K12 and F68. LNS changed to the amorphous phase and showed better release compared to that of the pure crystalline drug. Inclusion of MgO improved LNS extrudability and release and resulted in over 80% drug release in the buffer stage. Hot-melt extruded LNS was physically and chemically stable after 12 months of storage. Both formulations were studied for compatibility with Eudragit® L 100-55. The optimized formulation was compressed into a tablet followed by coating process utilizing a pan coater using L 100-55 as an enteric coating polymer. In a two-step dissolution study, the release profile of the enteric coated LNS tablets in the acidic stage was less than 10% of the LNS, while that in the buffer stage was more than 80%. Drug content analysis revealed the LNS content to be 97%, indicating the chemical stability of the enteric coated tablet after storage for 6 months. HME, which has not been previously used for LNS, is a valuable technique to reduce processing time in the manufacture of enteric coated formulations of an acid-sensitive active pharmaceutical ingredient as compared to the existing methods.

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Keywords

Lansoprazole; release; stability; hot-melt extrusion; enteric coating

INTRODUCTION

Lansoprazole (LNS), a *benzimidazole* derivative, is a proton pump inhibitor and BCS class II drug characterized by low solubility and high permeability.^{1–3} It is crystalline in nature⁴ and sensitive to acid, heat, and light.^{5, 6} Solid dispersion is an approach to enhance the solubility of poorly soluble molecules, which involves conversion of the drug from the crystalline to the amorphous phase.^{7, 8} To improve the solubility of LNS, many solid dispersion techniques have been used.^{3, 9} Furthermore, addition of an alkalizer can improve the solubility of LNS⁵, which increases with the increase in the pH.^{10, 11}

Hot-melt extrusion (HME) is one of the preferred techniques for improving the solubility of poorly soluble active pharmaceutical ingredients (APIs) by preparing solid dispersions.^{12, 13} Preparing a solid dispersion of a heat-labile API by using the HME method is challenging because of the temperature and shearing force.^{14–16} Therefore, for LNS, formulation using melting methods that require a high temperature is not applicable.⁹

LNS is sensitive to acid; thus enteric coating is necessary to avoid degradation by the gastric fluid. The stability of LNS is also affected by the free carboxyl group of the enteric polymer.¹⁷ Thus, stabilization can be achieved by adding an alkalizing agent to the drug layer to provide a suitable microenvironmental pH (pH), or by using an intermediate inert layer to separate the drug from the enteric coating.^{18, 19} The manufacturing of the LNS tablet undergoes many processing steps, including preparation of the granules followed by the undercoating and enteric coating processes and, finally, the tablet compression.²⁰ Each coating process is very time consuming as it involves a coating step, which is then followed by a drying step. Also, to improve the properties of the granules during tablet compression, the number of the coating layers should be increased.²¹ As the number of the coating layers increases, the processing time increases¹⁹ making the production of LNS tablets costly and time consuming. HME, on the other hand, is a continuous process that reduces formulation processing time and also helps in improving the physiochemical properties of the API. To date, no studies have reported the application of HME for the preparation of LNS formulations.

In this study, Kollidon® 12 PF (K12), Lutrol® F 68 (F68), and magnesium oxide (MgO) were used as excipients to process LNS using HME. K12 is polyvinylpyrrolidone (PVP) with a glass transition temperature (T_g) of 90°C; it is mainly used as a solubilizing agent. F68, which has a low melting point (55°C), works as a solubilizer and plasticizer in HME applications.²² MgO is used in the enteric coating formulation as stabilizing agent.¹⁸ It is also used to modulate the pH for solubility enhancement.²³ For the enteric coating process, Eudragit® L 100-55 was used as an enteric coating polymer. It is an anionic methacrylate copolymer which dissolves at a pH of 5.5 or higher²⁴.

The aim of the current work is to utilize the HME process to improve the physiochemical properties of LNS to prepare stable enteric coated tablets. In this study, LNS was extruded with polymers using the HME process and was further compressed into tablets followed by enteric coating using a pan coater.

MATERIAL AND METHODS

Material

LNS was kindly gifted by Lupin Pharmaceuticals Ltd (Pune, India). K12 and F68 were kindly gifted by BASF SE (Ludwigshafen, Germany). Triethyl citrate was obtained from Fisher Scientific (Pittsburgh, PA, USA). Avicel® 102 and Ac-Di-Sol® Croscarmellose Sodium were generously gifted by FMC Biopolymers (Philadelphia, PA, USA). Aerosil® 200 and Eudragit® L 100-55 were gifted by Evonik (Evonik Industries, Germany). Magnesium stearate was purchased from Spectrum Laboratory Products Inc. (Gardena, CA, USA). Magnesium oxide USP light and Talc were purchased from PCCA (Houston, TX, USA). All other chemical reagents used for HPLC, dissolution, and coating were of analytical grade.

Methods

Hot-melt extrusion—In the preliminary studies, low viscosity grade polymers such as K12 and HPMC E5 were used as a single polymeric carrier to extrude LNS. However, there was a need to add a plasticizer to decrease the extrusion temperature in order to avoid LNS degradation caused by high extrusion temperatures. Based on the literature and preliminary studies, K12 was finally chosen as a polymeric carrier for the extrusion process for many reasons, including the possibility of producing a solid dispersion and forming hydrogen bonds with LNS^{3,9}, its solubilizing effect as well as its low glass transition temperature (T_g). F68 was selected as a plasticizer and MgO as an alkalizer. Furthermore, a less shear generating screw design (Figure 1) was utilized to reduce the effect of the high-energy input of the HME technique. Using a V-Shell blender (MaxiBlend™, GlobePharma, North Brunswick, NJ, USA), the drug and the excipients were mixed for 10 min at 25 rpm prior to the extrusion process. LNS at a 10% drug load with K12 and F68 was melt-extruded with or without the alkalizer by using a co-rotating twin-screw extruder (11 mm Process 11, ThermoFisher Scientific). The formulation design and the processing conditions are shown in Table 1. The milling process was performed using a comminuting mill (Fitzpatrick, Model L1A). The drug contents of the physical mixtures and the extrudates were analyzed using HPLC.

Differential scanning calorimetry (DSC)—DSC studies were performed on PerkinElmer Diamond DSC system. Using a temperature range of 30°C to 200°C, 2–5 mg of the sample was placed in an aluminum pan and heated using a heating rate of 10°C/min. Pyris software (Perkin Elmer Life and Analytical Sciences, Connecticut, USA) was used to analyze the data.

Chromatographic analysis—Using Waters HPLC-UV system (Waters Corp, Milford, MA, USA), chromatographic analysis was performed at a wavelength of 288 nm utilizing

the stationary phase Phenomenex Luna[®] RP C18 column (250×4.6 mm; particle size, 5 µm). The mobile phase consists of KH₂PO₄ buffer (pH 4.5) and acetonitrile in a ratio of 54:46 (v:v%) using a flow rate of 1.0 ml/min.⁹

mpH measurement—To measure the _MpH of the formulation, the equivalent of 15 mg of LNS extrudates was placed in a dissolution medium (pH 6.8 phosphate buffer with 5 mM sodium lauryl sulfate [SLS]) for 5 min. Then, the _MpH of the sample was measured using an Oakton pH meter (pH Spear, Fisher Scientific).

***In vitro* release**—*In vitro* release studies were performed using Hanson SR8-plus[™] dissolution apparatus (Chatsworth, CA). The equivalent of 15 mg of LNS extrudates was filled into a gelatin capsule and drug release was studied in 900 ml of phosphate buffer (pH 6.8 with 5 mM SLS) for 60 min at 75 rpm and 37°C using USP Type II apparatus. The *in vitro* release study for the enteric coated LNS tablet was performed as described in the US Pharmacopeia. The acid stage medium was 0.1 N HCl while the buffer stage medium had pH 6.8 with 5 mM SLS at a paddle speed of 75 rpm for 60 minutes at 37°C using USP Type II apparatus for each stage. Samples were withdrawn at different sampling time points and equal amount of the fresh medium was added back to the vessels to maintain the sink condition. It was performed in triplicates and the samples were analyzed using HPLC. To assess the similarity between the dissolution profiles, the following similarity factor equation was used:²⁵

$$f_2 = 50 \cdot \log \left\{ 1 + \left(\frac{1}{n} \right) \sum_{t=1}^n (R_t - T_t)^2 \right\}^{-0.5} * 100$$

Where:

R_t and T_t are the percentage of drug dissolved at each time point for the reference and the test, respectively. n is the number of dissolution sampling times. The two dissolution profiles are considered similar if $f_2 \geq 50$.

Fourier transform infrared spectroscopy (FT-IR)—FT-IR studies were conducted on an Agilent Cary 660 FT-IR Spectrometer (Agilent Technologies, Santa Clara, CA) in the range of 4000-650 cm⁻¹ to study the interaction between the drug and the carrier for the physical mixtures and the extrudate samples. The bench was equipped with an ATR (Pike Technologies MIRacle ATR, Madison, WI), which was fitted with a single-bounce, diamond-coated ZnSe internal reflection element.

Compatibility with an enteric coating polymer—To prepare a stable enteric coated tablet of LNS without using an intermediate barrier layer, compatibility studies of the formulations with L100-55 were conducted. The extrudates of formulations F1 b and F2 were individually mixed with L100-55 in a ratio of 1:2 (w:w). The mixtures were further stored in a closed glass vial for 12 months under storage conditions of 25°C/60% RH. After 6 and 12 months, drug content analysis was used to assess the chemical stability of the formulation in the presence of the enteric polymer.

Preparation and evaluation of the LNS core tablet—The extrudate and the other tablet excipients mentioned in Table 2 were sieved using USP #35 mesh and mixed for 10 min using V-shell blender; further, magnesium stearate was added to the blend and lubricated for 2 min. Using standard concave tooling (10 mm), tablets were compressed utilizing a single punch tablet press (MCTMI, GlobePharma Inc., New Brunswick, NJ) at a compression force of 550 psi. The tablets were further evaluated for hardness, disintegration time, and friability using a Dr. Schleuniger hardness tester, a Dr. Schleuniger Pharmatron USP disintegration apparatus, and a Vander Kamp friabilator (Vankel Industries Inc., Chatham, NJ), respectively..

Enteric coating of tablets—The enteric coating solution consists of Eudragit® L100-55: triethyl citrate (TEC): talc: acetone: isopropanol: water in a ratio of 6.25: 0.625: 3.125: 34.29: 51.42: 4.29 (%w/w). The quantities and the method of preparation were based on the recommendation of the manufacturer to prepare a film coating for gastrointestinal targeting.²⁶ The coating process for the core tablets was performed utilizing LDCS-5 coater (Vector Freund, Marion, IA) using the following processing parameters: inlet air temperature (30°C), exhaust air temperature (28°C), pan speed (35 rpm), and pump speed (10 rpm).

Stability—To study their physical and chemical stability, the extrudates were stored in closed glass vials using 25°C/60% RH storage conditions for 12 months. DSC was utilized to assess the physical stability of the extrudates, while drug content analysis was used to investigate the chemical stability. The enteric coated tablets were stored in closed glass vials under stability conditions of 25°C/60% RH for 6 months and their chemical stability was assessed. The studies were performed in triplicate.

Scanning electron microscopy—To examine the surface morphology of the enteric coated tablet, a scanning electron microscope (SEM, JEOL, JSM-5600) was used. A tablet was mounted on adhesive carbon pads placed on aluminum stubs and sputter-coated with gold. The sputter coating process was performed using a Hummer® 6.2 sputter system (Anatech Ltd, Springfield, VA). The microscope was operated at an accelerating voltage of 10 kV.

RESULTS AND DISCUSSION

Hot-melt extrusion

LNS is a heat-labile API that degrades under high temperatures. To minimize the effect of temperature, a shortened and less stressful screw configuration was used. In addition, 30% of the plasticizer (F68) was used to decrease the extrusion temperature. Table 3 shows the effect of the extrusion temperature on the post-processing drug content. For the formulation (F1 a) prepared without alkalizer, using 80° C for the extrusion process resulted in a low drug content (68%) of the API, while decreasing the extrusion temperature to 65° C for (F1 b) improved the post-processing drug content of LNS to 86%. This confirms the sensitivity of LNS to temperature and indicates the significant effect of the extrusion temperature on the stability of LNS during the process. The thermal stability of LNS can be enhanced by using an alkaline stabilizer²⁷. Adding MgO to the formulation improved the extrudability of

LNS and resulted in about 97% post-processing drug content of the formulation (F2). This might be due to stability of drug in presence of MgO. Also, the presence of the alkalizer in the formulation reduces moisture absorption which further affects its stability.¹ All further studies were performed based on the drug content of each formulation.

DSC

The DSC studies indicated a melting endothermic peak of LNS at around 178°C, while the exothermic peak represented the decomposition of LNS (Figure 2). However, the formulations F1 b and F2 exhibited the absence of the melting peak, which indicates the transformation of LNS from the crystalline to the amorphous form within the matrix after processing using HME.

In vitro release

The release profile of LNS formulations F1 b and F2 processed using HME (Figure 3) showed enhanced release compared to that of the pure drug. This may be due to the conversion of LNS into an amorphous solid dispersion, which has higher water solubility than the crystalline form in addition to the solubilization effect of F68 and K12. The addition of the alkalizer (MgO) to F2 increased its m_pH and further improved the release compared to F1 b. Several studies have reported the effects of pH modulation on release behavior after addition of an acidifier or alkalizer.^{28, 29} For the APIs influenced by pH-dependent solubility, the addition of a pH modifier to the formulation can provide a suitable environment for API to dissolve in greater extent. Tabata *et al.* (1992) stated the relationship between the pH and the solubility of LNS, where solubility increases at pH 9 and above. The m_pH study showed the effects of adding the alkalizer to formulation F2. When F2 was exposed to the dissolution medium, the alkalizer (MgO) which molecularly dispersed within the matrix modulated the m_pH to 9.5 in comparison to m_pH of 7.36 in F1 b. The effect of the m_pH on the release was observed where, the formulation F2 has a higher release compared to F1 b due to the increased solubility of LNS at pH 9.5.

From the *in vitro* release studies, it was found that the solid dispersion of LNS using the HME method improved its release, which was further improved by including the alkalizer in the formulation.

Fourier transform infrared spectroscopy (FT-IR)

FT-IR studies were conducted to evaluate the drug-polymer interaction. The results in Figure 4 demonstrate the characteristic stretching peaks of LNS at 3215.92, 2984.31, 1579.58, 1280.49, 1116.62, and 1036.36 cm^{-1} , which represent the stretching of $-NH$, $-CH_2-$, $C=N$, $C-N$, ether band, and $S=O$.^{3, 9} To investigate the interaction between the API and the excipients after the processing using HME, the spectra of the LNS, physical mixtures, and extrudates were studied. The spectra, shown in Figure 4, confirmed the results reported in previous studies regarding the intermolecular interaction between K12 and LNS by an absence of the characteristics peak of LNS at around 3215 cm^{-1} of both F1 b and F2 formulations. This peak was clearly observed in the corresponding physical mixtures, which indicates the formation of hydrogen bonding between LNS and K12 after the HME process. The absence, shift, and decreased intensity of other characteristics peaks of LNS at 2984.31,

1579.58, 1116.62, and 1036.36 cm^{-1} in the extrudates compared to the physical mixtures might be a result of the intermolecular interaction between LNS and K12 or F68.^{3, 9} Presence of MgO in F2 did not show any difference in interaction compared to F1 b. The FTIR studies indicated that hydrogen bonding can occur during the preparation of LNS solid dispersion using HME.

Stability

The physical stability of the amorphous dispersions is critical, as they tend to recrystallize during storage. Proper carrier selection, which can form H- bonding with the API, can solve this problem and physical stabilize the API for longer storage times.³⁰ In this study, the physical stability of the extrudates was determined by DSC. The DSC studies (Figure 5) indicate that LNS was stable and present in the amorphous form after 12 months of storage at 25°C/60% RH for the F1 b and F2 formulations. The physical stability of these formulations was attributed to hydrogen bonding between LNS and the carriers as a result of HME. Also, hydrogen bonding has an influence on the chemical stability of the API.^{30, 31} Drug content analysis studies after 6 and 12 months (Table 4) indicated no drug degradation in the formulations, confirming the chemical stability of the drug. This is because the drug was dispersed within the carrier and they were molecularly interacted. To study the influence of extrusion process on the chemical stability of LNS in the formulation, the extrudate F1 b and its physical mixture were stored in a closed glass vial under accelerated stability conditions of 40°C/75% RH for 1 week. The result indicated that the drug content of the physical mixture was 84%, which indicated the degradation of LNS after 1 week of storage, while the extrudate exhibited no chemical degradation of the API. The stability study showed that the hydrogen bonding induced between the drug and the carrier during the extrusion process positively affected the physical and chemical stability of LNS.

Compatibility with an enteric coating polymer

Stable enteric coated dosage forms of proton pump inhibitors are critical because of their chemical instability to the enteric coated polymer, which has a free carboxylic group. Degradation occurs when the sulfoxide group present in proton pump inhibitors is attacked by the proton.³² Using an intermediate layer or adding an alkaline agent to the drug layer are two solutions to overcome this problem. Chen *et al.* (2004) prepared stable enteric coated omeprazole tablets with a single enteric coating layer by adding the alkaline agent within the drug layer. Tabata *et al.* (1992) hypothesized that LNS degradation would be less extensive when the environmental pH of the dosage form is around 9. In this work, F2, which contains an alkalizer, showed chemical stability during storage for 12 months, while F1 b was not able to resist the degradation effect of L 100-55 (Table 5). The stability of LNS in F2 is mainly due to the presence of the alkalizer (MgO), which provides a MpH of 9.5.

Based on the extrudability of material through HME, along with dissolution, stability, and compatibility studies, it was determined that F2 was the most optimal formulation.

Lansoprazole core tablet evaluation

The tablets of the extrudate F2 were compressed and evaluated for thickness, hardness, and friability, and were subjected to the disintegration test. The average thickness of the tablets

was 4.82 mm, the hardness of the tablets was 7.4 Kp and the friability was 0.62%. The disintegration time of the core tablets was within 8 minutes.

Enteric coating of the core tablet

Enteric coating of LNS tablets is required to maintain stability in the acidic environment of the stomach. LNS core tablets prepared by direct compression were further enteric-coated using Eudragit® L100-55. The coating process was performed until 9% weight gain was achieved. The SEM image of the enteric-coated tablet indicates that the film coat is homogenous and the surface of the tablet is smooth. In addition, the tablet surface is free from the pores or cracks, revealing the well-aligned coating process (image not shown). The enteric-coated tablets passed the disintegration test in 0.1 N HCl for 2 hours. The disintegration time in phosphate buffer was approximately 15 minutes.

In vitro release and stability of the enteric coated tablet

The *in vitro* release of the enteric coated LNS was evaluated according to US Pharmacopeia, where drug release in the acid stage should not be more than 10% in one hour, while its release in the buffer stage should be more than 80% in one hour. In this study, the release of the enteric coated tablet exhibited almost no release of LNS in the acid stage, indicating a resistance to drug release due to sufficient enteric coating. In the buffer stage, the thickness of the enteric layer influenced the disintegration of the tablet and further affected the release of LNS in the first 10 minutes as compared to the marketed formulation, which is a fast disintegrating tablet. After 40 min there was more than 80% release in the buffer stage, which meets USP requirements (Figure 6). By the end of the study, the release of LNS, at the last time point, in the buffer stage was significantly ($p < 0.05$) higher than the marketed formulation (Prevacid® Solutab™ 15 mg). The *in vitro* release study indicates that the conversion of LNS into an amorphous solid dispersion using HME and the solubilization effect of K12 and F68 positively influenced the release of LNS to a greater extent.

There was no significant change in drug content of the enteric coated tablet, indicating the stability of LNS in this formulation at 25°C/60% RH for 6 months (Table 6). The chemical stability of LNS in the enteric coated tablet can be attributed to many factors. The most important factor is the presence of the alkalizer in the extrudate, which allows an appropriate pH for LNS stabilization. Another factor is the dispersion of LNS within the polymeric matrix, which might work as a protective layer. The release profile of the enteric coated LNS after 6 months stability was similar ($f_2 = 64$) to the initial tablets, indicating formulation stability.

CONCLUSIONS

The current process for manufacturing stable LNS dosage form is a lengthy process due to its physiochemical properties and multiunit processing. Using hot melt extrusion to prepare the formulation not only improves the solubility and stability of LNS but also reduces processing time. Selection of the excipients for the extrusion process plays a key role in the quality of the extrudates and the stability of LNS. Extrusion with polymeric carrier K12 results in the formation of an amorphous solid dispersion of LNS with intermolecular

interaction influencing the stability of the API. Lutrol® F68 acts as a plasticizer and thereby reduces the extrusion processing temperature of heat-sensitive LNS as well as assists in solubilizing the drug. Inclusion of the MgO in the extrusion process had a significant effect on the extrudability and the release of LNS. Additionally, it imparts stability to the API in the presence of the enteric coating polymer. The core tablets of the optimized extrudates were enteric coated using Eudragit® L100-55 and this coating protected LNS in the acidic medium. The final enteric coated tablet of LNS passed the acidic stage test of the release study (less than 10%), and in the buffer stage, it released more than 80% of the drug, which meets USP requirements. In addition, the final dosage formulation was stable after 6 months of storage at 25°C/60% RH. From this novel work, we concluded that hot-melt extrusion technology is a valuable process in manufacturing enteric-coated lansoprazole tablets with respect to improved solubility and stability, and reduced processing time for manufacturing compared to the alternative process.

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Figure 1.
Modified screw design used for preparation of lansoprazole using hot-melt extrusion

Figure 2.
DSC graphs of pure lansoprazole, F1 b (10% LNS- 30% F68- K12), and F2 (10% LNS- 4% MgO- 30% F68- K12)

Figure 3.
Dissolution profiles of pure lansoprazole, F1 b (10% LNS- 30% F68- K12), F2 (10% LNS- 4% MgO- 30% F68- K12), and the core tablet in phosphate buffer (pH 6.8, 5 mM SLS)

Figure 4.
FT-IR analysis of pure lansoprazole, physical mixtures (F1 b and F2), and the extrudates (F1 b and F2)

Figure 5. DSC graphs of F1 b (10% LNS- 30% F68- K12) and F2 (10% LNS- 4% MgO- 30% F68- K12) after 12 months of storage (25°C/60% RH) and pure lansoprazole

Figure 6. Dissolution profile of lansoprazole marketed formulation and lansoprazole enteric coated tablet before and after 6 months of storage (25°C/60% RH). The acid stage (0.1 N HCl) was the first 1 hour and the buffer stage (phosphate buffer, pH 6.8, 5 mM SLS) was the second hour.

Table 1

Hot-melt extrusion formulation design and processing conditions

Formulations	Lansoprazole (%/w/w)	MgO (%/w/w)	Lutrol® F 68 (%/w/w)	Kollidon® 12 PF (%/w/w)	Processing parameters	
					Temperature (°C)	Screw Speed (rpm)
F1 a	10	-	30	60	80	100
F1 b	10	-	30	60	65	100
F2	10	4	30	56	65	100

Table 2

Composition of lansoprazole core tablet

Tablet Excipients	Weight (mg/tablet)
F2 extrudate (LNS)	150 (15)
Avicel® 102	104
Aerosil® 200	15
Ac-Di-Sol® Croscarmellose Sodium	30
Magnesium stearate	1
Total	300

Table 3

Post processing drug content for F1 a, F1 b, and F2.

Formulation	Drug content (%)
F1 a	68.23 $\pm$ 2.18
F1 b	86 $\pm$ 4.73
F2	97.41 $\pm$ 2.20

(mean $\pm$ SD, n = 3)

Table 4

Drug content analysis of F1 b (10% LNS- 30% F68- K12) and F2 (10% LNS- 4% MgO- 30% F68- K12) after 6 and 12 months of storage (25°C/60% RH).

Formulation	Duration of the sorage (months)	Drug content (%)
F1 b	6	96.21 ± 0.23
F1 b	12	96.91 ± 2.11
F2	6	98.83 ± 0.64
F2	12	99.12 ± 0.87

(mean ± SD, n = 3)

Table 5

Drug content analysis for the compatibility study of F1 b (10% LNS- 30% F68- K12) and F2 (10% LNS- 4% MgO- 30% F68- K12) mixed with the enteric coating polymer L100-55 in a ratio of 1:2 after 6 and 12 months of storage (25°C/60% RH)

Mixture	Duration of the sorage (months)	Drug content (%)
F1 b + Eudragit® L100-55	6	9.3 ± 1.2
F1 b + Eudragit® L100-55	12	0
F2 + Eudragit® L100-55	6	97 ± 2.3
F2 + Eudragit® L100-55	12	97 ± 5.1

(mean ± SD, n = 3)

Table 6

Drug content analysis of lansoprazole enteric coated tablet after 1, 3, and 6 months of storage (25°C/60% RH).

Formulation	Drug content (%)		
	1 month	3 months	6 months
Lansoprazole enteric coated tablet	97.84 ± 1.46	96.71 ± 3.14	97.23 ± 4.15

(mean ± SD, n = 3)