**RESEARCH PAPER**

# Formulation and evaluation of Oral Thin Film of Esomeprazole and Domperidone Using $3^2$Factorial Design

Atul Gupta[1]*, Vinesh Kumar[2], Anil Kumar Goyal[3], Barkha Kumawat[4], Jyoti Agarwal[5]

*L.B.S College of Pharmacy*
*Email:ID: atuljps@gmail.com*
***Corresponding Author***
*Atul Gupta, L.B.S. College of Pharmacy,*
*Email:ID: atuljps@gmail.com*
***Received:** 20th Feb, 2026; **Revised:** 4th Mar, 2026; **Accepted:** 25th Mar, 2026; **Available Online:** 10th Apr, 2026*

**ABSTRACT**
This study focused on the formulation and evaluation of oral thin films (OTFs) containing Esomeprazole, a proton pump inhibitor, and Domperidone, a dopamine antagonist, for the management of gastrointestinal disorders. OTFs were developed to address limitations of conventional oral dosage forms, particularly for patients with swallowing difficulties, and to improve solubility, bioavailability, and patient compliance. Film-forming agents such as Hypromellose, Carbomer 974, and Polyvinyl Alcohol were employed, and key formulation parameters—mechanical strength, disintegration time, and drug release—were optimized. Physicochemical evaluations included thickness, weight variation, folding endurance, swelling index, drug content uniformity, and in-vitro disintegration and dissolution studies. A $3^2$ full factorial design was used, with Hypromellose and Carbomer 974 concentrations as independent variables. Among the formulations, F3 exhibited optimal properties, with rapid disintegration (12 seconds), uniform drug content, and excellent dissolution profiles for both drugs. The findings highlight that OTFs offer a promising platform for delivering Esomeprazole and Domperidone, enabling precise dosing, rapid onset of action, and improved therapeutic efficacy, especially for pediatric and geriatric patients. This approach presents a viable alternative to conventional dosage forms in gastrointestinal therapy
**Keywords**: Oral Thin Films (OTFs), Esomeprazole, Domperidone, Drug Delivery, Bioavailability, Quality by Design, Drug Release.
**How to cite this article:** Gupta A, Kumar V, Goyal AK, Kumawat B, Agarwal J; Formulation And Evaluation Of Oral Thin Film Of Esomeprazole And Domperidone Using $3^2$ Factorial Design.Int J Drug Deliv Technol. 2026;16(26s):171 181. Doi: 10.25258/ijddt.16.26s.17
**Source of support:** Nil.
**Conflict of interest:** Nil.

## INTRODUCTION

The development of innovative drug delivery systems is a key focus in pharmaceutical research, aiming to overcome the limitations of traditional oral dosage forms like tablets and capsules. Oral thin films (OTFs) have emerged as a promising alternative, offering advantages such as rapid disintegration, ease of use, and improved patient compliance. These thin, flexible strips dissolve quickly in the oral cavity, providing precise dosage control, bypassing first-pass metabolism, and potentially enhancing bioavailability, particularly for poorly water-soluble drugs.[1-2]

Esomeprazole and domperidone are widely used in treating gastrointestinal disorders. Esomeprazole, a proton pump inhibitor, effectively reduces gastric acid secretion, while domperidone, a dopamine antagonist, improves gastrointestinal motility and alleviates nausea and vomiting. However, both drugs face challenges in conventional dosage forms due to poor solubility, low bioavailability, and patient adherence issues, particularly among elderly and pediatric patients who may struggle with swallowing tablets or capsules.[3-4]

This study aimed to formulate and evaluate oral thin films of esomeprazole and domperidone, focusing on achieving rapid disintegration, adequate mechanical strength, and optimal physicochemical properties. The formulation utilizes OTF technology to enhance the delivery and therapeutic efficacy of these drugs. Key formulation parameters, such as the concentration of film-forming polymers, emulsifiers, and plasticizers, were optimized to strike a balance between mechanical stability, drug release, and patient acceptability.[5]

The OTFs were comprehensively evaluated through various physicochemical and in-vitro tests, including thickness, weight variation, folding endurance, surface pH, swelling behavior, disintegration time, and drug content. In-vitro dissolution studies were conducted to assess the release profiles of both drugs and their correlation with formulation variables. The findings from this research contribute to the growing knowledge on OTF technology and provide valuable insights into its potential for enhancing the delivery of esomeprazole and domperidone.[6-7]

## METHODOLOGY

### Materials, Chemicals, and Reagents

The materials used in this study included Esomeprazole and Domperidone as active pharmaceutical ingredients (APIs). Film-forming agents such as Hypromellose, Carbomer 974 (Carbopol), and Polyvinyl Alcohol were used, with Hypromellose also acting as an emulsifier and plasticizer. Glycerin served as a plasticizer, while Benzoic Acid and

*Author for Correspondence:* atuljps@gmail.com.

Sodium Benzoate were included as preservatives. Citric Acid was used to adjust pH, and sweeteners like Sucrose and Sucralose enhanced palatability. Sodium Lauryl Sulfate acted as a surfactant, Clove was used for flavor, Beta-Cyclodextrin as a complexing agent, and Crosscarmellose Sodium and Crospovidone were included as superdisintegrants. Purified water was the vehicle for the formulation.

**Equipment and Instruments**

The research utilized various equipment, including an electronic balance (OHAUS) for weighing, a mechanical sifter (Sartorius) with sieves for particle size analysis, and stainless steel SS 316 vessels (Electrolab) for material handling. A hot plate (Effem) and mechanical stirrer (Remi Motor Pvt. Ltd.) were used for formulation preparation, while a digital pH meter (Lab India) measured pH and a magnetic stirrer (Equitron) ensured uniform mixing. Viscosity was measured with a Brookfield viscometer, and film thickness was determined using a Vernier caliper and thickness gauge (Sunshine Instruments). HPLC analysis was conducted with a Waters system, UV-visible spectroscopy with a Shimadzu spectroscope, and thermal analysis using a DSC 60 and FTIR 1800 (Shimadzu).

**Evaluation and Characterization of Drugs**

The organoleptic properties of Esomeprazole and Domperidone, including color, odor, and physical form, were observed visually. Identification tests were conducted using Infrared (FTIR) and UV spectroscopy. For FTIR, the drug samples were mixed with dried potassium bromide (KBr), and spectra were recorded. UV spectra were obtained by scanning 10 ppm solutions of the drugs in 0.1 N HCl across 200–400 nm. The melting point of the drugs was determined using the capillary method, and solubility was tested in pH 6.8 buffer, water, alcohol, and acetonitrile. Excess drug was dissolved, filtered, and analyzed using UV spectrophotometry. Drug content was quantified by HPLC, with a mobile phase prepared from potassium dihydrogen phosphate, methanol, and acetonitrile, and detection at 284 nm. DSC analysis was performed to evaluate thermal properties and drug-excipient compatibility, recording thermograms for pure drugs, excipients, and the optimized batch.[8-12]

**Drug-Excipient Compatibility:**

Compatibility studies were conducted using FTIR and pH analysis. FTIR spectroscopy was employed to examine potential interactions between Esomeprazole, Domperidone, and excipients by recording the IR spectra of the pure drugs, polymers, and their combinations in the range of 4000–400 $cm^{-1}$. Additionally, pH compatibility was assessed by dissolving drug-excipient mixtures in water and measuring the pH using a digital pH meter. These tests aimed to ensure the stability and suitability of the formulations.[13-15]

**Preparation of Preliminary Trial batches of Oral Thin Films (OTFs):**

Six preliminary trial batches of oral thin films (OTFs) for Esomeprazole and Domperidone were developed using the solvent casting method. The concentrations of HPMC K4M, Carbomer 974, and Polyvinyl Alcohol were varied. In the process, Hypromellose, Carbomer, PVA, glycerin, citric acid, benzoic acid, and sodium benzoate were dissolved in purified water at 60°C to form Solution A. Other excipients, including Sodium Lauryl Sulfate, Croscarmellose Sodium, Beta Cyclodextrin, Clove, and Sucralose, were dissolved separately to form Solution B. Both solutions were mixed, followed by the addition of the active pharmaceutical ingredients (APIs). The solution was vacuumed to remove air, cast into films, and dried. The resulting films were cut into 2.5 cm x 2.5 cm pieces.[16]

**Table No. 1 Preliminary Trial Batches Composition**

| Ingredients | PT1 | PT2 | PT3 | PT4 | PT5 | PT6 |
|---|---|---|---|---|---|---|
| Esomeprazole | 20 | 20 | 20 | 20 | 20 | 20 |
| Domperidone | 10 | 10 | 10 | 10 | 10 | 10 |
| Hypromellose | -- | -- | 10 | 15 | 10 | 15 |
| Carbomer 974 (Carbopol) | 10 | 5 | -- | -- | 10 | 5 |
| Polyvinyl Alcohol | 10 | 15 | 10 | 15 | -- | -- |
| Glycerin | 10 | 10 | 10 | 10 | 10 | 10 |
| Benzoic Acid | 2 | 1 | 2 | 1 | 2 | 1 |
| Sodium Benzoate | 1 | 2 | 1 | 2 | 1 | 2 |
| Citric Acid | 5 | 5 | 5 | 5 | 5 | 5 |
| Sucrose | -- | 3 | 3 | 3 | -- | -- |
| Sucralose | 3 | -- | -- | -- | 3 | 3 |
| Sodium Lauryl Sulfate | 2 | 2 | 2 | 2 | 2 | 2 |
| Clove | 2 | 2 | 2 | 2 | 2 | 2 |
| Beta cyclodextrin | 3 | 2 | 3 | 2 | 2 | 2 |
| Crosscarmellose Sodium | 3 | 3 | 3 | 3 | 3 | 3 |
| Crospovidine | 3 | 3 | 3 | 3 | 3 | 3 |
| Purified Water | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |

**Formulation of Oral Thin Film using $3^2$ full factorial design**

The quality target product profile (QTPP), which encompasses a summary of the quality attributes of the drug product for achieving the oral thin film to achieve the best therapeutic effects, was established in accordance with the QbD-based approach to drug product development. Numerous patient-centric critical quality attributes (CQAs) relating to the calibre of the completed product were established in order to achieve the QTPP.

The main components of the QTPP for creating OTF are outlined in the supplemental material, together with the appropriate justifications for the CQAs.

An optimization study was conducted for prepared OTF using a $3^2$ (two-factor; three-level) experimental design. Independent variables (factors) selected for the study

included concentrations of HPMC K4M (X1) and Carbomer 974 (X2), each varied at three levels (low, intermediate, and high). The selection of factor levels was based on preliminary trial batches conducted prior to the implementation of the factorial design.

**Table No. 2 Factors and levels of independent variables in $3^2$ factorial designs**

| Coded Level | Low (-1) | Intermediate (0) | High (+1) |
|---|---|---|---|
| $X_1$ (HPMC K4M) | 5 | 10 | 15 |
| $X_2$ (Carbomer 974) | 5 | 10 | 15 |

**Table No. 3 A $3^2$ factorial design experimental layout**

| Formulation code | Coded factor levels | |
|---|---|---|
| | $X_1$ (HPMC K4M) | $X_2$ (Carbomer 974) |
| F1 | 5 (-1) | 15 (+1) |
| F2 | 10 (0) | 15 (+1) |
| F3 | 15 (+1) | 15 (+1) |
| F4 | 5 (-1) | 10 (0) |
| F5 | 10 (0) | 10 (0) |
| F6 | 15 (+1) | 10 (0) |
| F7 | 5 (-1) | 5 (-1) |
| F8 | 10 (0) | 5 (-1) |
| F9 | 15 (+1) | 5 (-1) |

**Table No. 4 Formulation of Oral Thin Film**

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Esomeprazole | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| Domperidone | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Hypromellose | 5 | 10 | 15 | 5 | 10 | 15 | 5 | 10 | 15 |
| Carbomer 974 (Carbopol) | 15 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 5 |
| Glycerin | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Benzoic Acid | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 2 |
| Sodium Benzoate | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 1 |
| Citric Acid | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Sucralose | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Clove | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Beta cyclodextrin | 2 | 3 | 2 | 3 | 2 | 2 | 2 | 2 | 2 |
| Sodium Lauryl Sulfate | 2 | 3 | 2 | 3 | 2 | 2 | 2 | 2 | 2 |
| Crosscarmellose Sodium | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Crospovidine | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Purified Water | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |

**Evaluation of Oral Thin Films (OTFs):**[17-20]

- **Physical Appearance:** OTFs were visually and sensually evaluated for color, homogeneity, transparency, smell, texture, taste, and flavor.
- **Surface pH:** The pH was measured using a combined pH electrode on a slightly moistened film to ensure it remained near neutral to prevent oral mucosal irritation.
- **Thickness:** Thickness was measured at five points on each film using a digital gauge, with results reported as mean ± SD.
- **Weight Variation:** Ten films were individually weighed, and the average weight was calculated to check for consistency.
- **Folding Endurance:** Films were folded repeatedly at the same spot until they broke, with the number of folds recorded as folding endurance.
- **Swelling Property:** Films were weighed and immersed in pH 6.8 buffer, and the increase in weight was measured at intervals until constant weight was achieved.
- **Drug Content:** HPLC was used to determine drug content under specified chromatographic conditions (detection at 284 nm, run time of 20 min).
- **In-vitro Disintegration Studies:** Disintegration time was measured in water or buffer, typically ranging from 5 to 30 seconds, depending on formulation content.
- **Dissolution Studies:** Dissolution rates were assessed in 900 ml pH 6.8 buffer at 37°C ± 1°C using a USP basket apparatus at 50 rpm, with samples analyzed at regular intervals.

## RESULTS AND DISCUSSION

### Analytical Evaluation of Drug API

***Appearance***

The appearance of the drugs was consistent with their expected forms: Esomeprazole appeared as a white powder, while Domperidone was observed as a fine white powder, indicating the purity of the drugs.

***Identification Tests:***

Identification of Esomeprazole and Domperidone was performed using Infrared (IR) Spectroscopy and UV absorbance spectra.

- **IR Spectroscopy**:

- The IR spectrum of Esomeprazole (Figure No. 1) revealed characteristic peaks at 3445.22 $cm^{-1}$ (O-H stretching), 1726 $cm^{-1}$ (C=O stretching), and 1515.71 $cm^{-1}$ (Aromatic C=C stretching), among others, confirming its identity.
- For Domperidone (Figure No. 2), the prominent peaks at 2953 $cm^{-1}$ (C-H stretching), 1662 $cm^{-1}$ (C=O stretching), and 1557 $cm^{-1}$ (Aromatic C=C stretching) were observed, supporting its structural identity.

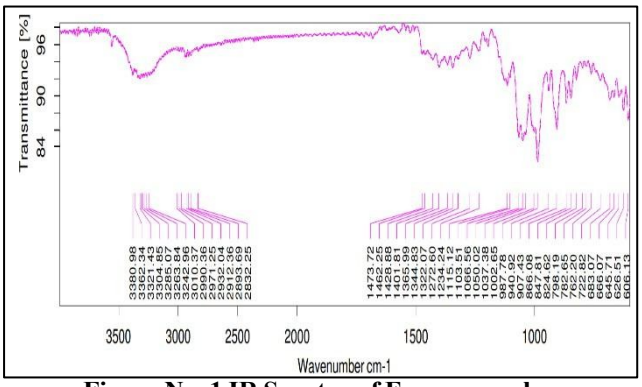


**Figure No. 1 IR Spectra of Esomeprazole**

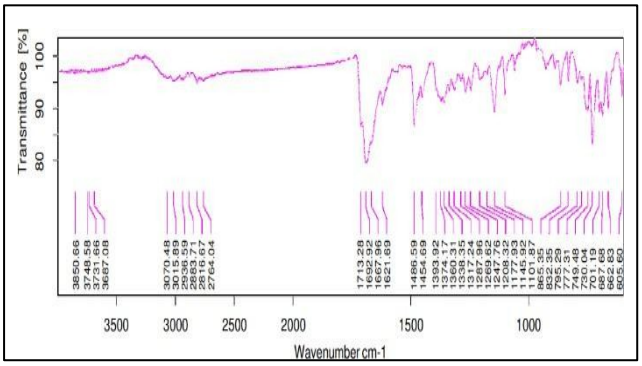


**Figure No. 2 IR Spectra of Domperidone**

- **UV Spectroscopy**:
  - Esomeprazole exhibited a λmax at 301 nm (Figure No. 3), which corresponds to its known absorbance, confirming its identity.
  - Domperidone showed a λmax at 285 nm (Figure No. 4), which is characteristic of the drug and supports its identification. The UV spectra of both drugs displayed distinct absorption peaks, useful for quality control purposes.

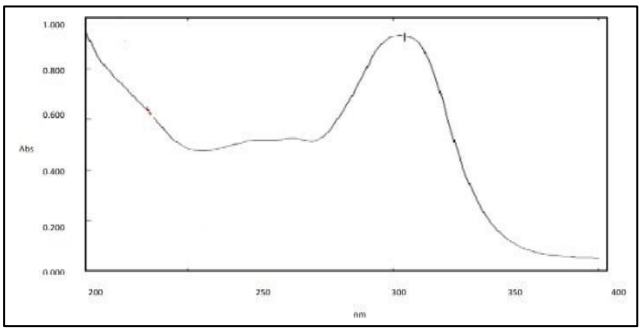


**Figure No. 3 UV Spectra of Esomeprazole**

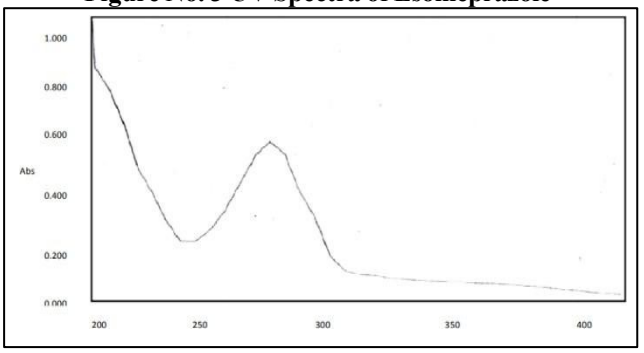


**Figure No. 4 UV Spectra of Domperidone**

***Solubility***

Esomeprazole and Domperidone were tested for solubility in various solvents.

- Esomeprazole was sparingly soluble in water, soluble in methanol and pH 1.2 buffer, and slightly soluble in pH 6.8 buffer.
- Domperidone, on the other hand, was practically insoluble in water, slightly soluble in methanol, and soluble in both pH 1.2 and pH 6.8 buffers.

***Melting Point***

The observed melting points for Esomeprazole (154.8°C) and Domperidone (241.9°C) matched the reported values, confirming the purity of both drugs.

***HPLC Analysis***

The purity of Esomeprazole (99.24%) and Domperidone (99.76%) was evaluated using High-Performance Liquid Chromatography (HPLC) (Figures No. 5 and No. 6). Both drugs were within the acceptable purity range, indicating minimal impurities and confirming their pharmaceutical-grade quality.

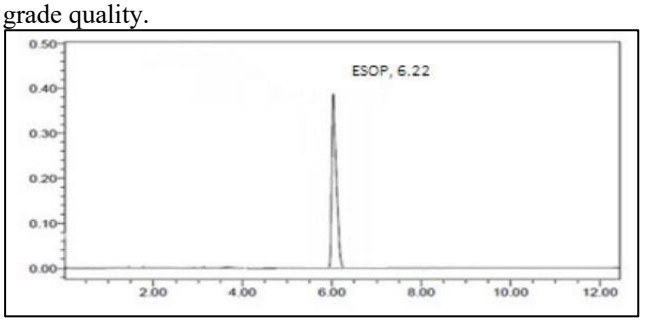


**Figure No. 5 Chromatogram of Esomeprazole Pure drug**

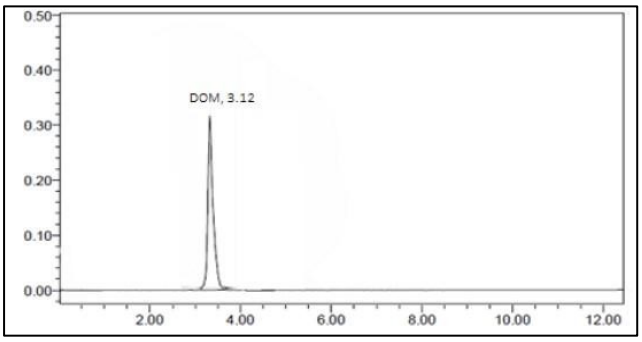


**Figure No. 6 Chromatogram of Domperidone Pure drug**

***DSC Analysis***

Differential Scanning Calorimetry (DSC) was used to evaluate the thermal properties of Esomeprazole and Domperidone.

- Esomeprazole exhibited a sharp endothermic peak at 176.48°C (Figure No. 7), confirming its crystalline structure and thermal stability.
- Domperidone showed an endothermic peak at 249.57°C (Figure No. 8), indicating its crystalline nature and thermal stability. Both drugs demonstrated high purity and minimal thermal transitions, suggesting compatibility with formulation processes.

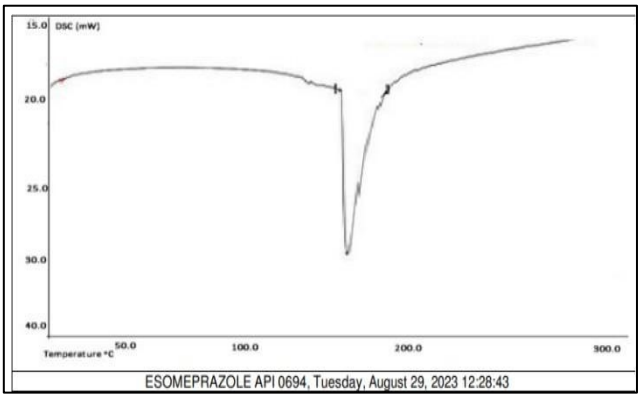


**Figure No. 7 DSC Thermogram of Esomeprazole Pure drug**

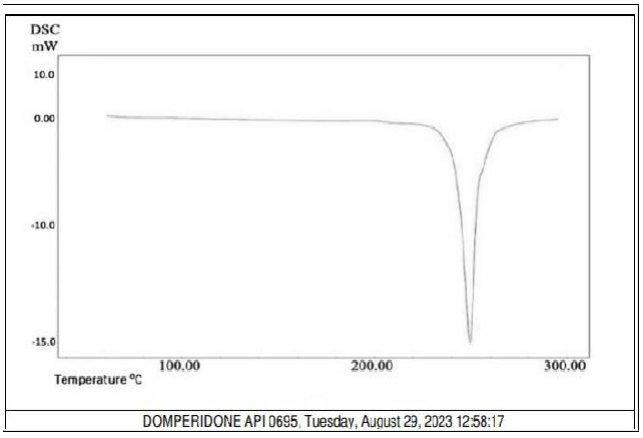


**Figure No. 8 DSC Thermogram of Domperidone drug**

***Drug-Excipients Compatibility Study***

The pH values of various excipients in combination with Esomeprazole and Domperidone were evaluated (Table No. 5). Most excipients were compatible, with pH values ranging from 4.4 to 7.6, indicating suitability for formulation without significant pH-induced instability.

**Evaluation of OTF Batches**

The preliminary evaluation of oral thin film (OTF) trial batches (PT1-PT6) containing Esomeprazole and Domperidone showed varying results across key parameters. PT1, PT4, PT5, and PT6 were colorless and transparent, while PT2 and PT3 were opaque. Surface pH ranged from 6.5 to 7.6, ensuring oral cavity compatibility. Film thickness ranged from 0.5 mm to 0.9 mm, with acceptable weight variation. Folding endurance was highest in PT5 and PT6, indicating better flexibility. Swelling properties ranged from 53.98% to 69.37%, with PT5 and PT6 showing higher swelling, which aids faster disintegration. Drug content was consistent across batches, with PT5 showing the highest drug content. PT5 also exhibited the shortest disintegration time (12 seconds), making it the most promising formulation for further development.

**Table No. 5 pH of Drug and Excipients Datasheet**

| **Excipient** | **Esomeprazole + Domperidone** |
|---|---|
| Drug: Hypromellose | 6.7 |
| Drug: Carbomer 974 | 7.2 |
| Drug: Glycerin | 6.4 |
| Drug: Polyvinyl Alcohol | 5.9 |
| Drug: Benzoic Acid | 4.9 |
| Drug: Sodium Benzoate | 7.6 |
| Drug: Clove | 5.3 |
| Drug: Citric Acid | 4.4 |
| Drug: Sucralose | 5.3 |
| Drug: Beta cyclodextrin | 6.2 |
| Drug: Croscarmellose Sodium | 5.7 |
| Drug: Polyplasdone | 6.8 |

**Table No. 6 Evaluation of Preliminary Trial Batches of OTF (PT1-PT6)**

| Batch | Appearance Transparency | Weight Variation | Folding Endurance | Swelling Properties (%) | Drug Content (Esomeprazole) | Drug Content (Domperidone) | In-vitro Disintegration Time (sec) |
|---|---|---|---|---|---|---|---|
| **PT1** | Colorless, Transparent | 42.75±0.376 | 189±2.154 | 62.52 | 95.75 % | 96.45 % | 15±1.534 |
| **PT2** | White Opaque | 48.96±0.846 | 145±3.945 | 57.06 | 96.34 % | 95.87 % | 35±1.573 |
| **PT3** | White Opaque | 44.45±0.231 | 161±3.652 | 53.98 | 94.56 % | 96.56 % | 28±1.574 |
| **PT4** | Colorless, Transparent | 43.53±0.469 | 137±3.102 | 57.77 | 96.66 % | 97.84 % | 29±1.457 |
| **PT5** | Colorless, Transparent | 42.46±0.453 | 196±1.156 | 69.37 | 98.87 % | 98.46 % | 12±1.684 |
| **PT6** | Colorless, Transparent | 40.58±0.421 | 191±0.448 | 66.84 | 96.43 % | 97.76 % | 13±1.844 |

The evaluation of oral thin film (OTF) batches F1 to F9 using a $3^2$ full factorial design highlighted the impact of formulation variables on key characteristics. Most batches were colorless and transparent, with F2 and F4 being opaque. Surface pH ranged from 6.5 to 7.6, indicating good oral compatibility. Thickness varied from 0.5 mm (F8) to 1.0 mm (F5), with consistent weight variation. Folding endurance was highest in F4 (196), and swelling properties ranged from 58.34% (F7) to 71.92% (F3). Drug content was uniform across all batches, with F3 showing the highest content (99.12% for Esomeprazole). In-vitro disintegration times ranged from 12 seconds (F3) to $3^2$ seconds (F7), with F3 having the shortest time. F3 stood out as the most promising batch due to its optimal transparency, neutral pH, high swelling, excellent drug content uniformity, and rapid disintegration, making it ideal for rapid drug release and patient comfort

.

**Table No. 7 Evaluation of OTF batches (F1 To F9) using $3^2$ Factorial design**

| Batch | Appearance Transparency | Folding Endurance | Swelling Properties (%) | Drug Content % (Esomeprazole) | Drug Content % (Domperidone) | In-vitro Disintegration Time (sec) |
|---|---|---|---|---|---|---|
| **F1** | Colorless, Transparent | 165±2.465 | 67.23 | 96.79 | 98.76 | 17 |
| **F2** | White Opaque | 174±1.764 | 68.36 | 97.48 | 98.23 | 13 |
| **F3** | Colorless, Transparent | 144±3.864 | 71.92 | 99.12 | 99.83 | 12 |
| **F4** | White Opaque | 196±1.156 | 63.63 | 95.12 | 97.37 | 25 |
| **F5** | Colorless, Transparent | 147±0.448 | 64.83 | 95.32 | 98.23 | 24 |
| **F6** | Colorless, Transparent | 185±2.154 | 66.23 | 96.67 | 98.51 | 22 |
| **F7** | Colorless, Transparent | 194±3.945 | 58.34 | 93.54 | 96.42 | 32 |
| **F8** | Colorless, Transparent | 161±3.652 | 59.53 | 93.54 | 96.43 | 28 |
| **F9** | Colorless, Transparent | 135±2.497 | 60.23 | 94.22 | 97.23 | 27 |

***In-Vitro Drug Release***

The in-vitro dissolution studies of Esomeprazole and Domperidone (Tables No. 8 and No. 9) showed that both drugs released gradually over time, with Esomeprazole achieving 97.53% cumulative release in 25 minutes and Domperidone reaching 98.87%. The dissolution profiles of both drugs indicated controlled release characteristics, with a good fit to various kinetic models (Figures No. 9, No. 10), suggesting potential for effective therapeutic delivery.

In conclusion, the analytical evaluation and formulation studies for Esomeprazole and Domperidone confirmed their high purity, stability, and suitability for oral thin film formulation, with efficient drug release profiles and minimal impurity levels.

**Table No. 8 In-Vitro Drug Release of Esomeprazole**

| Time (min) | % Cumulative Drug release of Esomeprazole | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 0 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 |
| 2 | 27.14 | 31.98 | 29.87 | 25.56 | 19.98 | 17.44 | 21.98 | 18.34 | 14.56 |
| 5 | 39.23 | 43.56 | 42.34 | 41.87 | 34.78 | 31.32 | 36.55 | 39.98 | 29.28 |
| 10 | 66.87 | 67.45 | 63.65 | 64.45 | 51.55 | 53.23 | 49.23 | 50.65 | 48.91 |
| 15 | 86.57 | 82.27 | 81.34 | 79.12 | 69.12 | 67.87 | 73.67 | 74.12 | 69.45 |
| 20 | 94.54 | 91.97 | 96.64 | 92.66 | 86.45 | 85.54 | 90.17 | 89.96 | 83.66 |
| 25 | 97.53 | 97.43 | 98.22 | 96.95 | 95.32 | 94.23 | 90.74 | 93.65 | 90.43 |

**Table No. 9 In-Vitro Drug Release of Domperidone**

| Time (min) | % Cumulative Drug release of Domperidone | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 37.56 | 26.48 | 39.48 | 35.44 | 29.29 | 27.8 | 31.09 | 28.48 | 24.01 |
| 5 | 49.71 | 41.45 | 52.16 | 51.23 | 44.75 | 41.49 | 46.56 | 49.71 | 39.4 |
| 10 | 76.25 | 53.11 | 73.79 | 74.48 | 61.81 | 63.27 | 59.28 | 60.51 | 58.87 |
| 15 | 84.65 | 77.68 | 87.21 | 82.37 | 66.43 | 74.34 | 78.45 | 66.36 | 73.95 |
| 20 | 91.23 | 91.2 | 98.45 | 90.34 | 77.23 | 80.35 | 81.23 | 76.34 | 84.12 |
| 25 | 96.23 | 98.43 | 98.87 | 92.76 | 89.54 | 93.76 | 88.95 | 89.35 | 88.54 |

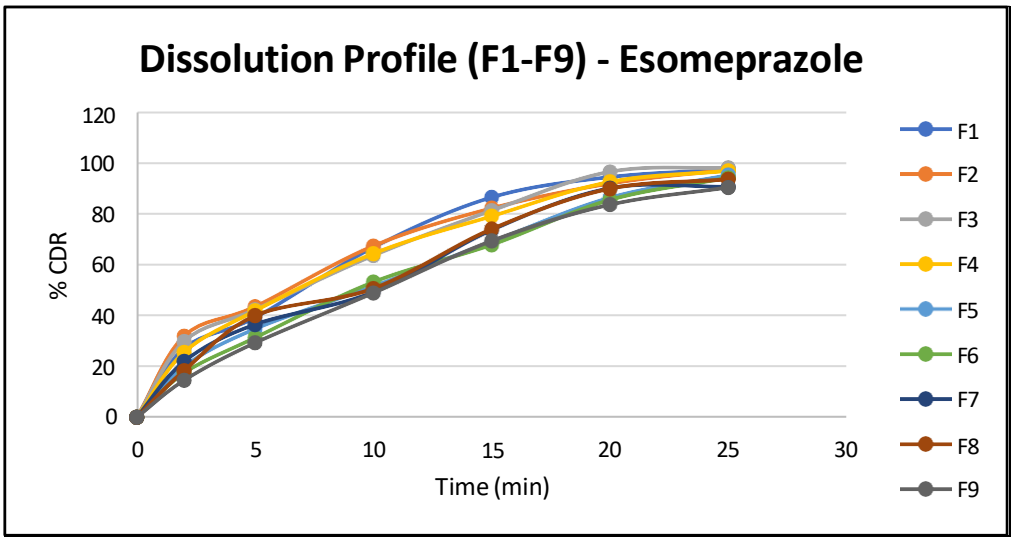


**Figure No. 9 Dissolution Profile of Esomeprazole**

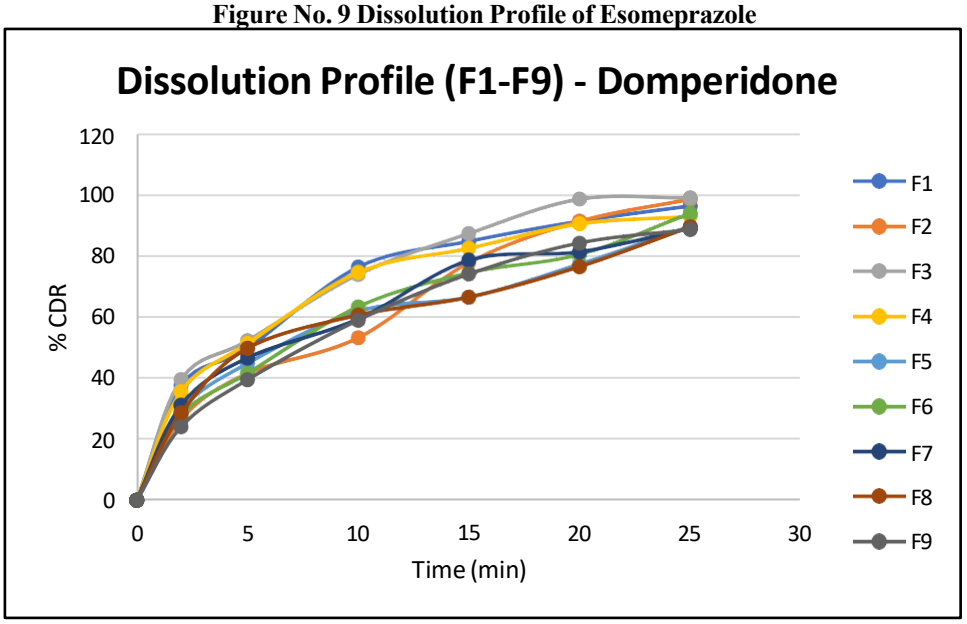


**Figure No. 10 Dissolution Profile of Domperidone**

**Statistical analysis and mathematical model fitting**

The evaluation of oral thin film (OTF) formulations using a 3D surface plot and statistical models provides insights into the effects of HPMC K4M and Carbomer 974 on key properties like swelling, disintegration, drug content, and cumulative drug release (CDR) for Esomeprazole and Domperidone.

1. **Swelling Properties**: Increased concentrations of HPMC K4M and Carbomer 974 enhance the swelling index, with a highly predictive model ($R^2$ = 0.9757, F-value = 120.49).
2. **In-Vitro Disintegration Time**: Higher polymer concentrations, particularly Carbomer 974, increase disintegration time. The model has an $R^2$ of 0.9634, confirming its significance.
3. **Drug Content**: Esomeprazole showed near-perfect model fit ($R^2$ = 0.9993), while Domperidone had a slightly lower fit ($R^2$ = 0.8971). Both models demonstrated strong predictive accuracy.
4. **Cumulative Drug Release (CDR)**: Higher Carbomer 974 concentrations delay drug release, while HPMC K4M promotes faster release. Esomeprazole's CDR model has an $R^2$ of 0.9339, and Domperidone's has an $R^2$ of 0.8767.
5. **Optimal Formulation**: The best formulation includes 15 mg of both HPMC K4M and Carbomer 974, yielding desirable swelling, rapid disintegration (12.56 seconds), and high drug content (99.12% Esomeprazole, 99.52% Domperidone), with near-complete drug release (99.11% Esomeprazole, 97.79% Domperidone). This formulation meets all target criteria with a desirability score of 1.000, making it ideal for further development.

**Table No. 10 Statistical analysis of generated model**

| Response | F value | P value | $R^2$ value | Adequate precision |
|---|---|---|---|---|
| Swelling Properties | 120.49 | 0.0001 | 0.9757 | 27.4972 |
| In-vitro Disintegration Studies | 78.98 | 0.0001 | 0.9634 | 22.0095 |
| Drug Content – Esomeprazole | 903.75 | 0.0001 | 0.9993 | 86.6961 |
| Drug Content – Domperidone | 26.14 | 0.0011 | 0.8971 | 13.5135 |
| %CDR – Esomeprazole | 42.42 | 0.0003 | 0.9339 | 16.6758 |
| %CDR - Domperidone | 21.33 | 0.0019 | 0.8767 | 10.0436 |

**Table No. 11 Solution Proposed by DesignExpert**

| No. | HPMC K4M | Carbomer 974 | Swelling Index (%) | In-vitro Disintegration Studies (sec) | Drug Content – Esomeprazole (%) | Drug Content – Domperidone (%) | %CDR – Esomeprazole | %CDR - Domperidone | Desirability |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 15.000 | 15.000 | 70.909 | 12.556 | 99.124 | 99.517 | 99.109 | 97.793 | 1.000 |

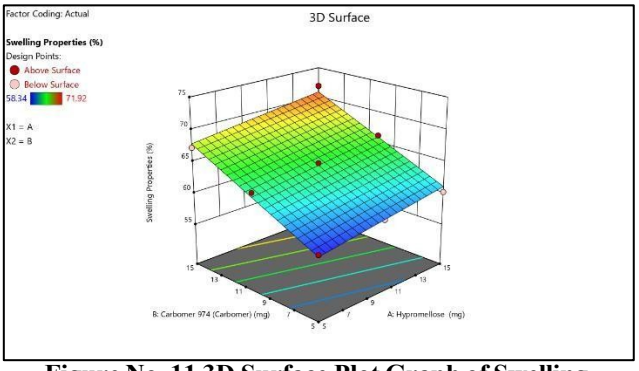


**Figure No. 11 3D Surface Plot Graph of Swelling Properties**

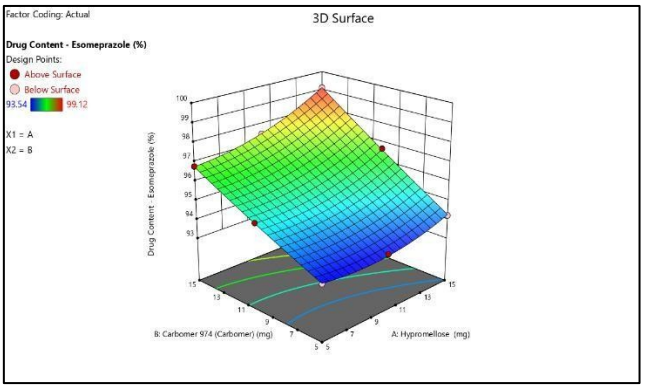


**Figure No. 13 3D Surface Plot Graph of Drug Content - Esomeprazole**

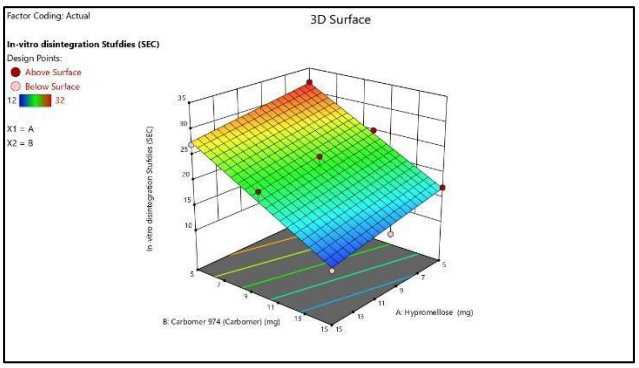


**Figure No. 12 3D Surface Plot Graph of In-vitro disintegration Studies**

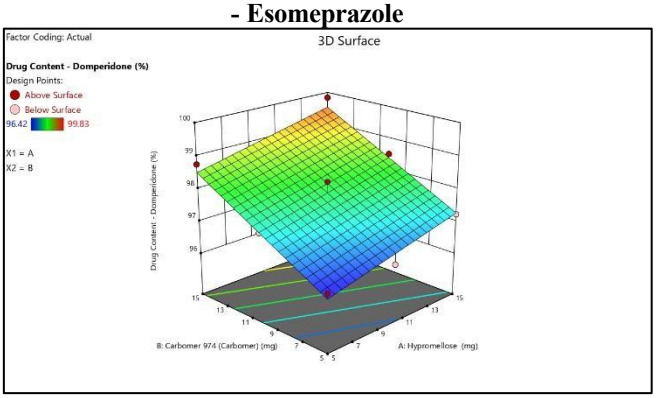

**Figure No. 14 3D Surface Plot Graph of Drug Content - Domperidone**

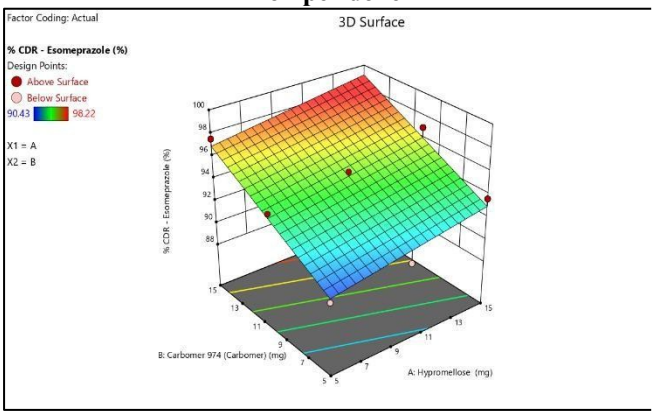


**Figure No. 15 3D Surface Plot Graph of % CDR - Esomeprazole**

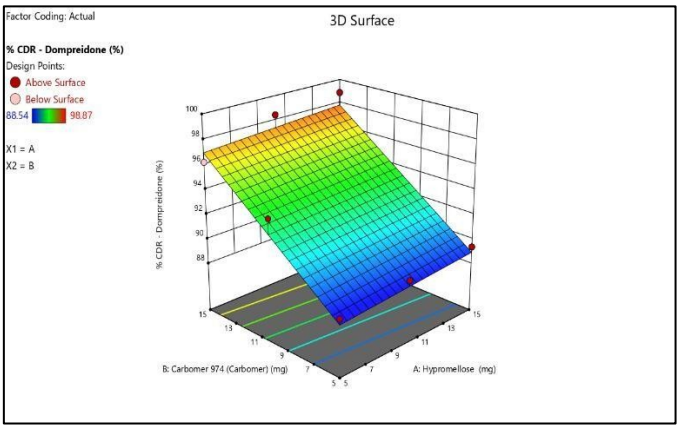


**Figure No. 16 3D Surface Plot Graph of % CDR - Domperidone**

## CONCLUSION

In this study, the development and evaluation of oral thin films (OTFs) for the dual-drug delivery of esomeprazole and domperidone were successfully carried out, addressing key challenges such as poor solubility and bioavailability of the active pharmaceutical ingredients (APIs). The use of OTF technology has demonstrated a promising alternative to traditional oral dosage forms, offering several advantages including rapid disintegration, precise dosage control, improved patient compliance, and potential enhanced bioavailability, particularly for the poorly water-soluble drugs like esomeprazole and domperidone. The formulation process, optimized using a $3^2$ full factorial design, allowed for the fine-tuning of critical factors such as polymer concentrations and their impact on film characteristics. Several formulation batches were prepared, evaluated, and compared for key parameters including appearance, thickness, weight variation, folding endurance, swelling properties, drug content, and in-vitro disintegration time. Among the formulations, Batch F3 emerged as the most promising, showing optimal transparency, high swelling properties, rapid disintegration time (12 seconds), and superior drug content uniformity. In-vitro dissolution studies further confirmed that the OTFs exhibited efficient and rapid drug release profiles, with the potential to significantly enhance the bioavailability of both esomeprazole and domperidone. The formulation was also shown to be physically stable, with no significant drug-excipient incompatibilities identified during the compatibility studies. Overall, the findings of this research suggest that OTFs are a viable and effective delivery system for esomeprazole and domperidone, offering the potential for enhanced therapeutic efficacy, improved patient adherence, and better management of gastrointestinal disorders. Future research could explore further optimization and clinical trials to confirm the real-world efficacy of these OTF formulations.

## CONFLICT OF INTEREST:

"We affirm that we have no conflicts of interest."

## ACKNOWLEDGEMENT:

We would like to thank L.B.S. College of Pharmacy for providing the facilities and resources that were utilized in the research project.

## REFERENCE

1. Park HR, Seok SH, Hwang KM, Kim JY, Park CW, Park ES. Formulation of sustained-release orodispersible film containing drug–resin complexes of donepezil hydrochloride. J Pharm Investig. 2022;52(2):259–72. DOI: 10.1007/s40005-022-00560-4.
1. Palakurthi SS, Jakka D, Pinnamraju DN. Preparation and evaluation of oral thin films of a natural product: Syzygium cumini seed powder. J Drug Deliv Ther. 2022;12(1-S):64–70. DOI: 10.22270/jddt.v12i1-S.5343.
2. Radicioni M, Caverzasio C, Rovati S, Giori AM, Cupone I, Marra F, Mautone G. Comparative bioavailability study of a new vitamin D3 orodispersible film versus a marketed oral solution in healthy volunteers. Clin Drug Investig. 2022;1–11. DOI: 10.1007/s40261-021-01113-7.
3. Özakar RS, Özakar E. Current overview of oral thin films. Turk J Pharm Sci. 2021;18(1):111–121. DOI: 10.4274/tjps.galenos.2020.76390.
4. Rathore L, Gehalot N, Jain V. A short review on advancement in fast dissolving oral thin films. Curr Res Pharm Sci. 2021;11(4):112–7. DOI: 10.24092/crps.2021.110404.
5. Gupta MS, Kumar TP, Gowda DV. Orodispersible thin film: a new patient-centered innovation. J Drug Deliv Sci Technol. 2020;59:101843. DOI: 10.1016/j.jddst.2020.101843.

6. Kanna S, Nadendla RR, Satyanarayana J, Karthikeya V, Sonu MV, Bhargavi PN. Formulation and evaluation of fast-dissolving oral film of rivaroxaban. J Young Pharm. 2023;15(4):687–95. DOI: 10.5530/jyp.2023.15.94.
7. He M, Zhu L, Yang N, Li H, Yang Q. Recent advances of oral film as platform for drug delivery. Int J Pharm. 2021;604:120759. DOI: 10.1016/j.ijpharm.2021.120759
8. El-Said IA, Aboelwafa AA, ElGazayerly ON. Optimization of taste-masked dapoxetine oral thin films using factorial design: in vitro and in vivo evaluation. Pharm Dev Technol. 2021;26(5):522–38. DOI: 10.1080/10837450.2021.1885174
9. Anji Reddy K, Karpagam S. In vitro and in vivo evaluation of oral disintegrating nanofiber and thin film containing hyperbranched chitosan/donepezil for active drug delivery. J Polym Environ. 2021;29(3):922–36. DOI: 10.1007/s10924-020-01893-3
10. Rathore L, Gehalot N, Jain V. A short review on advancement in fast dissolving oral thin films. Curr Res Pharm Sci. 2021;11(4):112–7. DOI: 10.24092/crps.2021.110404
11. Gupta MS, Kumar TP, Gowda DV. Orodispersible thin film: a new patient-centered innovation. J Drug Deliv Sci Technol. 2020;59:101843. DOI: 10.1016/j.jddst.2020.101843
12. Karki S, Kim HJ, Na SJ, Shin D, Jo K, Lee J. Thin films as an emerging platform for drug delivery. Asian J Pharm Sci. 2016;11(5):559–74. DOI: 10.1016/j.ajps.2016.05.004 .
13. Preis M, Woertz C, Schneider K, Kukawka J, Broscheit J, Roewer N, Breitkreutz J. Design and evaluation of bilayered buccal film preparations for local administration of lidocaine hydrochloride. Eur J Pharm Biopharm. 2014;86(3):552–61. DOI: 10.1016/j.ejpb.2013.12.020
14. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: a new approach to oral drug delivery system. Int J Pharm Investig. 2013;3(2):67–76. DOI: 10.4103/2230-973X.114897
15. Cilurzo F, Cupone I, Minghetti P, Buratti S, Gennari C, Montanari L. Nicotine fast dissolving films made of maltodextrins: a feasibility study. AAPS PharmSciTech. 2010;11(4):1511–7. DOI: 10.1208/s12249-010-9522-8
16. Cilurzo F, Cupone I, Minghetti P, Gennari CG, Montanari L. Fast dissolving films made of maltodextrins. Eur J Pharm Biopharm. 2008;70(3):895–900. DOI: 10.1016/j.ejpb.2008.06.032
17. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharm J. 2016;24(5):537–46. DOI: 10.1016/j.jsps.2015.02.024
18. Dixit RP, Puthli SP. Oral strip technology: overview and future potential. J Control Release. 2009;139(2):94–107. DOI: 10.1016/j.jconrel.2009.06.014
19. Cilurzo F, Cupone I, Minghetti P, Montanari L. Fast dissolving films for oral drug delivery: evaluation of mechanical properties and dosage uniformity. AAPS PharmSciTech. 2011;12(3):1101–8. DOI: 10.1208/s12249-011-9663-8