FORMULATION AND EVALUATION OF MOUTH DISSOLVING FILM OF LAMOTRIGINE BY CRYSTALLO-CO-AGGLOMERATION TECHNIQUE

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ABSTRACT:

Background: Lamotrigine is a Biopharmaceutical Classification System (BCS) Class II antiepileptic drug with poor aqueous solubility, which limits its dissolution rate and oral bioavailability. The present study aimed to develop mouth dissolving films (MDFs) of Lamotrigine using the crystallo-co-agglomeration technique to enhance drug dissolution and improve patient compliance.

Methods: Lamotrigine mouth dissolving films were prepared by the solvent casting method using crystallo-co-agglomerated drug. Nine formulations (F1–F9) were developed by varying the concentrations of hydroxypropyl methylcellulose (HPMC E5), polyvinyl alcohol (PVA), and polyethylene glycol (PEG 400). Preformulation studies, including organoleptic evaluation, solubility, melting point, FTIR, and DSC analyses, were carried out to assess drug characteristics and compatibility. The prepared films were evaluated for weight variation, folding endurance, disintegration time, surface pH, drug content, in vitro drug release, and accelerated stability.

Results: Preformulation studies confirmed the purity of Lamotrigine and its compatibility with the selected excipients. All formulations exhibited satisfactory physicochemical properties with uniform weight, acceptable mechanical strength, near-neutral surface pH, and uniform drug content. Formulation F7 demonstrated the best overall performance, showing a folding endurance of 232 ± 6, disintegration time of 24 ± 1.80 s, drug content of 99.82 ± 0.60%, and 100 ± 1.20% drug release within 10 min. Accelerated stability studies conducted for three months revealed no significant changes in the physicochemical characteristics or dissolution profile of the optimized formulation.

Conclusion: The combination of crystallo-co-agglomeration and solvent casting successfully produced Lamotrigine mouth dissolving films with improved dissolution characteristics, rapid disintegration, and good stability. The optimized formulation (F7) exhibited desirable pharmaceutical properties and represents a promising oral drug delivery system for improving the dissolution and patient acceptability of Lamotrigine. Further in vivo studies are warranted to confirm its pharmacokinetic and therapeutic

advantages.

Keywords: Lamotrigine; Mouth dissolving film; Crystallo-co-agglomeration; Solvent casting; Drug dissolution; Fast dissolving oral film; HPMC; Polyvinyl alcohol; Drug release; Stability study.

INTRODUCTION:

Epilepsy is one of the most common chronic neurological disorders affecting approximately 50 million people worldwide and is characterized by recurrent, unprovoked seizures resulting from abnormal electrical discharges in the brain. Effective management of epilepsy requires maintaining consistent plasma drug concentrations to prevent seizure recurrence and improve the patient's quality of life.[1] Antiepileptic drugs (AEDs) remain the primary therapeutic option for epilepsy; however, their clinical effectiveness is often influenced by poor aqueous solubility, limited oral bioavailability, and variable gastrointestinal absorption. These limitations can delay the onset of therapeutic action and reduce treatment efficacy, particularly in patients who require rapid symptom control.[2,3]

Lamotrigine is a second-generation antiepileptic drug widely prescribed for the management of focal and generalized seizures, Lennox–Gastaut syndrome, and bipolar disorder. It exerts its pharmacological action primarily by blocking voltage-gated sodium channels, thereby inhibiting the excessive release of excitatory neurotransmitters such as glutamate and aspartate. Despite its proven therapeutic efficacy and favorable safety profile, Lamotrigine is categorized as a Biopharmaceutical Classification System (BCS) Class II drug because of its poor aqueous solubility and high permeability. Although the drug is readily absorbed after dissolution, its dissolution rate is the limiting step governing its oral bioavailability. Consequently, improving the dissolution behavior of Lamotrigine remains an important strategy for enhancing its therapeutic performance.[4-6]

Several formulation approaches have been investigated to overcome the solubility limitations of poorly water-soluble drugs, including particle size reduction, solid dispersions, nanosuspensions, cyclodextrin inclusion complexes, lipid-based drug delivery systems, and crystal engineering techniques. Among these, crystallo-co-agglomeration has emerged as a simple, economical, and efficient particle engineering approach capable of simultaneously improving the micromeritic properties and dissolution characteristics of poorly soluble drugs. This technique combines crystallization and agglomeration into a single process, producing spherical agglomerates with enhanced wettability, improved flowability, better compressibility, and increased surface area.[7] The improved physicochemical properties of crystallo-co-agglomerated particles contribute to faster dissolution and enhanced drug availability without altering the chemical structure of the active pharmaceutical ingredient.[8]

In recent years, mouth dissolving films (MDFs) have gained considerable attention as an innovative oral drug delivery system because of their rapid disintegration, ease of administration, and improved patient compliance. MDFs are thin, flexible polymeric films that rapidly hydrate and dissolve upon contact with saliva, releasing the incorporated drug without the need for water. This dosage form is particularly beneficial for pediatric, geriatric, psychiatric, and dysphagic patients who experience difficulty

swallowing conventional tablets or capsules. Additionally, mouth dissolving films provide accurate dosing, portability, ease of handling, reduced choking risk, and faster onset of therapeutic action compared to conventional oral dosage forms.[9-10]

The performance of mouth dissolving films is largely dependent on the selection of suitable film-forming polymers and formulation excipients. Hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA) are extensively employed because of their excellent film-forming properties, flexibility, and compatibility with a wide range of pharmaceutical ingredients. Plasticizers, including polyethylene glycol (PEG 400), improve film elasticity and prevent brittleness, while superdisintegrants such as sodium starch glycolate facilitate rapid film disintegration by promoting water uptake and swelling. Additional excipients, including citric acid, sweeteners, and flavoring agents, further enhance patient acceptability by improving salivation and masking the unpleasant taste of the drug.[11-12]

Although mouth dissolving films have been successfully developed for several therapeutic agents, the formulation of Lamotrigine into this dosage form remains challenging because of its poor aqueous solubility. Simply incorporating the drug into a hydrophilic polymer matrix may not be sufficient to achieve the rapid dissolution required for immediate drug release. Therefore, combining a solubility enhancement technique with a rapidly disintegrating dosage form offers a promising strategy to overcome these limitations. Crystallo-co-agglomeration enhances the dissolution characteristics of Lamotrigine by improving particle wettability and reducing diffusion barriers, while the mouth dissolving film ensures rapid hydration and drug release in the oral cavity. The synergistic combination of these two approaches is expected to significantly improve the overall performance of the formulation.

The present study was undertaken to develop and evaluate mouth dissolving films of Lamotrigine using the crystallo-co-agglomeration technique. The prepared formulations were characterized for their physicochemical properties, drug–excipient compatibility, mechanical strength, disintegration behavior, drug content, in vitro dissolution profile, and stability. The study aimed to identify an optimized formulation capable of providing rapid drug release, improved dissolution characteristics, satisfactory mechanical properties, and enhanced patient compliance. The successful development of such a formulation may provide an effective alternative to conventional Lamotrigine dosage forms and contribute to improved therapeutic outcomes in the management of epilepsy and related neurological disorders.

MATERIALS AND METHODS:

MATERIALS:

Lamotrigine was obtained as a gift sample from Sun Pharmaceutical Industries Ltd., India. Hydroxypropyl methylcellulose (HPMC E5/E15) was procured from Colorcon Asia Pvt. Ltd., Goa, India, while polyvinyl alcohol (PVA) was purchased from Loba Chemie Pvt. Ltd., Mumbai, India. Polyethylene glycol 400 (PEG 400), glycerol, and methanol were obtained from Merck Life Science Pvt. Ltd., India. Sodium starch glycolate and crospovidone were procured from Signet Chemical Corporation Pvt. Ltd., Mumbai, India. Citric acid and aspartame were supplied by S.D. Fine Chemicals Ltd., Mumbai, India. A

commercially available flavoring agent was obtained from a local supplier in India. Distilled water was prepared in-house and used throughout the study. All chemicals and reagents used were of analytical reagent (AR) grade and were used as received without further purification.

Selection of Drug and Excipients

Lamotrigine was selected as the model drug due to its poor aqueous solubility (BCS Class II), which limits its dissolution rate and oral bioavailability. To improve its dissolution behavior and achieve rapid drug release, crystallo-co-agglomeration was employed prior to the development of mouth dissolving films (MDFs). Hydroxypropyl methylcellulose (HPMC E5/E15) and polyvinyl alcohol (PVA) were selected as film-forming polymers, while polyethylene glycol 400 (PEG 400) and glycerol served as plasticizers. Sodium starch glycolate and crospovidone were incorporated as superdisintegrants to accelerate film disintegration. Citric acid was used as a saliva-stimulating agent, whereas aspartame and a flavoring agent were added to improve the taste and patient acceptability of the films.[13-14]

Preformulation Studies

Preformulation studies were performed to evaluate the physicochemical properties of Lamotrigine prior to formulation development. The investigations included organoleptic evaluation, solubility analysis, melting point determination, UV spectrophotometric analysis, and Fourier transform infrared (FTIR) spectroscopy to establish the identity, purity, and compatibility of the drug.[15-18]

Organoleptic Evaluation

Lamotrigine was examined for its physical appearance, color, odor, and texture by visual inspection under normal laboratory conditions to confirm its identity and suitability for formulation.

Solubility Study

The equilibrium solubility of Lamotrigine was determined in distilled water, methanol, ethanol, and phosphate buffer (pH 6.8). An excess amount of drug was added to each solvent and shaken continuously for 24 h at room temperature. The resulting solutions were filtered, suitably diluted, and analyzed using a UV–Visible spectrophotometer.

Melting Point Determination

The melting point of Lamotrigine was determined using the capillary tube method with a digital melting point apparatus. The observed melting temperature was compared with the reported literature value to assess drug purity.

UV–Visible Spectrophotometric Analysis

A standard stock solution of Lamotrigine was prepared in methanol and subsequently diluted with phosphate buffer (pH 6.8). The solution was scanned over the wavelength range of 200–400 nm using a UV–Visible spectrophotometer to determine the wavelength of maximum absorbance (λmax), which was used for subsequent quantitative estimations.[19-22]

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopy was performed using the KBr pellet technique over the spectral range of 4000–400 cm^{-1} to identify the characteristic functional groups of Lamotrigine. The obtained spectrum was compared

with the reference spectrum to confirm the identity of the drug and evaluate its compatibility with the selected excipients.[23-24]

Analytical Method Development and Validation

A UV–Visible spectrophotometric method was developed for the quantitative estimation of Lamotrigine in bulk drug and mouth dissolving films. The method was validated according to ICH guidelines for its suitability in routine analysis during formulation development and evaluation.[25-27]

Determination of λmax

A standard stock solution of Lamotrigine was prepared in methanol and further diluted with phosphate buffer (pH 6.8). The solution was scanned over the wavelength range of 200–400 nm using a UV–Visible spectrophotometer to determine the wavelength of maximum absorbance (λmax), which was used for subsequent quantitative analysis.[28]

Calibration Curve

A calibration curve was prepared by diluting the standard stock solution with phosphate buffer (pH 6.8) to obtain solutions of different concentrations. The absorbance of each solution was measured at the selected λmax, and a calibration graph of absorbance versus concentration was constructed to establish linearity. The calibration equation was subsequently used for drug content estimation during formulation studies.[29]

Preparation of Crystallo-Co-Agglomerated Lamotrigine

Lamotrigine agglomerates were prepared using the crystallo-co-agglomeration technique to improve the drug's solubility, wettability, and flow properties. The optimized agglomerates obtained from the crystallization process were dried, characterized, and used for the preparation of mouth dissolving films.[30-36]

Formulation of Mouth Dissolving Films

Mouth dissolving films containing crystallo-co-agglomerated Lamotrigine were prepared by the solvent casting method. Film-forming polymers (HPMC E5/E15 and PVA), plasticizers (PEG 400 and glycerol), superdisintegrants (sodium starch glycolate and crospovidone), citric acid, aspartame, and flavoring agent were incorporated into the polymeric solution. The optimized drug agglomerates were dispersed uniformly in the casting solution, which was poured onto a suitable casting surface, dried under controlled conditions, and cut into films of uniform dimensions. A total of nine formulations (F1–F9) were prepared by varying the concentrations of polymers and plasticizers while maintaining a constant drug content.[37-40]

Table 1: Composition of Mouth Dissolving Films of Lamotrigine

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F8	F8	F9
Lamotrigine	2	2	2	2	2	2	2	2	2
HPMC E5	100	120	140	100	120	140	80	100	120
PVA	50	50	50	80	80	80	90	90	90

PEG 400	15	20	25	15	20	25	15	20	25
Sodium starch glycolate	10	10	10	12	12	12	15	15	15
Citric acid	5	5	5	5	5	5	5	5	5
Aspartame	8	8	8	8	8	8	8	8	8
Flavor (q.s.)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Distilled water (mL)	10	10	10	10	10	10	10	10	10

Preparation of Mouth Dissolving Films

Mouth dissolving films of Lamotrigine were prepared by the solvent casting method using crystallo-co-agglomerated Lamotrigine. HPMC (E5/E15) and PVA were dissolved in distilled water under continuous magnetic stirring to obtain a clear polymeric solution. The optimized Lamotrigine agglomerates were dispersed in methanol and incorporated into the polymer solution. PEG 400, glycerol, sodium starch glycolate, crospovidone, citric acid, aspartame, and flavoring agent were added with continuous stirring until a homogeneous and bubble-free casting solution was obtained. The solution was cast onto a leveled glass Petri dish and dried at 40–45°C for 24 h. The dried films were peeled off, cut into uniform strips (2 × 2 cm^2), and stored in a desiccator until further evaluation.

Evaluation of Mouth Dissolving Films[41-46]

The prepared mouth dissolving films were evaluated for their physicochemical properties, mechanical strength, drug content uniformity, disintegration behavior, and dissolution characteristics.

Weight Variation

Individual films of uniform dimensions (2 × 2 cm^2) were weighed using a calibrated analytical balance. The average weight and standard deviation were calculated from three randomly selected films.

Folding Endurance

The mechanical strength of the films was assessed by repeatedly folding each film at the same position until visible cracks or breakage occurred. The number of folds required to break the film was recorded as the folding endurance.

Disintegration Time

The disintegration time was determined by placing each film in 10 mL of phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C. The time required for complete disintegration was recorded, and the measurements were performed in triplicate.

Surface pH

The surface pH of the films was measured after moistening the film with distilled water for 1–2 min. A digital pH meter electrode was gently placed on the film surface, and the measurements were performed in triplicate.

Drug Content

A film strip of known dimensions was dissolved in methanol and suitably diluted with phosphate buffer (pH 6.8). The solution was filtered, and the absorbance was measured at 228 nm using a UV–Visible spectrophotometer. The drug content was calculated using the calibration curve.

***In Vitro* Dissolution Study**

The *in vitro* dissolution study was performed using the USP dissolution apparatus II (paddle method) containing 900 mL of phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C and stirred at 50 rpm. Samples were withdrawn at predetermined intervals, filtered, and analyzed spectrophotometrically at 228 nm. An equal volume of fresh dissolution medium was added after each sampling, and the cumulative percentage drug release was calculated.

Stability Study

The optimized formulation was subjected to stability studies according to ICH Q1A(R2) guidelines under accelerated (40 ± 2°C/75 ± 5% RH), intermediate (30 ± 2°C/65 ± 5% RH), and long-term (25 ± 2°C/60 ± 5% RH) storage conditions. At predetermined intervals, the films were evaluated for physical appearance, drug content, surface pH, disintegration time, and *in vitro* drug release.

RESULTS AND DISCUSSION:

Preformulation Studies

The preformulation studies confirmed that Lamotrigine possesses physicochemical characteristics suitable for formulation development. The drug exhibited acceptable organoleptic properties, high purity, and poor aqueous solubility, highlighting the necessity for solubility enhancement. Therefore, the crystallo-co-agglomeration technique was selected to improve the dissolution characteristics before developing the mouth dissolving film formulation.

Table 2: preformulation characteristics of Lamotrigine

Parameter	Observation	Significance
Appearance	White to off-white crystalline powder	Confirms drug identity
Odor	Odorless	Indicates purity
Water solubility	Practically insoluble	Confirms poor aqueous solubility
Phosphate buffer (pH 6.8)	Slightly soluble	Limited dissolution in physiological medium
Methanol	Freely soluble	Suitable solvent for analytical studies
Ethanol	Slightly soluble	Moderate solubility
Melting point	206–208°C	Indicates crystalline and pure drug
Biopharmaceutical classification	BCS Class II	Supports need for solubility enhancement

UV Spectrum of Drug Lamotrigine

The concentration range of Lamotrigine for the calibration was found to be 5-30 µg/ml at λ_{max} 281nm.

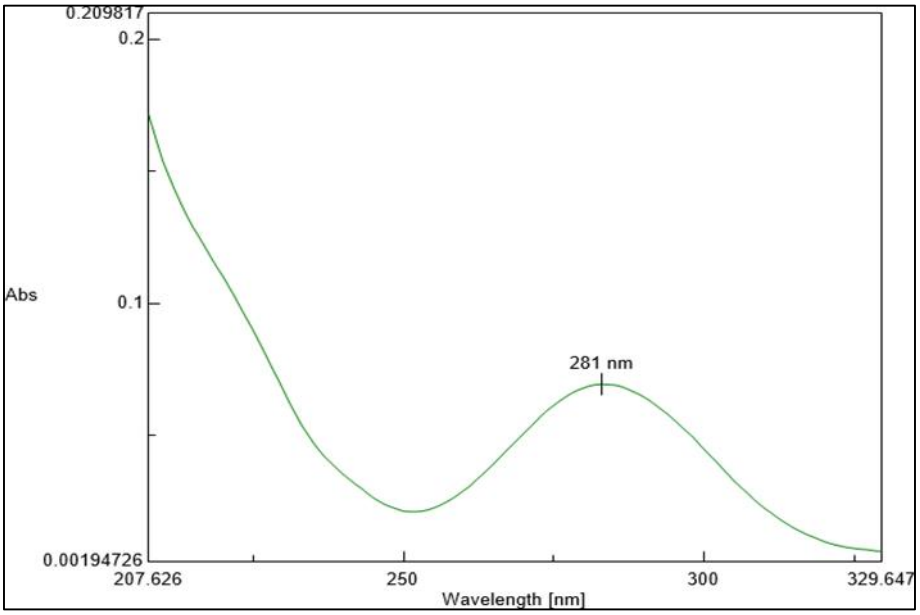

Figure 1: λmax of drug Lamotrigine (Maximum wavelength)

Calibration Curve of drug Lamotrigine

The regression equation was found to be y=0.032c+0.004 with regression coefficient 0.999 which is closer to 1 states the concentration is in linear proportion. The concentration range for the calibration was found to be 5-30 µg/ml at λ_{max} 281nm. Maximum wavelength was found to be 281nm for Lamotrigine.

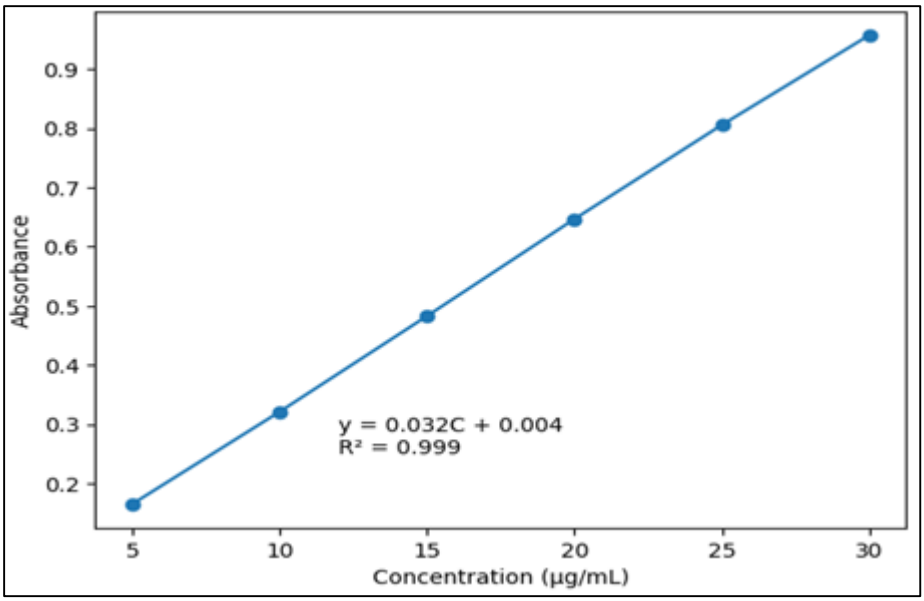

Figure 2: Calibration curve for Lamotrigine

Fourier Transform Infrared Spectroscopy (FTIR) Study

Fourier Transform Infrared (FTIR) spectroscopy was carried out to evaluate the possible interactions between Lamotrigine and selected excipients used in the formulation of mouth dissolving films. The FTIR spectra of pure drug and physical mixtures of drug with polymers and other excipients (HPMC, PVA, PEG 400, etc.) were recorded and analyzed. The characteristic peaks of Lamotrigine were identified and compared with those observed in physical mixtures. No significant shift or disappearance

of characteristic peaks was observed, indicating the absence of chemical interaction between the drug and excipients. Thus, the drug was found to be compatible with all selected formulation components.

FTIR Spectrum of Pure Lamotrigine

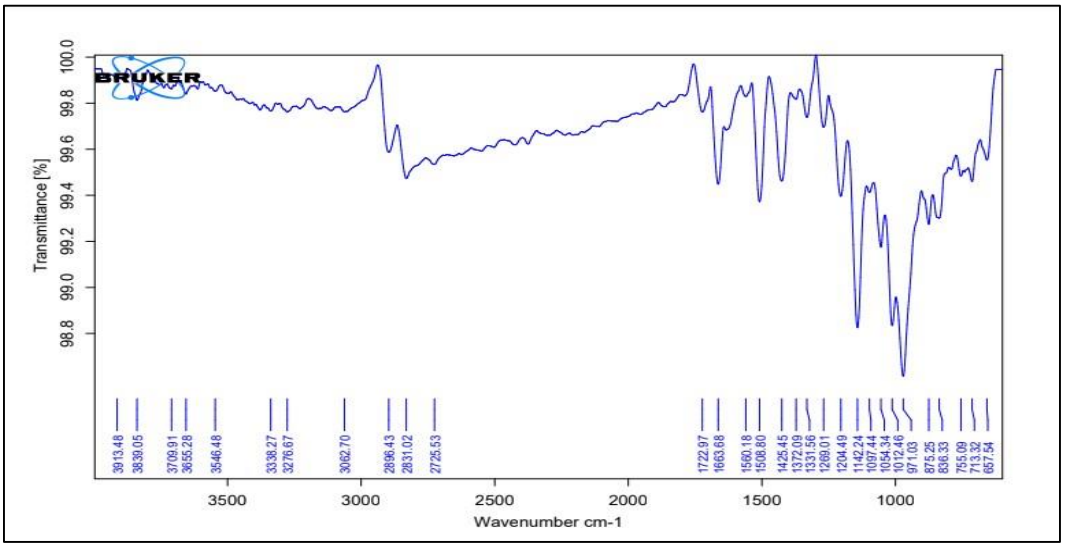

Figure 3: FTIR Spectrum of Lamotrigine

Drug–Excipient Compatibility Study

Fourier Transform Infrared (FTIR) Analysis

The compatibility of Lamotrigine with the selected excipients was evaluated by FTIR spectroscopy. The characteristic functional group peaks of Lamotrigine were retained in the physical mixture without any significant shift, disappearance, or appearance of new peaks, indicating the absence of chemical interactions. These findings confirmed the compatibility of Lamotrigine with the selected excipients, supporting their use in the formulation of mouth dissolving films.

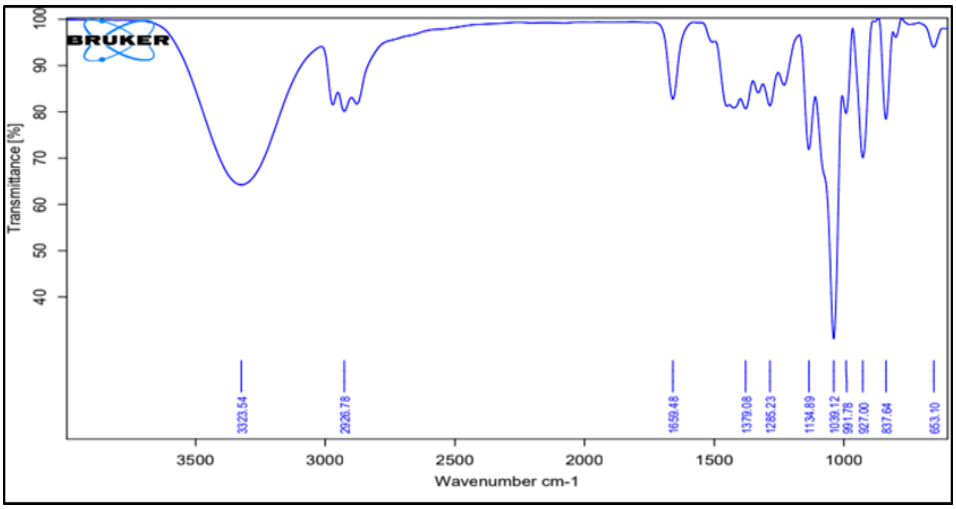

Figure 4: FTIR Spectra of Physical Mixture

Differential Scanning Calorimetry (DSC)

The thermal behavior of Lamotrigine and its physical mixture with excipients was evaluated using DSC. Pure Lamotrigine exhibited a sharp endothermic peak corresponding to its melting point, confirming its crystalline nature. The physical mixture showed the characteristic melting peak of Lamotrigine without any significant shift or disappearance, although a slight reduction in peak intensity was observed due to

the dilution effect of excipients. These results indicate the absence of significant drug–excipient interactions and confirm the thermal stability and compatibility of Lamotrigine with the selected formulation components.

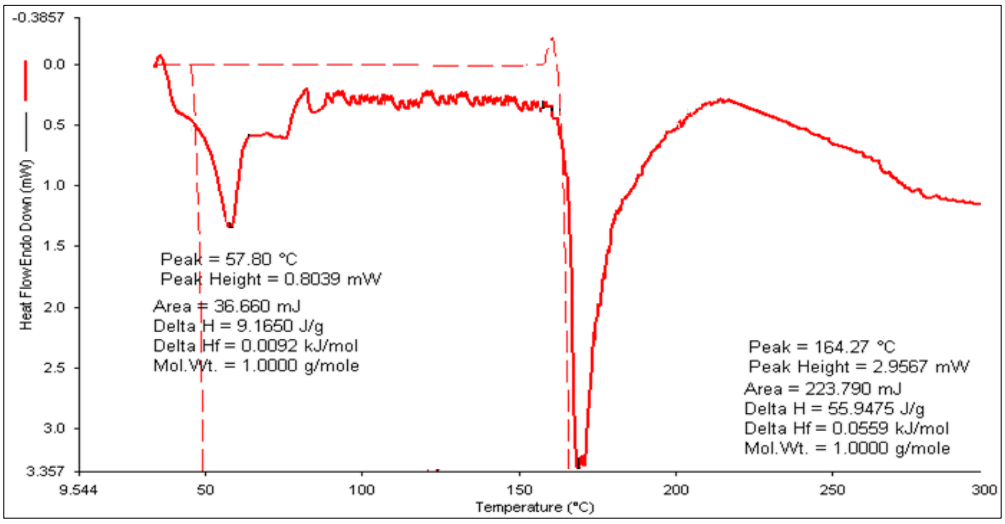

Figure 5: DSC Thermogram of Physical Mixture of Drug and Excipients

Formulation of Mouth Dissolving Films

Mouth dissolving films of Lamotrigine were successfully prepared by the solvent casting method using crystallo-co-agglomerated drug. Nine formulations (F1–F9) were developed by varying the concentrations of HPMC E5, PVA, and PEG 400 while maintaining a constant drug content. The prepared films were visually uniform, smooth, transparent, and free from air bubbles and visible drug crystallization, indicating successful film formation and homogeneous drug distribution.

Evaluation of Film Formation

All formulations (F1–F9) produced continuous films that were easily peeled from the casting surface without visible defects. The films were smooth, transparent, and showed uniform appearance with no evidence of air bubbles, cracks, or drug crystallization, confirming homogeneous dispersion of Lamotrigine within the polymeric matrix. Formulations containing higher concentrations of HPMC and PVA exhibited improved film integrity and handling characteristics, whereas lower polymer concentrations produced comparatively thinner and less robust films. The incorporation of PEG 400 effectively improved film flexibility and reduced brittleness, allowing the films to withstand repeated handling without damage. Overall, the solvent casting method combined with the crystallo-co-agglomeration technique yielded mouth dissolving films with satisfactory physical characteristics suitable for further physicochemical and performance evaluation.

Evaluation of Mouth Dissolving Films

The prepared mouth dissolving films (F1–F9) were evaluated for physicochemical properties including weight variation, folding endurance, disintegration time, surface pH, and drug content. The results demonstrated good uniformity, mechanical integrity, rapid disintegration, and satisfactory drug distribution among all formulations.

Weight Variation

The average weight of the films ranged from 45.0 ± 0.46 to 68.0 ± 0.93 mg. The gradual increase in film weight from F1 to F9 corresponded to the increasing polymer concentration. The low standard deviation values confirmed uniform film casting and reproducible formulation.

Folding Endurance

Folding endurance values ranged from 118 ± 4 to 268 ± 6 folds, indicating good flexibility and mechanical strength of all formulations. An increase in polymer concentration improved the mechanical properties of the films, while PEG 400 imparted adequate elasticity by reducing film brittleness.

Disintegration Time

The films disintegrated rapidly, with disintegration times ranging from 24 ± 1.80 to 52 ± 4.55 s. Faster disintegration was observed in formulations containing optimized concentrations of superdisintegrant and film-forming polymers. Formulation F7 exhibited the shortest disintegration time, indicating efficient hydration and rapid film breakdown.

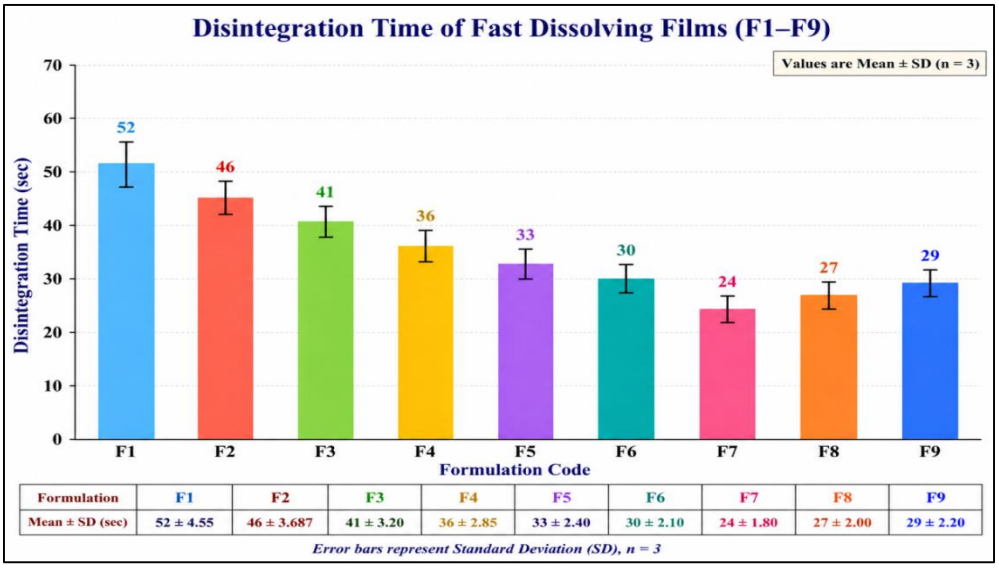

Figure 6: Disintegration times of Fast Dissolving Films

Surface pH and Drug Content

The surface pH of all formulations ranged from 6.18 ± 0.09 to 7.10 ± 0.07, remaining within the physiological range of the oral cavity and indicating minimal risk of mucosal irritation. Drug content varied between 94.35 ± 1.25% and 99.82 ± 0.60%, demonstrating uniform drug distribution and good content uniformity throughout the films.

Overall, formulation F7 exhibited the most favorable balance of mechanical strength, rapid disintegration, near-neutral surface pH, and high drug content, and was therefore selected as the optimized formulation for further studies.

Table 3: Physicochemical evaluation of Lamotrigine mouth dissolving films (mean ± SD, n = 3)

Formulation	Weight (mg)	Folding endurance	Disintegration time (s)	Surface pH	Drug content (%)
F1	45.0 ± 0.46	118 ± 4	52 ± 4.55	6.18 ± 0.09	94.35 ± 1.25

F2	48.0 ± 0.67	137 ± 5	46 ± 3.69	6.32 ± 0.08	95.48 ± 1.12
F3	52.0 ± 0.98	158 ± 6	41 ± 3.20	6.47 ± 0.07	96.72 ± 1.05
F4	55.0 ± 1.04	176 ± 5	36 ± 2.85	6.60 ± 0.06	97.40 ± 0.92
F5	58.0 ± 0.85	198 ± 6	33 ± 2.40	6.73 ± 0.05	98.15 ± 0.85
F6	60.0 ± 0.34	214 ± 5	30 ± 2.10	6.84 ± 0.05	99.05 ± 0.72
F7	62.0 ± 0.12	232 ± 6	24 ± 1.80	6.91 ± 0.04	99.82 ± 0.60
F8	65.0 ± 0.47	251 ± 5	27 ± 2.00	7.04 ± 0.06	98.75 ± 0.82
F9	68.0 ± 0.93	268 ± 6	29 ± 2.20	7.10 ± 0.07	97.65 ± 0.95

The physicochemical evaluation confirmed that all formulations met the essential quality requirements for mouth dissolving films. The increase in polymer concentration resulted in higher film weight and improved mechanical strength, while the optimized combination of polymers and superdisintegrant facilitated rapid disintegration. The surface pH of all formulations remained within the physiological range, indicating compatibility with the oral mucosa. Drug content values above 94% demonstrated uniform drug incorporation and reproducibility of the solvent casting process. Among the formulations evaluated, F7 exhibited the best overall performance and was selected as the optimized formulation for subsequent dissolution and stability studies.

***In Vitro* Dissolution Study**

The in vitro dissolution profiles of Lamotrigine mouth dissolving films demonstrated rapid and progressive drug release for all formulations (F1–F9). Drug release increased with time, indicating efficient hydration of the polymer matrix and rapid dissolution of the crystallo-co-agglomerated drug. Among all formulations, F7 exhibited the highest release profile, achieving 55.0 ± 1.1% drug release within 1 min and complete drug release (100.0 ± 1.2%) within 10 min. The enhanced dissolution of F7 may be attributed to the optimized ratio of HPMC, PVA, and sodium starch glycolate, which promoted rapid film hydration and drug diffusion. Formulations containing higher polymer concentrations (F8 and F9) exhibited slightly slower drug release, possibly due to the formation of a denser polymeric matrix that retarded drug diffusion.

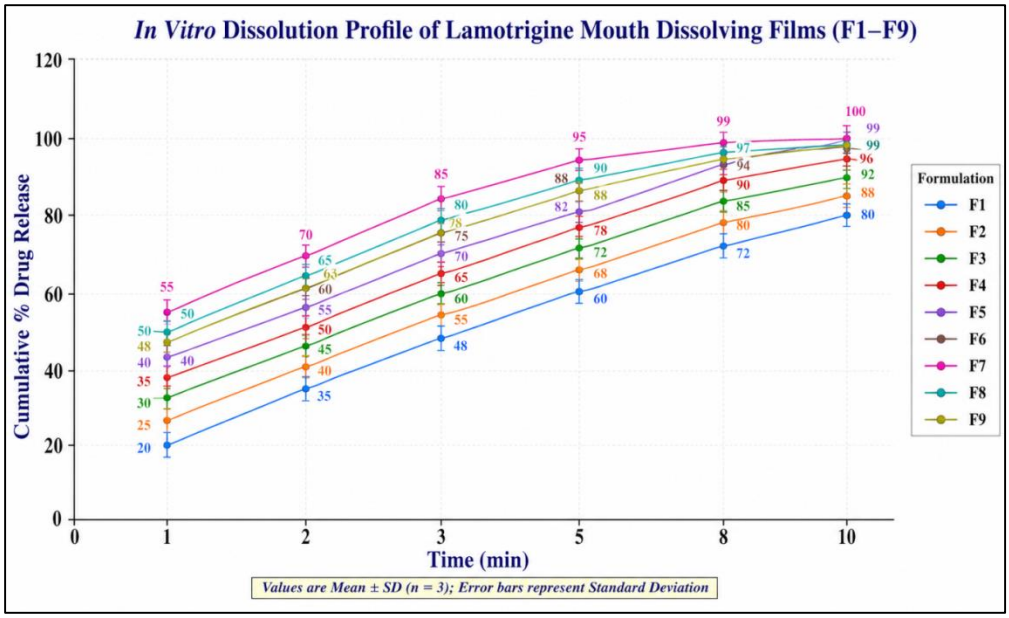

Figure 7: *In Vitro* Drug Release Profile of Fast Dissolving Films

Stability Study

The optimized formulation (F7) was subjected to accelerated stability testing at 40 ± 2°C/75 ± 5% RH for three months according to ICH guidelines. No significant changes were observed in physical appearance throughout the storage period. A slight increase in disintegration time and minor reductions in drug content and drug release were observed; however, all values remained within acceptable limits, demonstrating good physical and chemical stability of the formulation.

Table 4: Accelerated stability study of optimized formulation (F7) (mean ± SD, n = 3)

Storage period	Appearance	Disintegration time (s)	Drug content (%)	Drug release at 10 min (%)
Initial	Smooth, transparent	24 ± 1.80	99.82 ± 0.60	100.0 ± 1.20
1 Month	No change	25 ± 1.75	99.10 ± 0.65	99.20 ± 1.10
2 Months	No change	26 ± 1.70	98.45 ± 0.70	98.60 ± 1.15
3 Months	No change	27 ± 1.85	97.80 ± 0.75	97.90 ± 1.20

The stability study confirmed that the optimized formulation retained its physical appearance, drug content, and dissolution characteristics during storage. The minor changes observed over three months were within acceptable pharmaceutical limits, indicating that the formulation remained stable under accelerated storage conditions.

CONCLUSION:

Lamotrigine mouth dissolving films were successfully developed using the crystallo-co-agglomeration technique in combination with the solvent casting method. Preformulation studies confirmed the purity and identity of Lamotrigine, while FTIR and DSC analyses demonstrated the compatibility of the drug with the selected excipients, indicating the suitability of the formulation components. All prepared formulations (F1–F9) exhibited satisfactory physicochemical characteristics, including uniform weight, good mechanical strength, acceptable surface pH, and uniform drug content. The incorporation of

crystallo-co-agglomerated Lamotrigine improved the dispersion of the drug within the polymeric matrix and contributed to rapid film hydration and dissolution. Among the developed formulations, F7 demonstrated the most desirable performance, with optimum folding endurance, the shortest disintegration time (24 ± 1.80 s), high drug content (99.82 ± 0.60%), and complete drug release (100 ± 1.20%) within 10 min. The optimized formulation remained stable under accelerated storage conditions for three months without significant changes in appearance, drug content, disintegration time, or dissolution profile, confirming its physical and chemical stability. Overall, the developed mouth dissolving film of Lamotrigine represents a promising oral drug delivery system with the potential to enhance dissolution, provide rapid drug release, improve patient compliance, and offer an effective alternative to conventional oral dosage forms. Further *in vivo* pharmacokinetic and bioavailability studies are recommended to establish its clinical performance and therapeutic advantages.

CONFLICT OF INTEREST:

The authors declare that there are no conflicts of interest.

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