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Formulation And Evaluation Of Rapidly Disintegrating Oral Ultrathin Film Of Lamotrigine For Treatment Of Childhood Epilepsy

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Abstract
The advancement of Rapidly Disintegrating Oral Ultrathin Films (RDOFs) represents a novel and promising approach to conventional oral drug delivery systems. These films present a user-friendly, self-administerable platform that dissolves swiftly in the oral cavity, facilitating rapid drug absorption through the pre-gastric route and potentially leading to a quicker onset of therapeutic action. Their distinct advantages—including ease of administration and enhanced patient compliance—have made RDOFs increasingly attractive for both systemic and localized drug delivery. This research focuses on the design and evaluation of Lamotrigine-loaded RDOFs, targeting the treatment of pediatric epilepsy. Conventional oral formulations often pose challenges for children due to swallowing difficulties, necessitating the development of more acceptable and patient-centric dosage forms. The objective of this formulation was to enhance the drug's bioavailability and ensure better adherence to therapy. The development process incorporated the selection of suitable film-forming polymers, evaluation of the films' mechanical characteristics, and execution of in vitro disintegration and drug release assessments. The findings demonstrate that Lamotrigine-based RDOFs hold significant potential as an efficient and practical alternative for managing epilepsy in pediatric populations, offering improved bioavailability, simplified administration, and greater treatment compliance.

Keyword: *Rapidly Disintegrating Oral Ultrathin Films (RDOF), Childhood Epilepsy, Film-Forming Polymers, Drug Delivery System, Patient Compliance*

INTRODUCTION

Oral drug delivery remains the most widely adopted and preferred route in pharmaceutical therapeutics due to its convenience, safety, and cost-effectiveness. However, it presents notable challenges for specific patient populations, such as the elderly, children, and individuals with dysphagia or neurological conditions, who may experience difficulty in swallowing or chewing conventional solid dosage forms. To address these limitations, Fast Dissolving Tablets (FDTs) were introduced in the early 20th century as an innovative alternative to traditional formulations [1].

Fast-dissolving drug delivery systems offer distinct advantages by enabling the drug to disintegrate rapidly and dissolve in the saliva without requiring water for administration [2]. The oral mucosa's high permeability, coupled with its rich vascularization and thin membrane, facilitates rapid drug absorption and immediate systemic availability. This mechanism bypasses gastrointestinal degradation and first-pass hepatic metabolism, resulting in a faster onset of therapeutic action and improved bioavailability [3]. Furthermore, these systems enhance patient compliance, particularly among individuals who struggle with conventional tablets, such as those with dysphagia. Incorporating mucoadhesive polymers into oral thin films enhances mucosal adhesion, promoting better drug retention and absorption at the site of administration [4]. These advanced dosage forms—referred to by various names such as fast-dissolving, rapid-melt, or quick-disintegrating films—share a common functionality: rapid dissolution or disintegration in the oral cavity without the need for water. This technology has proven particularly beneficial for geriatric patients who typically manage multiple medications daily, including those with Alzheimer's

disease, Parkinsonism, bipolar disorder, schizophrenia, and other conditions that complicate oral medication intake [5].

Among oral fast-dissolving dosage forms, Oral Thin Films (OTFs) are gaining significant attention due to their portability, flexibility, and ease of administration. They are particularly useful for delivering medications across a wide range of therapeutic areas, including analgesics, antihistamines, anti-asthmatics, cardiovascular agents, neuroleptics, and drugs for erectile dysfunction. One notable therapeutic area is migraine management. Migraine, characterized by recurring episodes of intense headache and associated symptoms, is classified by the World Health Organization (WHO) as one of the most disabling neurological conditions.

Zolmitriptan (ZMT), a 5-hydroxytryptamine (5-HT) receptor agonist and a BCS Class III drug, is widely used in the treatment of acute migraine attacks, with or without aura, and in cluster headaches. It effectively alleviates symptoms such as headache, nausea, and sensitivity to light or sound. Available commercial formulations include oral tablets (2.5 and 5 mg), orally disintegrating tablets (2.5 mg), and nasal sprays (5 mg) [6]. However, intranasal administration is hindered by challenges like mucociliary clearance and poor drug permeability across the nasal epithelium, highlighting the need for more effective delivery alternatives such as OTFs [7].

Recently, fast-dissolving films have emerged as a viable substitute for orally disintegrating tablets, offering the additional benefit of eliminating the risk of choking and circumventing existing patent limitations. These films are typically composed of plasticized hydrocolloids or polymer blends, manufactured using techniques like solvent casting or hot-melt extrusion [8]. However, several formulation and processing challenges remain, including foaming during film formation due to heat or solvent evaporation, cracking during cutting, and poor moisture stability. Furthermore, OTFs must exhibit appropriate tensile strength, flexibility, and non-adhesiveness to ensure efficient handling and packaging [9].

ADVANTAGES OF ORAL FAST-DISSOLVING FILMS

1. Enhanced stability, durability, and rapid dissolution compared to traditional solid dosage forms.
2. Eliminates the need for water and avoids first-pass metabolism, thereby improving bioavailability.
3. Reduced dose requirements and potential for fewer side effects.
4. Convenient for on-the-go administration, particularly in emergency or travel situations.
5. Rapid disintegration due to large surface area facilitates quick drug release.
6. Portable, flexible, and easy to store or transport.
7. Ideal for geriatric, pediatric, or mentally impaired patients with swallowing difficulties.
8. Suitable for conditions requiring immediate relief such as motion sickness, acute pain, allergic reactions, or coughing.
9. Offers dose accuracy and long-term stability in solid form.
10. Direct absorption through the oral mucosa enhances onset and efficacy while avoiding hepatic metabolism [10].

ANATOMY OF THE ORAL CAVITY

The oral cavity offers a surface area of approximately 100 cm^2, with the buccal mucosa exhibiting a thickness ranging from 500 to 800 μm. It comprises three major mucosal types: lining mucosa, masticatory mucosa, and specialized mucosa. The lining mucosa, which constitutes about 60% of the total oral surface, covers areas such as the lips, cheeks, soft palate, sublingual region, and the underside of the tongue. Masticatory mucosa (25%) is found in regions like the hard palate and gingiva and is characterized by its resistance to mechanical stress. Specialized mucosa (15%) resides on the dorsal surface of the tongue and plays a critical role in taste sensation [11].

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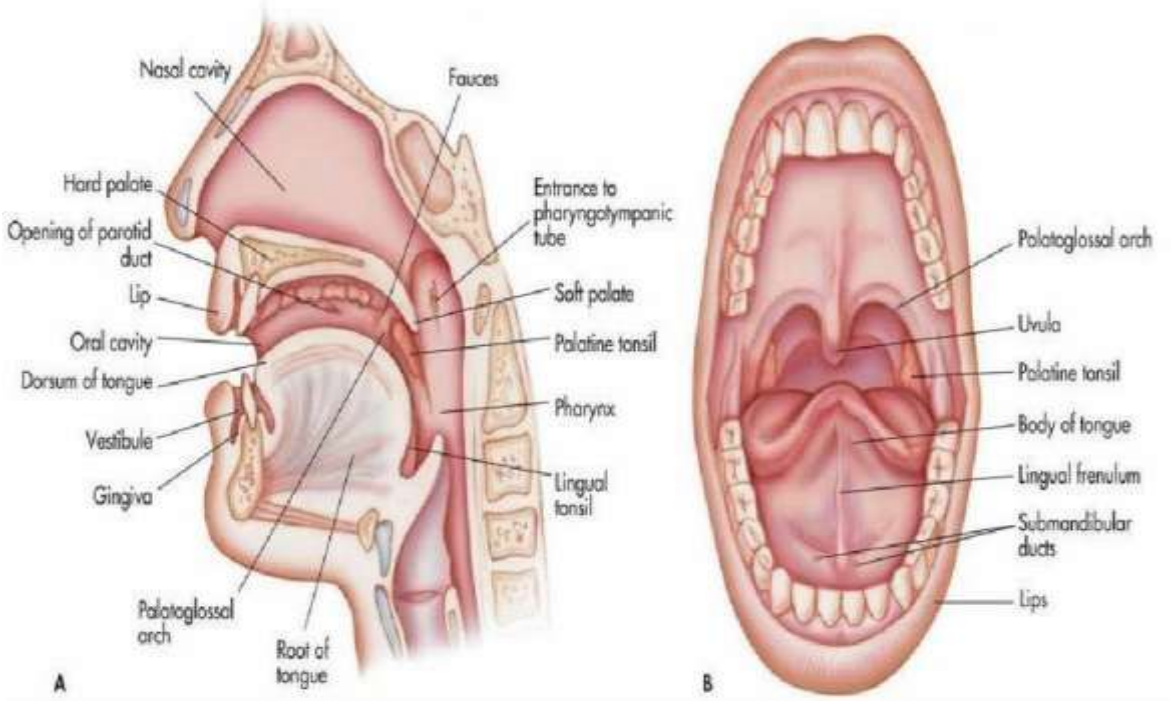

Figure 1: Anatomy of the oral cavity.

TONGUE

The tongue is a voluntary, muscular organ that resides on the floor of the oral cavity. It is anchored at its base to the hyoid bone and connected to the floor of the mouth via a fold of mucous membrane known as the frenulum. The upper surface is lined with stratified squamous epithelium and is covered with numerous projections known as papillae, which contain sensory nerve endings responsible for taste perception, often referred to as taste buds. Among the three types of papillae present, vallate papillae are the largest and most prominent. Typically numbering between 8 and 12, they are arranged in an inverted V-pattern near the posterior region of the tongue, making them easily visible [12].

ORAL MUCOSA

The **oral mucosa** consists of multiple layers, starting with an outer covering of **stratified squamous epithelium**, followed by the **basement membrane**, **lamina propria**, and the **submucosa**, which forms the deepest layer. In terms of permeability, the oral mucosa lies between that of the **skin (epidermis)** and **intestinal lining**, with the **buccal mucosa** demonstrating significantly higher permeability—estimated to be 4 to 4000 times greater than the skin. This variation in permeability across different regions of the oral cavity is attributed to the diverse anatomical structures and specific functional roles of the various types of oral mucosa [13].

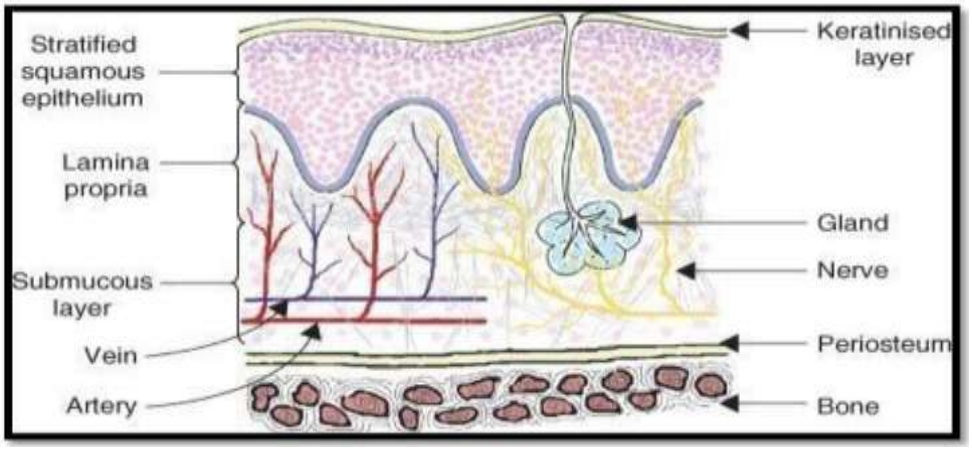

Figure 2: Cross-section of oral mucosa

Theories of Muco/Bioadhesion

Several theoretical models have been proposed to describe the mechanisms underlying mucoadhesion or bioadhesion. These theories explain the nature of interaction between a mucoadhesive polymer and the mucus layer:

1. **Electronic Theory**

This theory is based on the difference in electronic structures between the mucoadhesive polymer and the mucus glycoproteins. When these surfaces come into contact, **electron transfer** occurs, leading to the formation of a **charged double layer** at their interface. This results in **electrostatic attractive forces**, facilitating adhesion and potential interpenetration of the two surfaces [14].

2. **Adsorption Theory**

According to this theory, adhesion is achieved through **primary and secondary chemical interactions**—such as **covalent bonding** and **non-covalent forces** including van der Waals interactions, electrostatic forces, hydrogen bonding, and hydrophobic effects. The initial interaction is mostly attributed to these **non-covalent bonds**, which establish contact between the polymer and mucus [15].

3. **Wetting Theory**

Wetting theory emphasizes the importance of the **spreading ability** of a bioadhesive material across the biological surface. It is particularly relevant for **liquid-based mucoadhesive systems**, where polymers with **moderate wettability** have shown better adhesion properties to surfaces like **human endothelial cells** [16].

4. **Diffusion Theory**

This model proposes that adhesion occurs through **mutual diffusion** and **entanglement** of polymer chains. Upon contact, the polymer chains of the mucoadhesive system diffuse into the glycoprotein network of mucus, forming an interpenetrated, entangled structure. Factors affecting this include **polymer flexibility**, **chemical similarity**, **surface contact**, and the **diffusion coefficient** of the polymer [17].

5. **Fracture Theory**

Fracture theory focuses on the **mechanical aspect** of adhesion, particularly the force required to **detach** the mucoadhesive system from the mucus surface. The **work of fracture**—i.e., the energy needed to separate the two surfaces—is greater when the polymer has **longer network strands** or a **lower degree of cross-linking**, which enhances adhesive strength [18].

MATERIALS AND METHODS

Materials Used

The following drug and excipients were employed in the formulation and evaluation of fast-dissolving oral films (as shown in Table below):

Component	Name
Drug	Lamotrigine
Polymer	Konjac Gum
Plasticizers	Glycerol, Propylene Glycol, PEG 400
Sweetener	Aspartame
Flavoring Agent	Strawberry
Acidifying Agent	Citric Acid
Solvent	Methanol

Methods of Preparation

Several techniques can be utilized individually or in combination for the preparation of mouth-dissolving films, including:

- **Solvent Casting**
- **Semisolid Casting**
- **Hot Melt Extrusion**
- **Solid Dispersion Extrusion**
- **Rolling Method**

Solvent Casting Technique

The **solvent casting method** was employed in this study for film formulation. In this approach:

1. Excipients are initially **dissolved in distilled water**.
2. Water-soluble polymers are then incorporated, followed by the **addition of the drug**, with continuous stirring to form a homogeneous mixture.
3. The solution is then **poured into Petri plates** pre-treated with glycerol and **dried at a controlled temperature**.
4. Dried films are carefully **cut into 2 cm × 2 cm squares**.

Step-by-Step Procedure:

- Accurately weigh the **drug (Lamotrigine)** and dissolve it in **10 mL of distilled water**.
- Subject the solution to **ultrasonication** until the drug dissolves completely.
- Weigh the required quantity of excipients and mix them into the solution under **continuous stirring**.
- Add the **polymer** (Konjac gum) based on batch specification and stir until uniform.
- Perform **ultrasonication** again to remove entrapped air bubbles.
- Apply **glycerol** to the surface of the Petri plate.
- Pour the final mixture onto the plate and allow it to **dry uniformly** under controlled temperature.
- Once dried, **cut the film** into squares measuring **2 × 2 cm** using a clean blade.

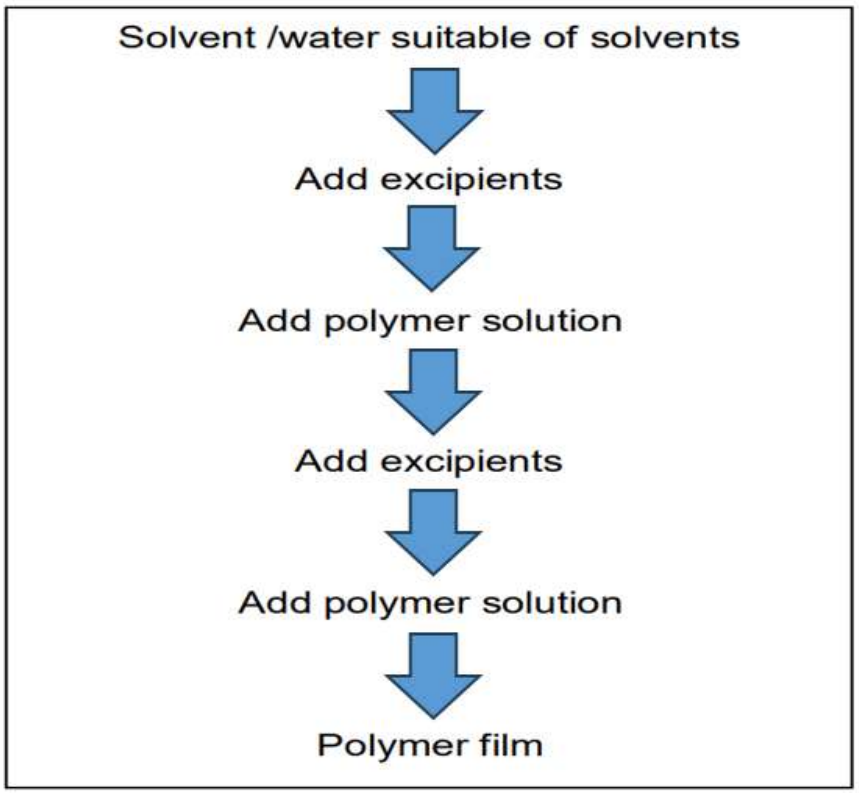

Figure 3: Solvent casting method flow

Advantages of the Solvent Casting Method

1. **Improved Uniformity and Clarity**

This method offers superior uniformity in film thickness and greater clarity when compared to extrusion techniques.

2. **Enhanced Surface Properties**

Films produced via solvent casting typically exhibit a **glossy finish** and are free from surface defects such as die lines.

3. **Superior Flexibility and Mechanical Strength**

The resulting films display excellent **flexibility and mechanical integrity**, contributing to better handling and performance.

The **ideal thickness** for finished films typically ranges between **12 to 100 µm**, although this may vary depending on the required active pharmaceutical ingredient (API) loading and dissolution characteristics.

Disadvantages of the Solvent Casting Method

1. **Solubility Constraints**

The selected polymer must be **soluble in a volatile solvent or water**, which may limit material choices.

2. **Formulation Requirements**

It is essential to formulate a **stable solution** with appropriate **solid content and viscosity** for successful casting.

3. **Film Formation Challenges**

A **homogeneous film** must be consistently formed, and it must **detach cleanly** from the casting substrate without damage or distortion.

Formulation and Development of Fast-Dissolving Oral Film

Formulation Overview

Konjac gum was selected as the **film-forming polymer** due to its excellent filmogenic properties and high biocompatibility. The plasticizers used included **glycerin, propylene glycol, and polyethylene glycol 400 (PEG 400)** to enhance flexibility and disintegration characteristics.

Additional excipients included:

- **Citric acid** as a **saliva-stimulating agent**
- **Aspartame** as a **sweetener**
- **Strawberry flavor** for **improved palatability**

Preparation Method

The fast-dissolving oral films of **Lamotrigine** were formulated using the **solvent casting technique** as follows:

1. The required amount of **Konjac gum** was **dispersed in 40 mL of water**, stirred continuously using a magnetic stirrer.
2. The **final volume was adjusted to 10 mL** using distilled water to obtain the desired concentration.
3. **Lamotrigine**, the active pharmaceutical ingredient, was **levigated with an appropriate volume of PEG 400** and then incorporated into the polymeric solution.
4. The resulting mixture was **homogenized thoroughly** to achieve a uniform solution.
5. The solution was carefully **cast onto a Petri dish** (total area: **66.31 cm²**) and placed in a **hot air oven at 40°C for 24 hours** to dry.
6. After drying, the films were **punched into circular units** measuring **2 cm in diameter** (area = **6.28 cm²**), each containing **10 mg of Lamotrigine** [46].

	OTF1	OTF2	OTF3	OTF4	OTF5	OTF6	OTF7	OTF8	OTF9
Konjac Gum (mg)	50	100	150	200	250	300	350	400	450
glycerine (mg)	100	200	300						
Propylene glycol (mg)				100	200	300			
Polyethylene glycol							100	200	300

400(mg)									
Aspartame (mg)	10	10	10	10	10	10	10	10	10
Lamotrigine (mg)	10	10	10	10	10	10	10	10	10
Citric acid (mg)	8	8	8	8	8	8	8	8	8
Strawberry	5	5	5	5	5	5	5	5	5
Distilled water	10	10	10	10	10	10	10	10	10

Evaluation and characterization of oral fast dissolving films
1. Physical appearance and surface texture
2. Weight uniformity
3. Uniformity of thickness
4. Folding endurance
5. Surface pH
6. In-vitro disintegrating time
7. Uniformity of drug content
8. *In-vitro* dissolution study Scanning electron microscopy (SEM)
9. Scanning electron microscopy (SEM)
10. Comparison between marketed and preparation oral film
11. Stability studies

RESULT AND DISCUSSION

Several methods are available for the development and evaluation of fast dissolving oral film containing Lamotrigine drugs. These formulations were intended to produce immediate release of drugs in the oral region. The result and discussion under different heading as follows.

Preformulation study

Melting point determination

Table 1: Melting points determination of drugs and polymer

Sr. no	By capillary method	Observed melting points	Methods used
1.	Lamotrigine	216-218°C	By capillary method
		216°C	Electronic melting point apparatus
		216°C	Differential scanning colorimetry
2.	Konjac gum	247°C	By capillary method

Differential scanning calorimetry-

The DSC thermogram of pure drug and polymer utilized in the system of formulation are presented in following figure no.7

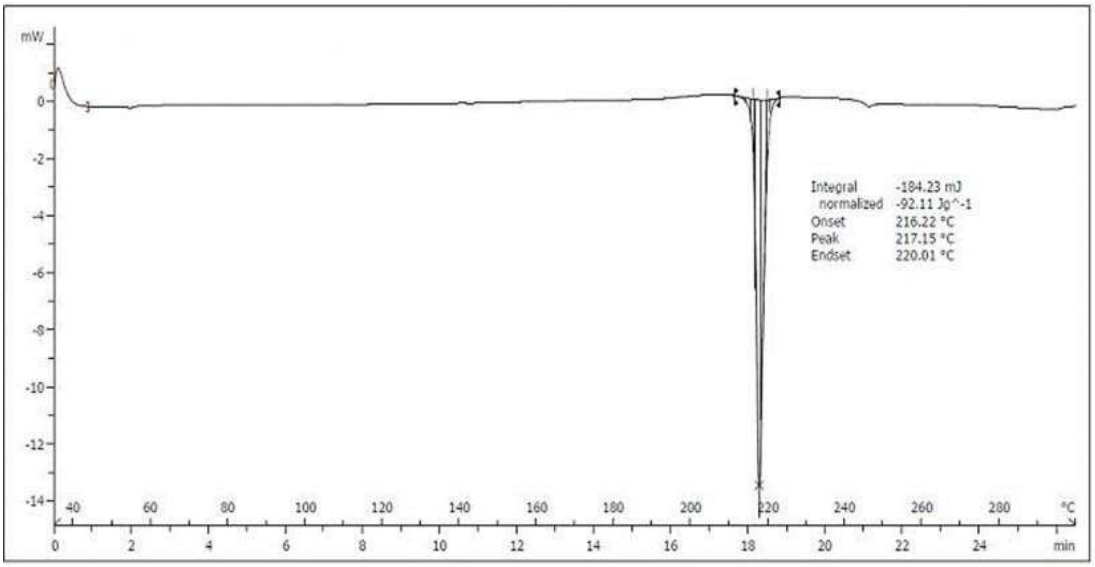

Figure 4: DSC graph of Lamotrigine

Interpretation of DSC of Lamotrigine

Peak	217.15°C
Onset	216.22°C
End set	220.01°C

UV Spectroscopy method

Lamotrigine solution was scanned at 400 nm to 200 nm, an absorbance maximum was observed at 310 nm as shown in Figure that was reported absorbance maximum of Lamotrigine in methanol.

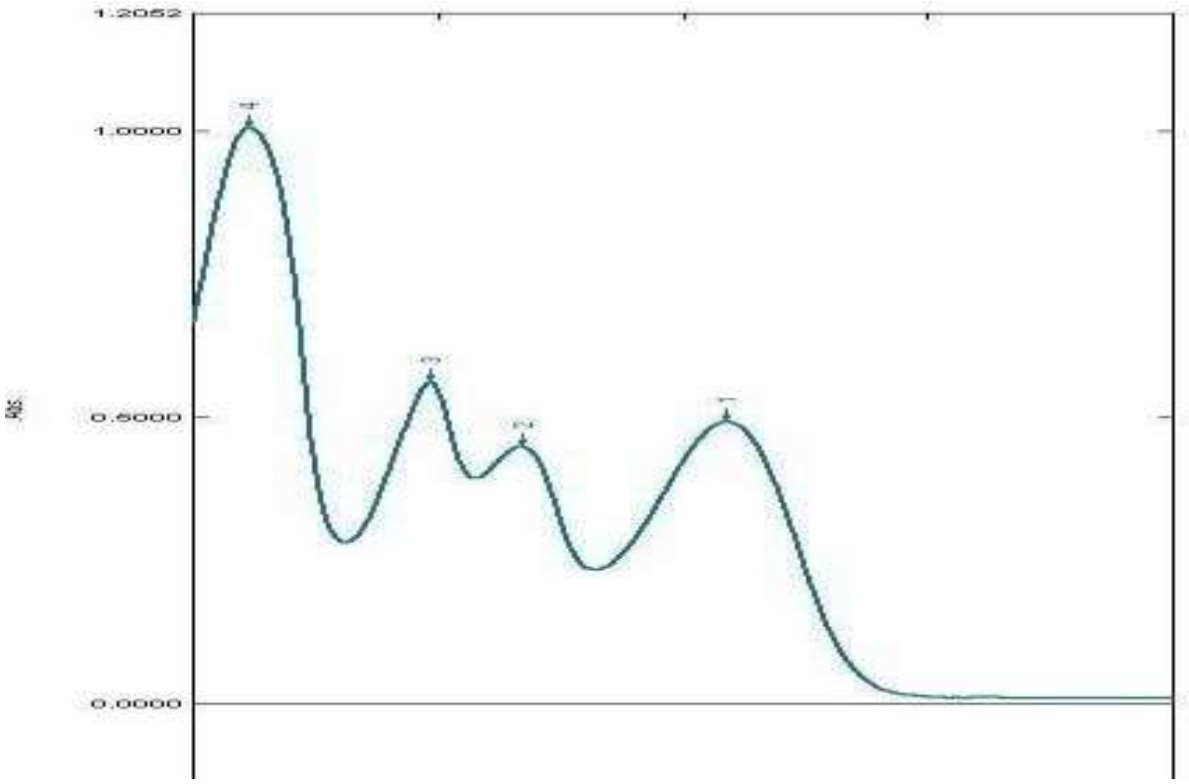

Figure 5: UV spectrum of Lamotrigine solution in methanol

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Calibration curve for Lamotrigine in PBS pH 6.8

Calibration curve of Lamotrigine in PBS pH 6.8 was plotted calibration curve of Lamotrigine with the correlation coefficient 0.999 and regression value of y=0.033x+0.007.

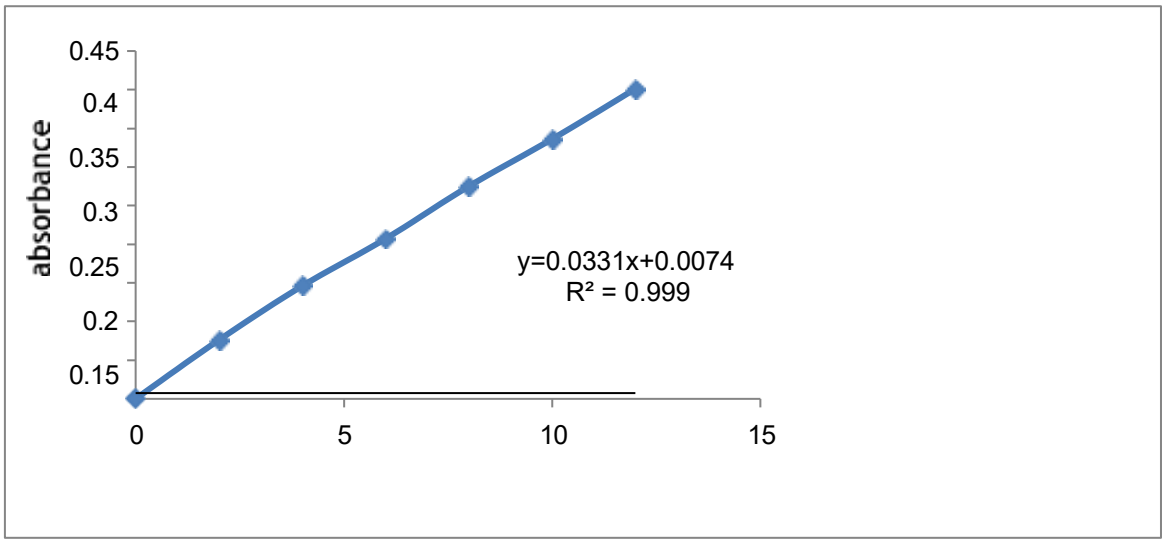

Figure 6: Standard calibration curve of Lamotrigine in PBS pH 6.8.

Table 2: Concentration Vs Absorbance of Lamotrigine

Sr. No.	Concentration µg/ml	Absorbance
1	2	0.076
2	4	0.146
3	6	0.207
4	8	0.275
5	10	0.336
6	12	0.401

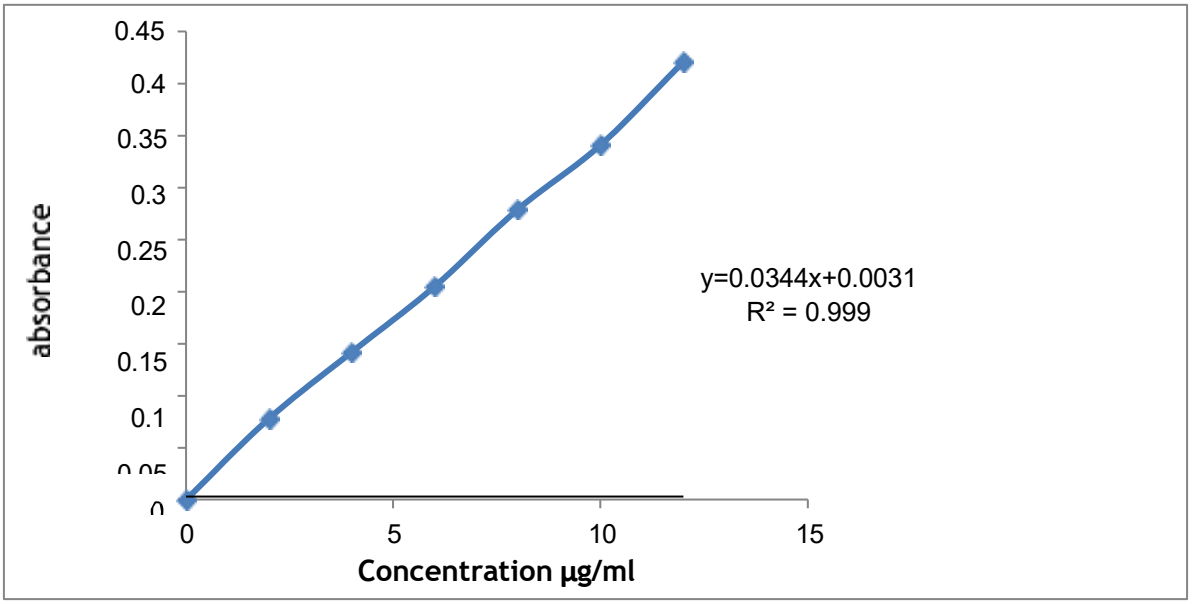

Figure 7: Standard calibration curve of Lamotrigine in methanol

Table 3: Concentration Vs Absorbance of Lamotrigine

Sr. No.	Concentration µg/ml	Absorbance

1	3	0.136
2	6	0.260
3	9	0.388
4	12	0.516
5	15	0.650
6	18	0.750

Drug –excipients Interaction studies

As described in the methodology FT-IR studies were carried out on pure drug Lamotrigine and polymer.IR spectra Lamotrigine with Combination of konjac gum is shown in figure

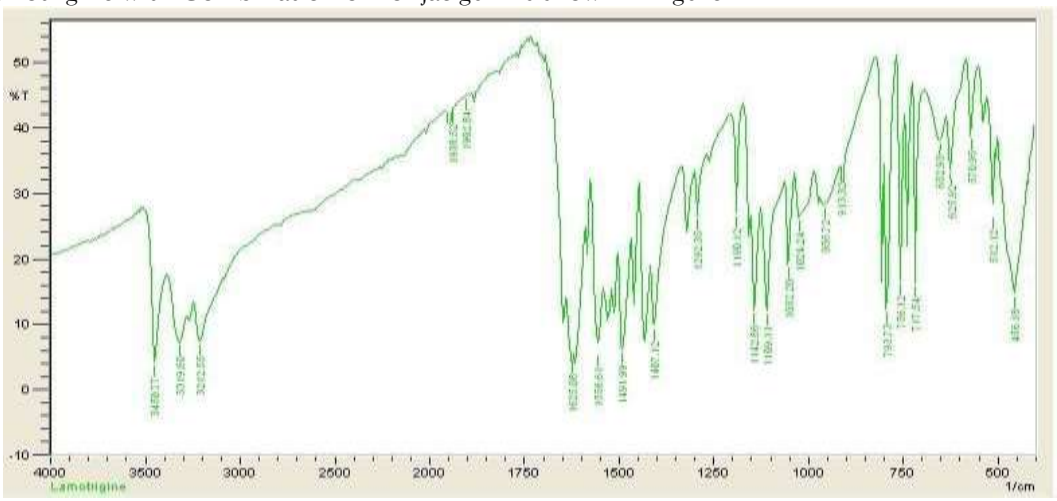

Figure 8: Infra –Red spectra of Lamotrigine

Table 4: Interpretation of IR spectra of Lamotrigine

Functional group	Observed peaks	Peak ranges
Ar C-H stretch	3086.21	3010-3100
N-H bend	1579.75	1450-1600
C-H bend	665.46	690-710
bend	759.98	730-770

Infra –Red spectra of konjac gum

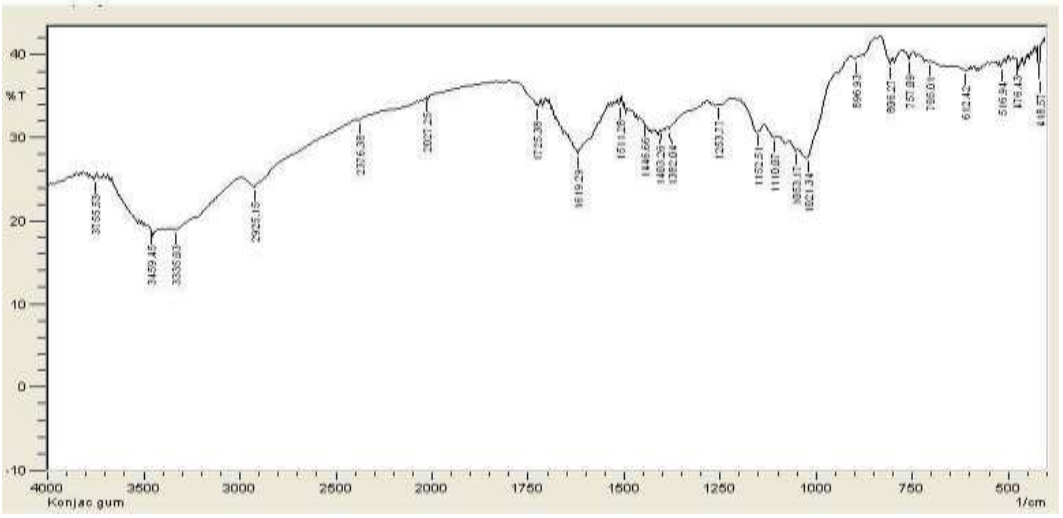

Figure 9: Infra-Red spectra of konjac gum

Table 5: Interpretation of IR spectra of Konjac gum

Functional group	Observed peaks	Peak ranges
O-H stretch	3313.82	2500-3500
C-H stretch	2924.18	2850-3000
C=O stretch	1674.26	1640-1690
C-O stretch	1153.40	1125-1205
C-F stretch	1023.31	1000-1350

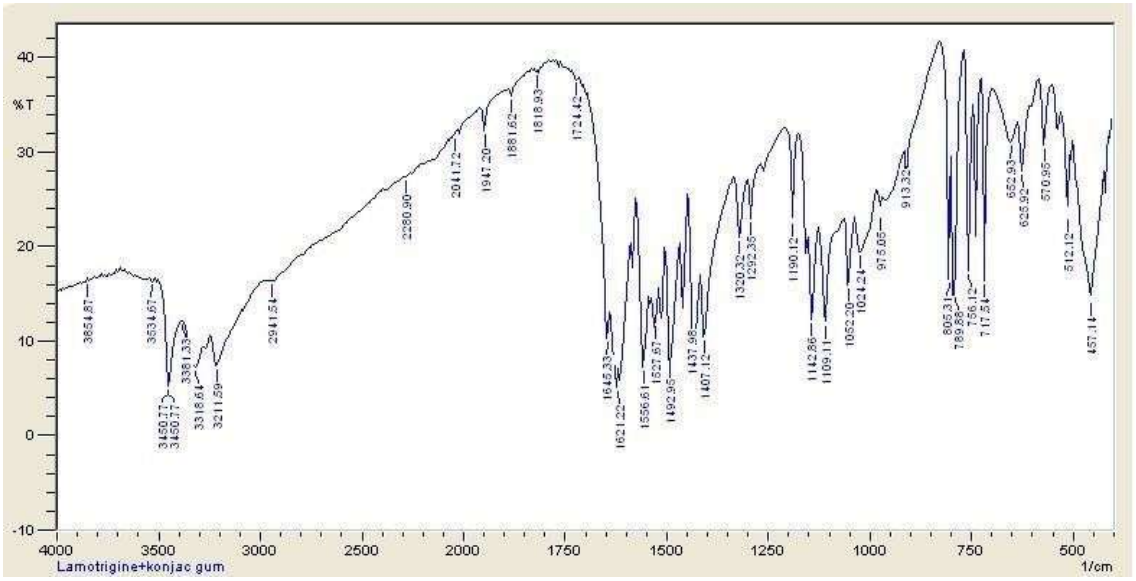

Figure 10: Infra-Red spectra of Lamotrigine and konjac gum

Table 6: Interpretation of IR spectra of drug + gum

Functional group	Observed peaks	Peak ranges
C-H stretch	2945.40	2850-3000
C-O stretch	1182.40	1125-1205
C=O stretch	1687.77	1640-1690
C-F stretch	1014.59	1000-1350
N-H stretch	3321.53	3310-33350
C-H bend	838.45	690-710

Formulations of films

Formulation of oral fast dissolving oral film by solvent casting method.

Figure 11: Formulations of oral fast dissolving films. Prepared batches OTF1-OTF9

Evaluation Parameters of prepared films

1. Physical appearance and surface texture: The results of Physical appearance and surface texture are shown in below table no. 7

Table 7: Physical appearance and surface texture

Formulation code	Physical appearance	Surface texture
OTF1	White in colour	Smooth
OTF2	White	Very smooth
OTF3	White	Smooth
OTF4	White	Very smooth
OTF5	Light brown	Smooth
OTF6	White	Very smooth
OTF7	Light brown	Smooth
OTF8	White	Very smooth
OTF9	White	Very smooth

2. Thickness uniformity of films

The thickness of drug loaded film were measured with the help of Digital calliper the mean values are shown in table no. 8

Table 8: Thickness ranges of prepared films

Formulation code	Mean thickness(mm)
OTF1	0.06±SD
OTF2	0.04±SD
OTF3	0.05±SD
OTF4	0.06±SD
OTF5	0.03±SD
OTF6	0.04±SD
OTF7	0.05±SD
OTF8	0.02±SD
OTF9	0.03±SD

3. Folding endurance of prepared films

Folding endurance was measured by manually for the prepared films. A strip of film (2×2cm) was cut evenly and repeatedly folded at same place till it broke.

Table 9: Folding endurance of prepared films

Formulation code	Folding Endurance
OTF1	163±SD
OTF2	180±SD
OTF3	177±SD
OTF4	190±SD
OTF5	196±SD
OTF6	210±SD
OTF7	263±SD
OTF8	289±SD
OTF9	272±SD

4. Weight uniformity of prepared films

Drug loaded film was tested for uniformity of weight and the results are given The weight of all the prepared films was found to quite uniform. Standard deviation of all the films ranged between 126-142.The change in the concentration of polymers and plasticizer did not show the difference in the weight of film.

Table 10: Weight uniformity of prepared films

Formulation code	Average weight (mg)
OTF1	52.4±SD
OTF2	54.3±SD
OTF3	54.8±SD
OTF4	51.5±SD
OTF5	49.3±SD
OTF6	48.6±SD
OTF7	40.9±SD
OTF8	35.4±SD
OTF9	41.3±SD

5. In-vitro disintegration time

This study represents an indication of onset of action of drug desired for OTF formulation. Fig. illustrates the in-vitro disintegration study of LMT loaded Konjac Gum based OTF in phosphate buffer (pH 6.8) at specific time interval. The mean time for complete disintegration of OTF was obtained below 5sec and completely disappearance into solution was within 10sec indicating that as the concentration of plasticizer increased, the disintegration time of film was also increased

0sec disintegration **5sec disintegration** **7 sec disintegration** **10sec disintegration**

Figure 12: *In-vitro* disintegration time

Table 11: Disintegration time of prepared films

Formulation code	Disintegration time(sec)
OTF1	21±SD
OTF2	23±SD
OTF3	23±SD
OTF4	20±SD
OTF5	18±SD
OTF6	20±SD
OTF7	13±SD
OTF8	10±SD
OTF9	15±SD

7. Surface pH determination

The surface pH of OTF batches was found in the range of 6–7 pH, close to neutral pH, indicating that the films were irritation free to tongue, the mucosal lining of oral cavity and easily acceptable for patients.

Table 12: Surface pH determination of prepared films

Formulation code	pH
OTF1	6.7±SD
OTF2	6.2±SD
OTF3	6.7±SD
OTF4	6.4±SD
OTF5	6.5±SD
OTF6	6.3±SD
OTF7	6.5±SD
OTF8	6.6±SD
OTF9	6.7±SD

Uniformity of drug content

The content uniformity test is commonly employed for unit dosage forms. In order to make sure about the uniform dispersion of drug in film. The drug content was carried out. The drug content was analysed at 270 nm for Lamotrigine by using phosphate buffer 6.8 pH. All the formulations showed more than 80% of the drug loading indicating much of the drug is not lost. The results indicated that the drug was uniformly dispersed.

Table 13: Uniformity of drug content

Formulation code	Drug content for LMT (%)
OTF1	87.7±SD
OTF2	80±SD
OTF3	82.3±SD
OTF4	92.5±SD
OTF5	97.5±SD
OTF6	62.5±SD
OTF7	97.5±SD
OTF8	99.2±SD
OTF9	80±SD

In-vitro drug release study

In –vitro drug release study of various formulations was carried out in PBS pH 6.8. The release data of formulations are shown the samples were diluted and Analysed using UV-Spectrophotometer at 310 nm for Lamotrigine.

In-vitro drug release study for LMT

Table 14: In-vitro drug release study for LMT

Time(sec)	OTF1	OTF2	OTF3	OTF4	OTF5	OTF6	OTF7	OTF8	OTF9
0	0	0	0	0	0	0	0	0	0
5	39.48	58.33	49.08	32.68	57.69	44.10	70.36	71.09	69.35
10	61.77	71.65	61.59	42.38	71.29	60.14	85.32	90.45	77.98
15	71.38	78.36	71.20	49.99	75.73	70.74	91.01	95.94	87.69

Scanning electron microscopy (SEM)

To characterized uniform or rough dispersion of all ingredient in konjac gum based OTF. SEM study was performed for sample LMT loaded konjac gum based OTF with all ingredient batch OTF8 apparent in the morphologies of sample were identified. It shows that proper homogenization solution of all ingredient in konjac gum based OTF before casting on glass Petri plates following its subsequent drying.

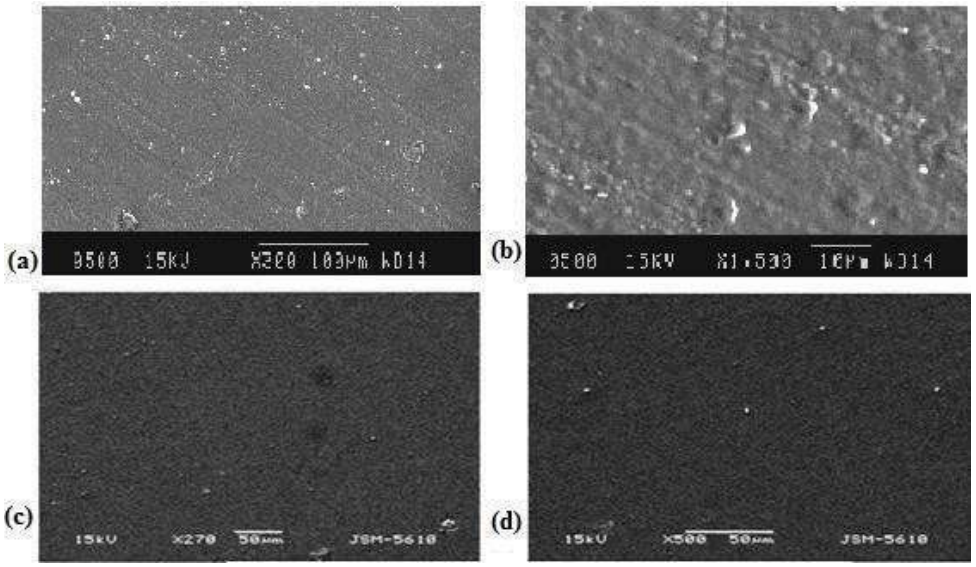

Figure 13: SEM images of LMT loaded konjac gum based OTF with all ingredients measured at magnifications, (a) X300 (b) X1500 (c) X270 (d) X500

Table No. 15: Comparison between marketed oral film and lab scale preparation oral film

Parameter	Marketed oral film	Lab scale preparation oral film
Thickness	0.04mm	0.02mm±SD
In-vitro Disintegration time(sec)	15	10±SD
Drug content	97.4%	99.2%±SD
Weight uniformity (mg)	43.5	0.02±SD
Folding endurance	254	289±SD
Surface pH	6.6	6.6±SD
In-vitro dissolution	91.83%	95.94%±SD

Stability studies

The optimized formulation of OTF8 was evaluated at the time interval of 30 and 90 days for all the parameters like, Appearance, Weight, Thickness, Drug content. The observations of the stability studies of optimized formulation OTF8 are shown and it did not show any significant change in these parameters after stability studies. This confirms the stored film formulation were stable for the storage period.

Table 16: Evaluation parameters of optimize batch (OTF8) after stability study

Duration	Visual Appearance	Weight films of (mg)	Thickness films of (mm)	% Drug for LMT content
0 days	Transparent	35.4±SD	0.03±SD	99.2±SD
30 days	Transparent	35.3±SD	0.03±SD	98.8±SD
60 days	Transparent	35.3±SD	0.03±SD	98.6±SD
90 days	Transparent	35.3±SD	0.03±SD	98.2±SD

CONCLUSION

A taste-masked, fast-dissolving oral film of Lamotrigine was successfully developed at the laboratory scale using **Konjac gum** as a natural, biodegradable film-forming polymer, **PEG 400** as a plasticizer, and **aspartame** as a sweetening agent via the solvent casting method. Preliminary trial batches demonstrated that PEG 400 and aspartame are compatible, inert, and effective in maintaining the overall quality and flexibility of the Konjac gum-based thin films.

The formulated films exhibited excellent palatability, smooth handling, and ease of administration. PEG 400 positively influenced the mechanical properties of the Konjac gum films while slightly reducing the drug release

rate. Both PEG 400 and aspartame enhanced the palatability, mouthfeel, and handling characteristics of the oral thin films.

Among the batches tested, the optimized formulation (Batch OTF8), containing 200 mg PEG 400 and 10 mg aspartame, showed superior mechanical strength, easy peelability from the casting surface, excellent palatability, and smooth mouthfeel. Additionally, the films demonstrated excellent stability when stored in tightly sealed aluminum sachets at **40 ± 2°C** and **75 ± 5% relative humidity**.

In conclusion, Konjac gum is a promising film-forming agent for the development of Lamotrigine oral thin films, with PEG 400 and aspartame serving as compatible plasticizer and sweetener, respectively. This formulation approach can be feasibly scaled up for commercial manufacturing, considering the critical factors affecting oral thin film development.

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