e-ISSN: 2320-4230, p-ISSN: 2961-6085

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 14, Issue 3; 2026, 21-30

Formulation and In Vitro Evaluation of Propranolol Hydrochloride Sublingual Films for Effective Hypertension Control

Dheeraj Bansiwal[1*], Yati Mishra[2], Mukesh Mehra[3], Jagdish Chandra Nagar[4]

[1,2,3]Department of Pharmaceutics, Kota College of Pharmacy, Ranpur, Kota, 325003
[4]Department of Pharmacology, Kota College of Pharmacy, Ranpur, Kota, 325003

Received: 21-03-2026 / Revised: 11-04-2026 / Accepted: 20-04-2026
Corresponding author: Dheeraj Bansiwal
Conflict of interest: No conflict of interest.

Abstract:

The objective of the present investigation was the formulation and evaluation of an oral fast-dissolving sublingual film of Propranolol HCl. This study aimed to formulate a rapid dissolving sublingual film of propranolol HCl by employing HPMC E15 as a film-forming agent, propylene glycol as a plasticizer, and cross-povidone as a disintegration agent. A fast-dissolving film was fabricated using the solvent casting technique. The stability studies of the patch were conducted for the optimized batch in accordance with the ICH guidelines. The medication and excipients underwent characterization according to the Indian Pharmacopoeia (IP). Investigation of drugs and excipients using Fourier Transform Infrared Spectroscopy (FT-IR). The films underwent physicochemical characterization, including assessment of weight Variation, thickness, tack test, drug content homogeneity, surface pH, folding endurance, disintegration time, in vitro drug release, and stability testing. Out of all the formulas (F1 to F9) that were created, batches F4 and F5 exhibited the highest quality, with a release of 109.86% and 104.73%, respectively during a 10-minute timeframe. The statistically optimized formulation was assessed using FT-IR (Fourier transform-infrared spectroscopy) investigations, which revealed no chemical interactions between the medication and polymer. Therefore, the propranolol HCl quick-dissolving film may serve as a superior substitute for tablets and capsules in achieving better oral bioavailability for the management of hypertension.

Keywords: Fast dissolving sublingual film, Propranolol HCl, solvent casting method, Drug release, Fast onset of action.

Introduction

In the late 1970s, fast-dissolving drug delivery systems were introduced as an alternative to traditional oral dosage forms (tablets, capsules, syrups). Because the oral cavity has a lot of blood vessels and lymphatic drainage, it has a larger surface area for absorption and allows for better permeability **(Laffleur & Keckeis, 2020).**

Mouth dissolving films (MDFs), also called fast dissolving, rapid melt, fast disintegrating, Oro-dispersible thin films, are solid dosage forms that dissolve or break apart quickly in the mouth without water or a solution.

Thin films were given different names, such as oral film, oral soluble film, wafer, oral strip, Oro-dispersible film (ODF), buccal

film, mucoadhesive films, ophthalmic film, and transmucosal film. Some films are made to dissolve quickly in the mouth for fast gastrointestinal absorption. Others, like buccal, sublingual, and ophthalmic thin films, are made to deliver a drug at the administration site. Drugs with high mucosal permeability have been shown to work well for buccal and sublingual delivery with films. MDFs help both cancer patients and people with trouble swallowing (dysphagia). The main goal of MDFs is to make drugs more bioavailable, have better permeability, start working quickly, and make it easier for patients to follow instructions. **(Sevinç Özakar & Özakar, 2021).**

Tablets and capsules are the most often used types of oral solid dose. A significant number of patients, especially children and geriatric individuals, encounter challenges in swallowing tablets and hard gelatin capsules, resulting in non-compliance with their prescribed medication. Dysphagia, a condition characterized by difficulty in swallowing, affects approximately 35% of the overall population. Swallowing tablets or capsules may become challenging in some situations, such as motion sickness, abrupt allergic reactions, coughing, fear of choking, or when water is not readily available. In order to surmount these challenges, numerous expedited dissolving medication delivery systems have been devised. In order to address the limitations of fast dissolving tablets, an appropriate approach is to employ a rapid dissolving film instead **(Hummler et al., 2023)**. Fast dissolving films closely resemble ultra-thin strips of postage stamps in terms of their shape, size, and thickness. The fast-dissolving film is applied directly onto the patient's tongue or any oral mucosal tissue. Upon contact with saliva, the film quickly hydrates and attaches to the area where it is applied. Subsequently, it swiftly breaks down and dissolves to liberate the drug for absorption through the oral mucosa. The fast-dissolving drug delivery system (FDDS) is ideal for medications that undergo significant first pass metabolism. It enhances bioavailability while minimizing the need for frequent dosing to achieve peak levels in the bloodstream. This approach minimizes adverse/side effects and also improves cost-effectiveness.

Most fast-dissolving oral films are ultra-thin films (50–150 m) about the size of a postage stamp. When they come in contact with saliva, they dissolve in the mouth within a minute, allowing the drugs to be absorbed quickly and immediately **(Rajagopalan et al., 2024).**

Materials and Method

Materials

Preparation of PRH sublingual films:

For the processing of the film, the solvent casting method was utilized. The appropriate amount of film- forming polymer was allowed to hydrate in a minimum amount of water for 3 to 4 hours before being uniformly dispersed to produce a transparent solution. The needed quantity of plasticizer is then added to the film-forming solution. Other ingredients, including a medication sweetener and a saliva-stimulating agent, were dissolved one at a time in the previously prepared film-forming solution to form a clear aqua solution. The aqueous solution was not disturbed until the trapped air bubbles were eliminated. The aqueous solution was poured into a 70.56 cm^2 glass petri dish and dried at room temperature. During the process, the petriplates were placed on a level surface to prevent variations in thickness. Approximately 24 hours were required for the film to dry at room temperature. The dried film was taken from the mold carefully and trimmed to the desired size for testing. The film was

preserved until further use in airtight plastic bags. Formulations F1-F9 were prepared by varying the concentration of Propranolol hydrochloride, HPMC E15, Cross povidone, Citric acid, Aspartame, P.E.G 400, and Distilled water (Mohammed Fitri et al., 2026) were depicted in (Table 1).

Table 1. **Composition of PRH sublingual films**

FORMULA CODE	F1	F2	F3	F4	F5	F6	F7	F8	F9
Propranolol hydrochloride (mg)	13.2	13.2	13.2	13.2	13.2	13.2	13.2	13.2	13.2
HPMC E15 (mg)	200	250	300	150	175	350	400	450	500
Cross povidone (mg)	16	16	16	16	16	16	16	16	16
Citric acid (mg)	50	50	50	20	20	20	50	50	50
Aspartame (mg)	10	10	10	10	10	10	10	10	10
P.E.G 400 (%)	0.4	0.4	0.4	0.4	0.4	0.4	0.2	0.2	0.2
Distilled water	Q.s.	Q.s.	Q.s.	Q.s.	Q.s.	Q.s.	Q.s.	Q.s.	Q.s.

Evaluation of PRH sublingual film:

a) **Physical appearance and surface texture**

Inspection of films by sight and touch is included in this process.

b) **Thickness of film**

Thickness of all the formulations was determined with calibrated micrometer screw gauge was used at five distinct positions (the center and four corners). There were three samples from each batch taken out and tested for thickness.

c) **Surface pH study**

An oral strip was tested for any potential side effects by measuring the pH of its surface. This was accomplished by employing a combined pH electrode. With the help of water, the oral film was moistened just enough. An electrode was positioned on the surface of the oral film in order to assess its pH. The experiment was replicated thrice, and the mean outcomes were presented.

d) **Folding endurance**

Folding endurance was assessed by continuously folding the film at a specific point until it reached its breaking point. Folding endurance is quantified as the maximum number of repetitive folds a film can endure at a certain place without experiencing any ripping.

e) **Drug content Uniformity**

The 2 cm by 2 cm film was submerged in 100 ml of distilled water. After total solubilization, the solution was adequately diluted, filtered, and UV-analyzed. The average of three films was used to determine the amount of drug per film unit**.**

f) **Weight determination**

Three films of each formulation were picked randomly and weighed separately, than the mean weight of each batch's films was computed**.**

g) **Moisture loss studies**

The film's physical stability and integrity were evaluated by measuring the percentage of moisture loss. This study assessed the film's ability to lose moisture by inserting films with known weight and predetermined size (2 cm×2 cm) in a desiccator filled with anhydrous calcium chloride for a duration of three days.

$$\text{Percent moisture loss} = \frac{\text{Initial weight} - \text{Final weight} \times 100}{\text{Initial weight}}$$

h) **In-vitro disintegrating studies**

Drop method:

With this technique, one drop of distilled water was pipette onto the oral film. Because of this, the films were mounted on a glass slide and placed on a Petri dish. The time it took for the film to disintegrate and form a hole was recorded.

Petri dish method:

A film was placed on a Petri dish containing 2 ml of distilled water and allowed to dissolve for a specified time. The results were then recorded. Under both procedures, drug-tainted films were analyzed.

i) **Dissolution studies**

Drug release profiles from MDFs were tested using the following dissolution procedures because any pharmacopoeia does not regulate them.

Beaker stirring method

The dissolving medium used in the in vitro studies was artificial saliva (125 ml) in a 150 ml glass beaker. Double-sided tape was used to attach the film to the beaker's one-side. The medium was stirred at 200 rpm by employing a magnetic bar. At intervals of 10, 20, 30, 40, 50, 60, 80, 100, 120sec, 5 ml samples were removed and replaced with 5 ml of a new dissolving medium. UV absorbance at 214 nm was used to examine the substances under test. There were three separate runs of the dissolution experiment to ensure accuracy.

USP Type II Apparatus

USP Dissolution Test Apparatus II was utilized to measure the release rate of the propanol hydrochloride fast-dissolving film. The dissolution test was conducted using 300 ml of artificial saliva with a pH of 6.8 at 37±.50°C with a paddle speed of 50 revolutions per minute. At 1-minute intervals, 5 ml of the solution was withdrawn from the dissolving equipment and replaced with the same volume of fresh dissolution medium. Whatman filter paper was used to process the aliquots.

At 214 nm, the filtered solution's absorbance was measured. It is recommended that the aliquot be taken at a distance of not less than 1 cm from the vessel wall when dissolving. Equation generated from the standard curve or percent drug release formula can be used to compute cumulative percentage release (%).

$$A = \frac{\text{Conc. of Std.} \times \text{Dilution factor}}{\text{Abs. of Std.}}, \quad B = (A - \text{Value} \times 100) \times \frac{1000}{\text{Label claim}}$$

Stability studies:

The accelerated stability experiments were performed in accordance with ICH Q1A (R2) recommendations. The selected formulations, F4 and F5, were evaluated in an expedited stability assessment. Each film was heat-sealed within an aluminum pouch

after being wrapped in butter paper and aluminum foil.

Twenty-one days stability testing was conducted at 40 ±2°C and 75%± 5% Rh. The physical and chemical characteristics of the samples were measured after 15 days. Physical appearance, in-vitro disintegration time, tensile strength, and drug content were all evaluated twenty-one days after being stored at 40 ±2°C and 75%± 5% Rh using the similarity factor to determine how the variables changed over time.

Scanning electron microscopy:

Scanning electron microscopy (SEM) analysis of the prepared films and the pure drug revealed distinct surface morphological differences. A thin layer of gold, about 20 nm thick, was vacuum-deposited onto an aluminum stub, which served as the sample mount. Microphotographs were taken at the appropriate magnifications while the scanning electron microscope was run at an accelerated voltage**.**

Results

Preparation of standard Calibration curve of Propranolol Hydrochloride:

The standard solution of 10µg/ml of Propranolol hydrochloride; was scanned over 200-400 nm, and taking similar concentration the calibration curve was made in phosphate buffer (pH 6.8) and the reading are mentioned in the below (Table 2), whereas the graphical representation has been shown in (figure 1). Spectra of Propranolol hydrochloride in phosphate buffer (pH 6.8) is depicted in (figure 2).

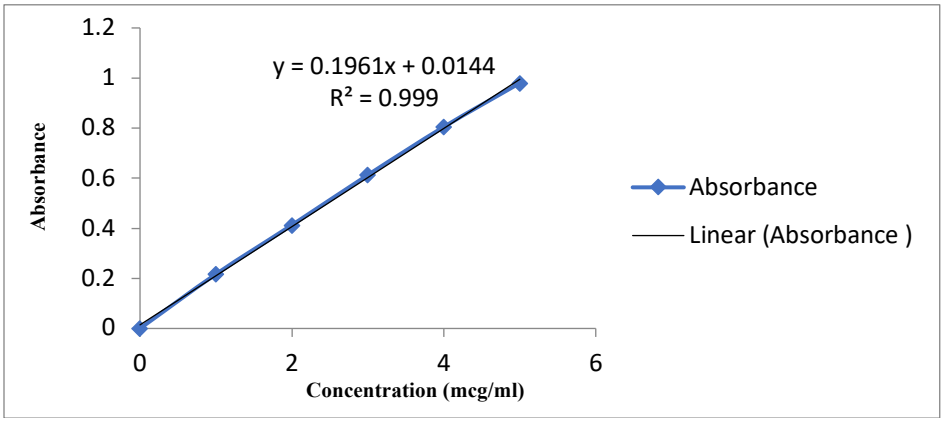

Figure 1. Calibration curve of Propranolol HCl

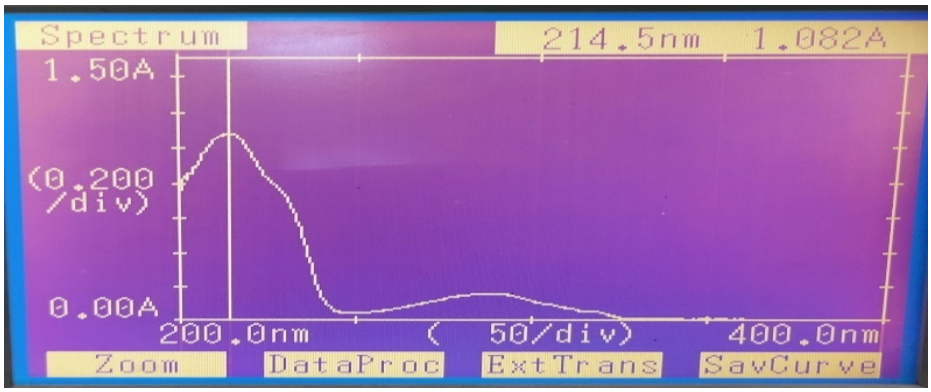

Figure 2. UV Spectra of Propranolol HCl in PBS (pH 6.8)

Compatibility study

Compatibility studies

Fourier transformed infrared spectrophotometer Perkin-Elmer spectrum was used to measure the FTIR of pure medication and physical mixing of formulation ingredients of the optimal batch. FTIR spectroscopy was conducted to detect interactions between drugs and polymers. The current study investigates the infrared (IR) analysis of Propranolol hydrochloride in its pure form, as well as its interactions with several substances including HPMC E-15 polymer, HPMC E-15 alone, propylene glycol, citric acid, aspartame, and cross povidone. The physical mixture contained the same amount of each formulation ingredient as the optimized batch. The pure medication and physical mixture were combined separately with IR-grade Potassium bromide (KBr.). This mixture was scanned over a 4000 to 400 cm-1 wave number range. The Propranolol hydrochloride spectra displayed prominent bands at specific wavelengths, as illustrated in (Figure 3). The combination of Propranolol hydrochloride and polymers exhibited strong spectral peaks at the specific wavelengths depicted in (Figure 4)

A. **FTIR Spectra of Propranolol hydrochloride**.

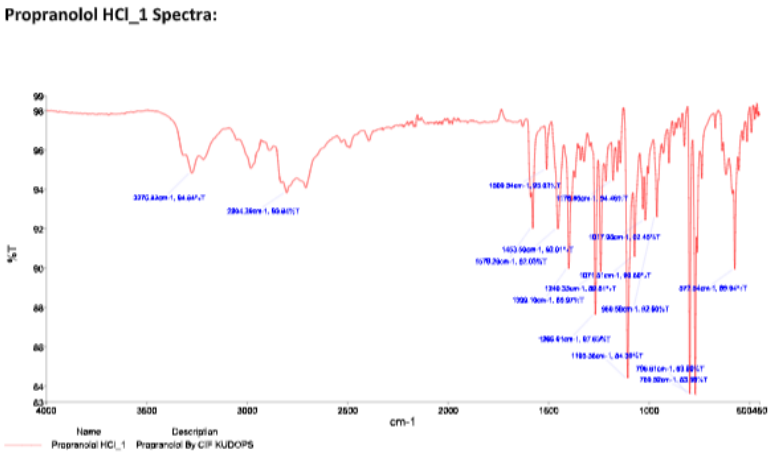

Figure 3: FTIR Spectra of Propranolol hydrochloride

B. **FTIR Spectra of Propranolol Hcl + Polymer mixture**

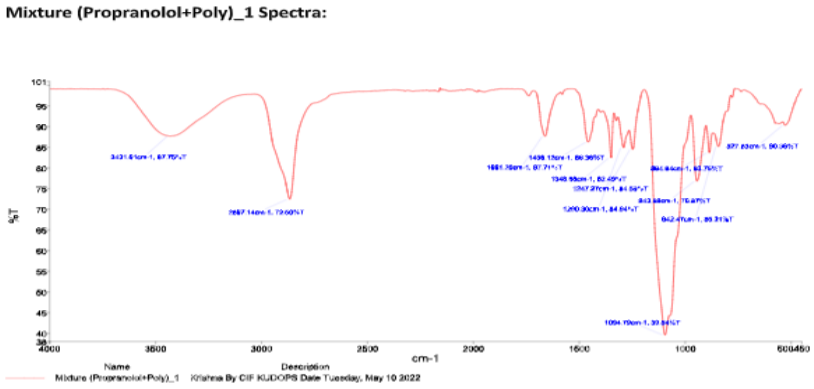

Figure 4. FTIR Spectra of Propranolol hydrochloride + Polymer mixture

The FT-IR of PRH and polymer mixture was performed in the range of 4000-400cm-1 and characteristic peaks were observed at 3431.61 O-H stretching (alcohol and phenol), 2867.14 C-H (alkane stretch), 1661.2 N-H (primary and secondary amine bend), 1456.12 -CH2- bend (alkene), 1348.98 C-N (amines), 1094.79 C-O (alcohols, esters, ethers, carboxylic acid, and anhydrides), 884.84 C-H [aromatic (out of plane bend)]. The FTIR study indicates that propranolol hydrochloride was compatible with the polymers.

Evaluation of sublingual films

Table 3. Physicochemical characterization of PRH sublingual film

S. no	Formulation Code	Appearance	Thickness (mm)	Surface pH	Folding endurance	Weight variation	Drug content
1	F1	Semi-transparent	0.15±0.005	6.75±0.03	275±2.51	50.40±1.04	92.66±2.32
2	F2	Transparent with air bubbles	0.16±0.005	6.82±0.06	283±3.15	52.27±1.59	90.67±4.167
3	F3	Greasy look	0.16±0.088	6.78±0.05	293±2.15	54.21±1.15	91.86±3.59
4	F4	Homogeneous and transparent	0.12±0.005	6.85±0.06	295±4.13	46.23±2.85	95.46±2.18
5	F5	Homogeneous and transparent	0.13±0.005	6.86±0.07	298±3.56	48.12±1.14	94.26±3.73
6	F6	Transparent	0.17±0.005	6.72±0.02	287±2.15	56.31±1.44	91.28±3.41
7	F7	Transparent	0.19±0.088	6.39±0.36	288±5.10	58.34±1.53	92.38±2.31
8	F8	Transparent	0.20±0.022	6.67±0.77	290±5.10	60.12±1.13	93.83±4.51
9	F9	Greasy look	0.23±0.022	6.46±0.81	285± 3.2	61.23±2.67	93.72±4.32

The physiochemical characterization of the film were performed and the obtained results are depicted in (table 3). homogeneous and transparent while F5, F6, F7, and F8, were transparent and passed the appearance test while other formulations F1, F2, F3, and F9 failed the appearance ttest Thickness of all formulation was lying between 0.12±0.005 to 0.23±0.022mm. Thickness of film is directly proportional to the disintegration time of the film.

The pH of the film's surface was measured with a pH meter, and the average value was recorded. All of the lots have surface pH values between 6.39±0.36 and 6.86±0.07. It was found that raising the polymer concentration raised the surface pH.

The weight of the formulations was determined by electronic balance. The result showed that the weight of formulations ranged from 0.12±0.005 mg to 023±0.022 mg. This indicates that there is no significant weight variation in all formulations.

The folding endurance of a film is assessed based on its capacity to resist tearing when subjected to folding. The average folding endurance of all the films was measured by repeatedly applying pressure to a small strip of film until it broke. The folding endurance of different batches exhibits significant variation, with a consistent pattern indicating that higher concentrations of polymers lead to increased endurance. The drug content for all formulations fell within the range of 100±15%. After comparing all the formulations, it was determined that formulation F4 was the most optimal and superior formulation among all.

In-vitro disintegrating studies of PRH sublingual films

Table 4. In-vitro disintegrating studies of PRH sublingual films

Formulation code	Disintegration time (sec)	
	Drop method	Petridish method
F1	18.6±1.25	18.2±1.02
F2	19..8±2.15	19.2±2.12
F3	19.5±3.01	19.1±1.15
F4	15.7±1.15	13.1±1.15
F5	18.8±2.15	17.5±3.12
F6	20.7±2.08	19.9±2.01
F7	23.9±1.02	21.6±2.21
F8	24.1±2.10	22.1±1.01
F9	26.5±3.15	24.7±3.07

In-vitro disintegration investigations were conducted for each formulation (F1-F9) using drop and the Petri dish methods and results are depicted in (table 4). The disintegration time varied from 15.7±1.15 to 26.1±3.15 in the drop technique, and from 13.1±1.15 to 24.7±3.07. In both approaches, formula F4 demonstrated the least disintegration time.

In-vitro dissolution studies

The Figure 5shows that drug release at the end of 10 min ranged from 52.97% to 109.8% for F1 to F9. All formulations exhibited a comparable release profile, characterized by a rapid initial release, followed by a consistent release rate, and reaching a plateau after approximately 10 minutes. The initial rapid release rates are differed in all formulations because of the variation in polymers content. The formulation F4 has a drug release of 109.8% which may be due to the greater swelling of the hydrophilic polymer. Formulation F9 has a low drug-release. The reason may be the higher polymer concentration and less concentration of plasticizer.

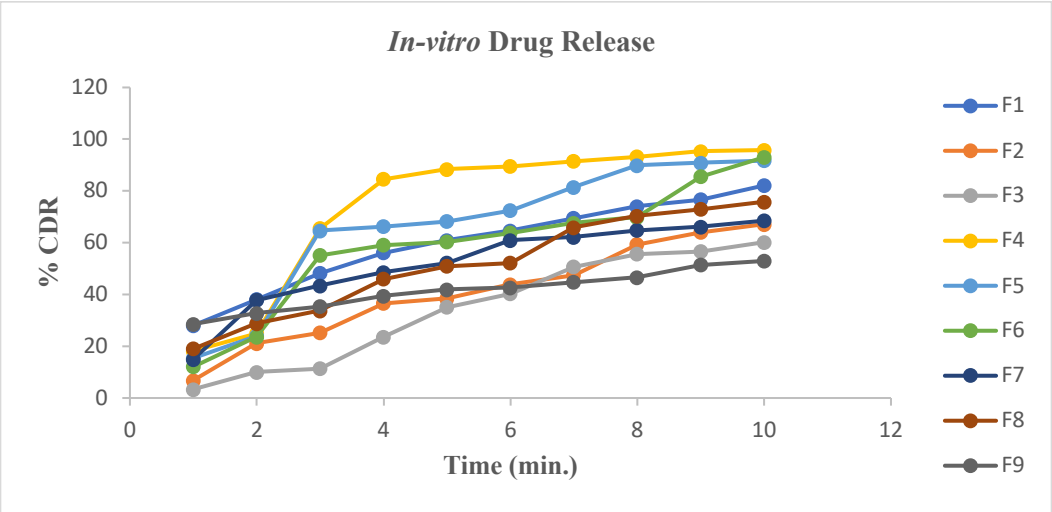

Figure 5. Determination of in-vitro release of different formulations of propranolol hydrochloride fast dissolving film (F1-F9)

Stability studies of sublingual films:

ICH-guided stability investigations were performed. The improved formulation and medication release remained unchanged. Fast-dissolving film formulations F4 and F5 were tested for 3 weeks (21 days) in a stability chamber. Enough film formulation was stored in a stability container and kept at 45°C and 75% RH. On the 21st day of drug content estimation, samples were taken and assessed for appearance, thickness, weight, folding durability, disintegration duration, surface pH, content uniformity, and in-vitro disintegration investigations. The results of stability studies are tabulated below (Table 5).

Table 5. Stability studies of optimized formulation

Parameter	Initial		Final	
	F4	**F5**	**F4**	**F5**
Thickness (mg)	0.12	0.13	0.12	0.13
Weight variation	46.23	48.10	46.19	48.00
Folding endurance	291	275	289	273
Surface pH	6.85	6.78	6.85	6.78
Disintegration time(sec.)	13	17	13	17
Percentage drug content (%)	109.8	104.7	109.8	104.7

Conclusion

As a non-selective beta-adrenergic antagonist, propranolol hydrochloride is subjected to substantial hepatic first pass metabolism, which results in a reduction of its bioavailability to 25%. The development of oral thin films of propranolol hydrochloride allows for the avoidance of the first pass metabolism that occurs in the liver, and it also allows for the reduction of doses in the control of hypertension. The solvent casting method was utilized to successfully manufacture oral thin films of propranolol hydrochloride. The polymer

used was HPMC E5, and the procedure was successful. In terms of peel ability, tackiness, weight variation, surface pH, folding durability, moisture loss, film softening upon storage, disintegration time, and medication content, the formulations that were created demonstrated satisfactory results. Within thirty seconds, the films that were made crumbled, and according to the evaluation parameters, formulations F4 and F5 demonstrated a faster release than the other formulations. There were no interactions between the medication and the polymer between the films that were created, and they were clear and had a smooth surface. It is possible to draw the conclusion that the fast-dissolving film of propranolol hydrochloride that was generated by the solvent casting approach exhibited satisfactory levels of drug release and mechanical qualities that were acceptable. Oral thin film of propranolol hydrochloride was found to be a better formulation for the control of hypertension. This is because oral thin film is a potential novel dosage form that might be used for pediatrics, geriatrics, and other groups.

Conflict of Interest:

The authors have no conflicts of interest regarding this investigation**.**

Acknowledgments:

The authors would like to thank

References

1. Hummler, H., Stillhart, C., Meilicke, L., Grimm, M., Krause, E., Mannaa, M., Gollasch, M., Weitschies, W., & Page, S. (2023). Impact of Tablet Size and Shape on the Swallowability in Older Adults. Pharmaceutics, 15(4), 1042. https://doi.org/10.3390/PHARMACEUTICS15041042/S1
2. Laffleur, F., & Keckeis, V. (2020). Advances in drug delivery systems: Work in progress still needed? International Journal of Pharmaceutics: X, 2, 100050. https://doi.org/10.1016/J.IJPX.2020.100050
3. Mohammed Fitri, T. F., Osman, A. F., Adnan, S. A., & Suryanto, H. (2026). Polymer buccal films as innovative approach in drug delivery systems: a review. Materials Research Express, 13(4), 042001. https://doi.org/10.1088/2053-1591/AE417A
4. Rajagopalan, S., Rajendhiran, D., Mohamed, I. A., & Sherbudeen, S. B. (2024). Fast dissolving oral thin films: an innovative herbal drug delivery system. International Journal of Research in Medical Sciences, 12(8), 3085–3090. https://doi.org/10.18203/2320-6012.IJRMS20242250
5. Sevinç Özakar, R., & Özakar, E. (2021). Current Overview of Oral Thin Films. Turkish Journal of Pharmaceutical Sciences, 18(1), 111. https://doi.org/10.4274/TJPS.GALENOS.2020.76390