Formulation And Evaluation of Thiamine Hydrocholoride Buccal Films

Smita A. Navale*[1], Pooja A. Pagale[2], Srushti D. Nishad[3], Pranjal U. Pandhare[4]

[1]Assistant Professor, Department of Pharmaceutics. JBVP'S Vidya Niketan College of Pharmacy, Lakhewadi. Tal. – Indapur, Dist. – Pune (413103), Maharashtra, India.

smitanavalevncop@gmail.com

[2,3,4]Student of JBVP'S Vidya Niketan College of Pharmacy, Lakhewadi, Tal. – Indapur, Dist. – Pune.

ABSTRACT:

The present study aimed to formulate and evaluate mucoadhesive buccal films of Thiamine Hydrochloride to improve bioavailability and therapeutic effectiveness by bypassing hepatic first-pass metabolism. Buccal drug delivery offers advantages such as rapid drug absorption, improved patient compliance, and avoidance of gastrointestinal degradation. The buccal films were prepared by the solvent casting method using HPMC as a film-forming polymer along with suitable excipients. Different formulations (F1–F6) were developed and evaluated for physicochemical parameters including physical appearance, weight variation, thickness, surface pH, swelling index, and moisture absorption. Compatibility studies using UV spectroscopy confirmed the absence of interaction between the drug and excipients. The λmax of Thiamine Hydrochloride was found at 246 nm in pH 6.8 phosphate buffer, and the calibration curve showed good linearity in the concentration range of 5–30 µg/mL following Beer–Lambert's law. The prepared films were smooth, flexible, transparent, and showed satisfactory physicochemical properties with acceptable stability and mucoadhesive characteristics. Overall, the formulated mucoadhesive buccal films demonstrated potential as an effective alternative delivery system for improving the bioavailability and therapeutic efficacy of Thiamine Hydrochloride.

KEYWORDS:

Buccal Film, Controlled Drug Release, UV Spectroscopy, Calibration Curve, Drug-Excipient Compatibility, Mucoadhesion, Permeation Study.

INTRODUCTION:

Oral medication delivery is the most popular approach because of patient compliance and ease of use. Nevertheless, a lot of medications have drawbacks like low bioavailability, gastrointestinal breakdown, and significant liver first-pass metabolism. Alternative routes, such as buccal drug delivery, have drawn a lot of attention recently as a means of overcoming these obstacles. Drugs are administered via the cheek's mucosal lining using the buccal route. Because of its high vascularization, relative permeability, and direct route to systemic circulation, the buccal mucosa avoids hepatic first-pass metabolism. This approach is especially beneficial for medications that experience substantial metabolic degradation or are unstable in the gastrointestinal environment.

Mucoadhesive buccal films are one of the more sophisticated and patient-friendly buccal drug delivery systems. Buccal films are thin, flexible, polymer-based formulations that are intended to stick to the buccal

mucosa and release the medication either quickly or gradually. By ensuring close contact with the absorption site, these films increase absorption and prolong the duration of drug residence. They also offer advantages like portability, precise dosing, ease of administration, and increased patient compliance, particularly in dysphagic, elderly, and pediatric patients. [1]

Vitamin B1, also referred to as thiamine hydrochloride, is a water-soluble vitamin that is necessary for healthy nerve function and the metabolism of carbohydrates. It functions as a coenzyme in a number of biochemical processes, most notably transketolation reactions and the decarboxylation of alpha-keto acids. Serious disorders like beriberi, Wernicke's encephalopathy, and Korsakoff syndrome can result from thiamine deficiency. Maintaining appropriate systemic levels of thiamine is essential because of its therapeutic significance.

Thiamine hydrochloride has some drawbacks when taken orally, despite its clinical importance. Because of active transport mechanisms that can become saturated at higher doses, it has variable absorption and is vulnerable to degradation in the gastrointestinal tract. A potential remedy for these problems is the creation of a buccal film containing thiamine hydrochloride. The formulation increases bioavailability by avoiding hepatic first-pass metabolism and gastrointestinal degradation by delivering the medication directly through the buccal mucosa. Additionally, mucoadhesive polymers like polyvinyl alcohol (PVA), sodium alginate, Carbopol, and hydroxypropyl methylcellulose (HPMC) aid in extending the dosage form's residence time at the absorption site. [2]

Solvent casting, hot-melt extrusion, and semi-solid casting are common methods used to create buccal films. Film-forming polymers, plasticizers (such as glycerol and polyethylene glycol), permeation enhancers, sweeteners, and flavoring agents to increase palatability are among the formulation's essential ingredients. The performance of buccal films depends on various factors, including polymer type, drug-polymer compatibility, film thickness, surface pH, swelling behavior, and mucoadhesive strength

In addition to improving thiamine hydrochloride's pharmacokinetic profile, the creation of a buccal film is in line with contemporary drug delivery trends that emphasize non-invasive, patient-centered methods. This dosage form is especially helpful for people with neurological disorders, children, and elderly patients who have trouble swallowing traditional tablets or capsules.

The water-soluble vitamin thiamine hydrochloride, also known as vitamin B1, is necessary for the metabolism of carbohydrates and the healthy operation of the nervous system. It participates as a coenzyme in a number of biochemical processes that produce energy. Serious conditions like beriberi and Wernicke-Korsakoff syndrome can result from a thiamine deficiency. For general health, maintaining appropriate thiamine levels through diet or supplementation is essential. Whole grains, legumes, nuts, and some meats are foods high in this vitamin, so it's crucial to include a range of these foods in your meals. In order to increase thiamine hydrochloride's bioavailability and therapeutic efficacy, the current study focuses on the creation and assessment of buccal films. [3]

Fig.no.1: Thiamine Hydrochloride

DRUG PROFILE: [4-6]

Parameter	Description
Drug Name	Thiamine Hydrochloride
Category	Water-soluble Vitamin
Synonym	Vitamin B1
Molecular Formula	$C_{12}H_{17}CIN_40S$-HCI
Molecular Weight	337.27 g/mol
Appearance	White or almost white crystalline powder
Odor	Slight characteristic odor
Taste	Bitter taste
Solubility	Freely soluble in water; slightly soluble in alcohol
Melting Point	Approximately 248-250°C (decomposes)
PH	Acidic
Partition Coefficient	Hydrophilic drug
Category Of Drug	Vitamin supplement
Mechanism Of Action	Acts as coenzyme in carbohydrate metabolism
Uses	Treatment and prevention of Vitamin B1 deficiency, beriberi, neuropathy
Half Life	Approximately 1-1.5 hours
Bioavailability	Limited due to poor storage and degradation in GI tract
Route Of Administration	Oral, injectable, buccal
Storage Condition	Store in cool, dry place away from light
Advantages In Buccal Delivery	Avoids first-pass metabolism, improves patient compliance, rapid absorption

MATERIALS AND METHODS:

Materials:

Table no.1: Materials used in formulation of thiamine HCL buccal films [7]

Sr.no.	Materials	Category/Use
1	Thiamine hydrochloride	Active pharmaceutical ingredient
2	HPMC	Film forming polymer
3	Sodium Saccharin	Sweetening agent
4	Citric Acid	Saliva stimulating agent
5	Tween 80	Surfactant / penetration enhancer
6	Orange flavor	Pleasant citrus taste
7	Distilled Water	Solvent

Methods:

Preliminary trials for choosing a suitable polymer and plasticizer:

Preliminary trials were conducted to select suitable concentrations of polymer and plasticizer for thiamine hydrochloride buccal films prepared by the solvent casting method. Different concentrations of HPMC (2%, 3%, and 4% w/v) were evaluated for film-forming ability and mechanical properties. The 3% w/v

HPMC formulation produced smooth, transparent, flexible, and easily peelable films and was selected for further studies. Further trials with PEG 400 and glycerol (0.6%, 0.9%, and 1.2% w/v) showed that 0.6% films were brittle, while 1.2% films were soft and sticky. The formulation containing 3% w/v HPMC with 0.9% w/v plasticizer showed optimum flexibility, folding endurance, and appearance, and was selected for optimization studies. [8]

Formulation:

In the solvent casting method, HPMC and other excipients are dissolved in distilled water to form a uniform viscous solution, while thiamine hydrochloride is dissolved separately and mixed under continuous stirring. The solution is cast into petriplates or glass moulds and dried to form thin buccal films, which are then peeled and cut into suitable sizes. The films are stored in airtight containers or aluminum foil packs to protect them from moisture and light. This method is preferred because it produces films with uniform drug distribution, smooth surface, and good mechanical strength. [9]

Composition of Thiamine Hydrochloride Loaded Mouth Dissolving Films:

Thiamine Hydrochloride loaded mouth dissolving films were formulated using the solvent casting method with the objective of developing a rapidly dissolving oral film capable of improving patient compliance and enhancing drug delivery through the oral cavity. Six different formulations, namely F1 to F6, were prepared by varying the concentration of the polymer and surfactant while keeping the drug concentration constant. The composition of all formulations was designed to obtain films with optimum mechanical strength, flexibility, surface smoothness, rapid disintegration, and satisfactory drug release characteristics.

Table no.2: Composition of Thiamine Hydrochloride loaded mouth dissolving films

Ingredients(mg)	F1	F2	F3	F4	F5	F6
Thiamine HCL	50	50	50	50	50	50
HPMC	525	525	550	580	530	500
Sodium Saccharin	10	10	10	10	10	10
Citric Acid	10	10	10	10	10	10
Tween 80	0.5	0.3	0.4	0.5	0.4	0.5
Orange flavor (ml)	Qs	Qs	Qs	Qs	Qs	Qs
Distilled Water	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml

Dose calculation of the amount of drug per batch:

Dose of drug per film = 6.35 mg Area of one film = 9 cm^2

Area of petri plate = 70.84 cm^2

Drug to be added per batch = (Dose of drug per film × Area of petri plate) ÷ Area of one film

= (6.35 x 70.84) ÷ 9

=50 mg

Standard calibration curve of Thiamine Hydrochloride:

A standard calibration curve of Thiamine Hydrochloride was prepared to determine the concentration of drug present in an unknown sample using UV-visible spectrophotometry. In this method, a stock solution of Thiamine Hydrochloride was prepared by dissolving an accurately weighed quantity of drug in pH 6.8 phosphate buffer. From the stock solution, different standard concentrations (5-30 µg/mL) were prepared

by suitable dilution with the same buffer solution. The absorbance of each solution was measured at the Amag of Thiamine Hydrochloride, i.e., 246nm, using a UV-visible spectrophotometer against pH 6.8 phosphate buffer as blank. A graph was plotted between concentration (X-axis) and absorbance (Y-axis), which showed a straight-line obeying Beer-Lambert's law. The calibration curve was found to exhibit good linearity within the selected concentration range and was used for estimation of drug content in buccal film formulations containing Thiamine Hydrochloride. [10]

Evaluation of Thiamine HCL film:

1) Physical appearance:

Formulated mouth dissolving films were assessed for their appearances either they are transparent or opaque by visual inspection or surface texture was assessed by contact or feel of the film. [11]

2) Weight uniformity:

The individual weight each of 3-5 films of 3×3 cm^2 for each formulation on an electronic weighing balance. The average weight was calculated. [12]

3) Thickness:

The average thickness of the film was determined by using digital Vernier Caliper (Digimatic, Mitutoyo, Japan) with a least count of 0.01 mm. The thickness was determined at five different places of the film and the average was taken and the standard deviation was calculated. [13]

4) Surface pH:

The surface pH was determined by placing one film in a glass vial, adding 1 ml of distilled water and wait for 30 Sec. The pH value obtained by bringing electrodes of pH meter (Lab, India) in contact with the moistened surface of the film. All measurements were performed in triplicate. It is essential that the strip should have an almost uniform pH value. [14]

5) Swelling index:

The swelling index of a buccal film is evaluated to determine its hydration capacity and swelling behavior, which affect mucoadhesion and drug release. The film is initially weighed (W_0) and placed in phosphate buffer pH 6.8 at 37 ± 0.5°C. After specific time intervals, film is removed, excess moisture is blotted gently, and the swollen film is reweighed (W_t). [15-16]

Swelling Index (%) = $(Wt - W_0) / W_0 \times 100$ Where:

Wt = weight of swollen film at time Wo = initial weight of film

6) Moisture absorption test:

The moisture absorption test of a buccal film is carried out to determine the ability of the film to absorb moisture under humid conditions, which influences the stability and physical properties of the film. The film is weighed initially (W_1) and then placed in a desiccator containing a saturated solution of aluminum chloride or potassium chloride to maintain relative humidity (about 75–84%) for 24 hours at room temperature. After the specified period, the film is removed and reweighed (W_2). [17-18]

Moisture Absorption (%) = $(W_2 - W_1) / W_1 \times 100$ Where:

W_1 = Initial weight of the film

W_2 = Final weight of the film after moisture absorption

RESULTS AND DISCUSSION:

Drug excipients compatibility study by UV spectroscopy:

The drug–excipient compatibility study of Thiamine Hydrochloride was carried out using UV–Visible spectroscopy in order to determine the possible interaction between the drug and selected excipients used in the buccal film formulation. It is shown in below fig. (fig. no.3 and 4). The UV spectrum of pure thiamine hydrochloride showed a characteristic absorption maximum (λmax) at 246 nm in phosphate buffer pH 6.8. The physical mixture of thiamine hydrochloride with excipients such as HPMC, citric acid, sodium saccharin, and Tween 80 also exhibited a similar λmax at 246 nm without any significant shift in wavelength or major change in absorbance pattern. The obtained spectra confirmed that there was no chemical incompatibility or interaction between the drug and excipients. Therefore, the selected excipients were found to be compatible with thiamine hydrochloride and suitable for the preparation of buccal films by the solvent casting method. [19]

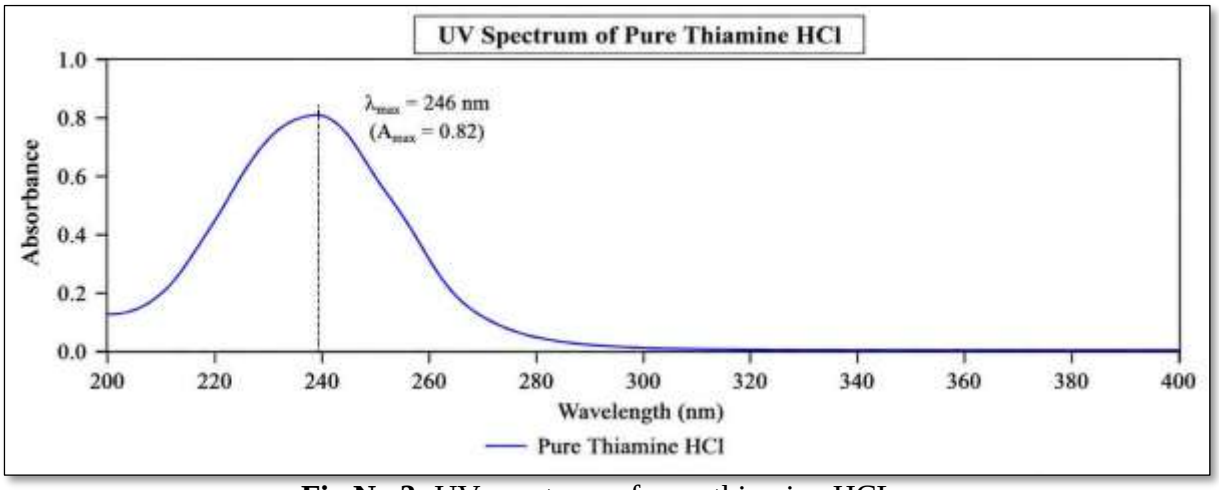

Fig.No.3: UV spectrum of pure thiamine HCL

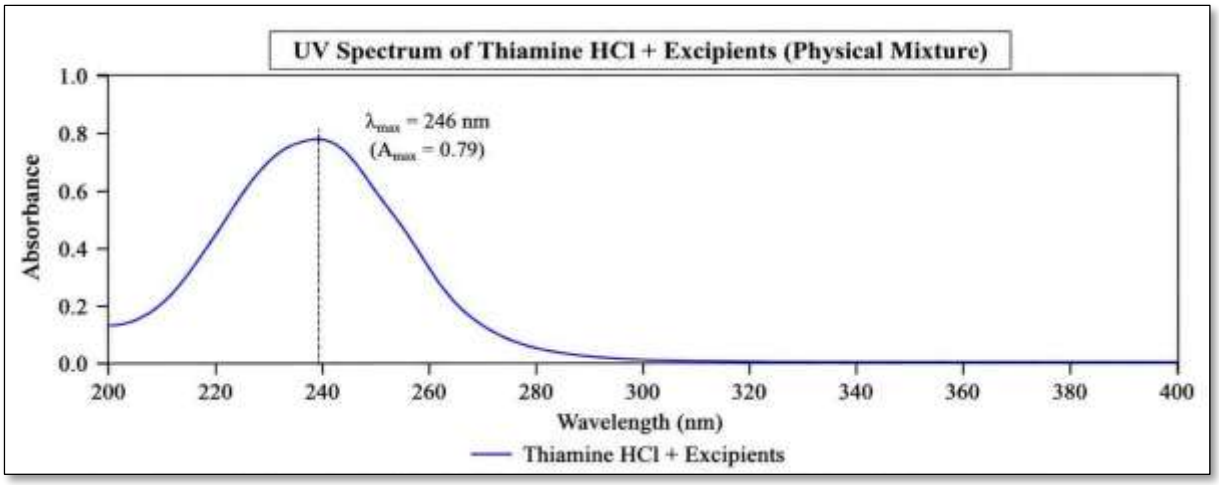

Fig.No.4: UV spectrum of pure thiamine HCL and excipients

Standard calibration curve of Thiamine Hydrochloride in 6.8 phosphate buffer:

A standard calibration curve of Thiamine Hydrochloride in pH 6.8 phosphate buffer showed good linearity in the concentration range of 5–30 µg/mL at 246 nm. The absorbance values were found to increase proportionally with concentration, confirming that the drug follows Beer–Lambert's law within the selected range. Hence, the developed UV spectrophotometric method was considered suitable for

estimation of Thiamine Hydrochloride in buccal film formulations. [10]

Table no. 3: Standard calibration curve of Thiamine HCL in 6.8 phosphate buffer

Sr.No.	Concentration (µg/mL)	Absorbance at 246 nm
1	5	0.112
2	10	0.224
3	15	0.336
4	20	0.448
5	25	0.559
6	30	0.671

Evaluation of films:

1) Physical appearance:

The prepared Thiamine HCl buccal films were found to be smooth, flexible, transparent and uniform in appearance without any air bubbles or cracks. The surface texture of the films was satisfactory. [11]

Table no.4: Physical appearance of buccal film

Parameter	Observation
Color	Slightly white
Surface texture	Smooth
Flexibility	Flexible
Transparency	Transparent / Translucent
Air bubbles	Absent
Cracks	Absent

2) Weight uniformity:

The films showed uniform weight variation, indicating uniform distribution of drug and excipients throughout the film matrix. The average weight of the films was found within acceptable limits. The average weight of the films was found in the range of 45–55 mg, indicating uniform distribution of drug and polymer in the film. [12]

3) Thickness:

The thickness of the buccal films was found to be uniform at different points of measurement, which indicates proper casting and even distribution of polymer solution. Low standard deviation confirmed uniform film thickness. The thickness of the films was found in the range of 0.12–0.25 mm with low standard deviation, showing uniform casting of films. [13]

4) Surface pH:

The surface pH was noted by pH meter near the surface of the fast- dissolving film and allowing equilibrating for 30 Sec and the surface pH of all fast-dissolving film was found to in between 6.58-6.89 pH. All batches show pH towards a neutral range, which is evidence for the absence of oral mucosal irritation. [14]

5) Swelling index:

The films exhibited satisfactory swelling behavior, which helps in proper adhesion and controlled drug release at the buccal site. The swelling index increased gradually with time due to hydration of polymers. The swelling index of the films was observed in the range of 20–45
%, indicating satisfactory hydration and mucoadhesive behavior of the polymeric film. [15-16]

6) Moisture absorption test:

The percentage moisture absorption of buccal films is generally found in the range of 2–10%, depending on the type and concentration of polymer and plasticizer used. Films showing moderate moisture absorption indicate good flexibility, stability, and resistance to brittleness without becoming excessively sticky. [17-18]

Future Scope of Thiamine HCL Buccal Film:

1.Improvement of bioavailability by avoiding first-pass metabolism. 2.Development of sustained and controlled release buccal films.

3. Use of novel polymers and permeation enhancers for better mucoadhesion and drug permeation.[20]

4. Application of advanced technologies like inkjet printing and 3D printing for personalized dosing.[21]

5. Combination buccal films containing B-complex vitamins.

6. In vivo pharmacokinetic and clinical studies for therapeutic effectiveness.[22] Stability studies and large-scale industrial manufacturing.

7. Better patient compliance in pediatric and geriatric patients due to ease of administration.[23]

CONCLUSION:

The present study successfully formulated and evaluated mucoadhesive buccal films of Thiamine Hydrochloride using the solvent casting method. The prepared films showed satisfactory physicochemical properties such as uniform thickness, acceptable weight variation, smooth appearance, flexibility, suitable surface pH, good swelling behavior, and moderate moisture absorption. UV compatibility studies confirmed that there was no interaction between thiamine hydrochloride and the selected excipients. The calibration curve of thiamine hydrochloride in pH 6.8 phosphate buffer showed good linearity at 246 nm. Overall, the developed buccal films demonstrated good potential for improving bioavailability, therapeutic efficacy, and patient compliance by bypassing first-pass metabolism and providing effective buccal drug delivery. [24-25]

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