WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Formulation & Evaluation of Nifedipin Buccal Tablet.

**** Mahek M. Shaikh, Pratik B.Bhange , Megha T. Salve***

Email ID: mahekmshaikh17@gmail.com
Shivajirao Pawar College Of Pharmacy, Pachegaon
Dr. Babasaheb Ambedkar technical University .

ABSTRACT :

The present study focuses on the formulation and evaluation of Nifedipine buccal tablets to overcome the challenges of poor water solubility and extensive first-pass hepatic metabolism. Buccal drug delivery offers a promising route for systemic drug administration by enabling direct absorption through the richly vascularized oral mucosa, thereby bypassing hepatic metabolism and enhancing bioavailability [19,]. Various formulations were developed using polymers such as HPMC and Carbopol, aiming to optimize key parameters including mucoadhesive strength, swelling behavior, and sustained drug release. Comprehensive evaluations were performed to assess weight variation, hardness, friability, surface pH, and in-vitro release profiles. FTIR studies confirmed the absence of drug-excipient interactions, supporting formulation compatibility. The optimized formulation exhibited favorable mucoadhesive properties and sustained release behavior, indicating its potential to reduce dosing frequency and improve therapeutic outcomes in the treatment of hypertension and angina [23]. Buccal delivery of Nifedipine may serve as an effective and patient-friendly alternative to conventional oral dosage forms.

Key words: Buccal drug delivery, Mucoadhesive tablet, Controlled release, Sustained release, Bioavailability enhancement ,First-pass metabolism, Mucoadhesive polymer , Calcium channel blocker .

Introduction:

Hypertension, which includes stroke, accelerated coronary and systemic ather concerned osclerosis, heart failure, chronic kidney disease, lowering blood pressure with antihypertensive medications, reducing target organ damage, and the prevalence of cardiovascular disease occurrence, is the most prevalent modifiable risk factor for death and disability.[1] A common calcium channel blocker used to treat hypertension and angina pectoris is nifedipine. Its significant first-pass metabolism and poor water solubility, which combined result in low and unpredictable bioavailability, limit its clinical use.[2,3]. This study is with creation and assessment of buccal tablets containing the calcium channel blocker nifedipine, which is used to treat angina and hypertension.[6]The objective is to use a mucoadhesive buccal administration technique to increase Nifedipine's bioavailability.[7] Buccal tablets are a type of mucoadhesive drug delivery system designed to be administered in the buccal cavity, where they adhere to the mucosal surface and allow for the systemic absorption of drugs through the rich vascular network of the buccal mucosa. This route bypasses first-pass hepatic metabolism, enhancing bioavailability and allowing for controlled or sustained drug release[13 Direct medication absorption through the mouth cavity's mucosal barrier is made possible by buccal drug delivery systems (BDDS), which can greatly increase a medicine's bioavailability and therapeutic effectiveness. The main indication for nifedipine is the treatment of cardiovascular diseases like angina and hypertension. A controlled-release formulation is necessary to maintain therapeutic plasma concentrations and lower dose frequency because of its short half-life and significant hepatic metabolism.[12]Because buccal administration avoids the hepatic first-pass impact and provides quick and long-lasting systemic distribution, it is a prospective substitute route.[4,5]The dihydropyridine class of calcium channel blockers, including nifedipine, is commonly used to treat these disorders due to its strong antihypertensive and vasodilatory properties.[8]Numerous assessments were conducted, including in-vitro drug release profile, swelling index, hardness, friability, disintegration, physicochemical characterisation, and homogeneity of drug content.[9]The improved formulation showed favorable pharmacotechnical and physical characteristics, suggesting that it could be a viable buccal delivery method for nifedipine.[10,11] These systems not only enhance mucosal adhesion and retention time but also allow for controlled and targeted drug delivery, reducing dosing frequency and improving therapeutic outcomes.[26]

Rationale:

1. Bypass of First-Pass Metabolism:

Drugs administered via the buccal route directly enter systemic circulation, avoiding hepatic first-pass metabolism and thus improving bioavailability [13]

2. Rapid Onset of Action:

the buccal mucosa is highly vascularized, allowing for faster absorption and a quicker onset of therapeutic action [14]

3. Improved Patient Compliance:

Buccal tablets are non-invasive, painless, and easy to administer-especially useful for children, the elderly, and unconscious patients [15].

4. Sustained and Controlled Release:

Use of mucoadhesive polymers in BDDS can prolong the residence time of the drug, allowing controlled and sustained drug release [16].

5. Avoidance of Gastrointestinal Degradation:

Since the drug does not pass through the Gl tract, it avoids enzymatic degradation and irritation issues associated with oral routes [17].

6. Improved Bioavailability for Drugs Like Nifedipine:Nifedipine suffers from low solubility and extensive first-pass metabolism.buccal delivery improves its bioavailability and therapeutic profile [18].

Classification of Hypertension

TABLE:1. Based on Blood Pressure Readings (According to ACC/AHA 2017 Guidelines)

Category	Systolic BP (mmHg)	Diastolic BP (mmHg)
Normal	Less than 120	and Less than 80
Elevated	120–129	and Less than 80
Stage 1 Hypertension	130–139	or 80–89
Stage 2 Hypertension	140 or higher	or 90 or higher
Hypertensive Crisis	Higher than 180	and/or Higher than 120

2. **Based on Etiology**

A. Primary (Essential) Hypertension

• No identifiable medical cause.
• Accounts for approximately 90–95% of cases.
• Associated with genetic, dietary, and lifestyle factors.

B. **Secondary Hypertension**

• Caused by an underlying medical condition. Common causes include:
- Chronic kidney disease
- Endocrine disorders (e.g., hyperaldosteronism, pheochromocytoma)
- Coarctation of the aorta
- Medications (e.g., oral contraceptives, NSAIDs)
- Obstructive sleep apnea

TABLE;2. Based on Severity (WHO/ISH Classification)

Grade	Systolic BP (mmHg)	Diastolic BP (mmHg)
Grade 1 (Mild)	140–159	90–99
Grade 2 (Moderate)	160–179	100–109
Grade 3 (Severe)	180 or higher	110 or higher

4. Based on Age of Onset

• Adult-Onset Hypertension: Most common type, typically associated with lifestyle factors.
• Pediatric/Adolescent Hypertension: Often secondary to renal or endocrine causes.
• Gestational Hypertension: Develops during pregnancy; includes conditions such as preeclampsia and eclampsia.

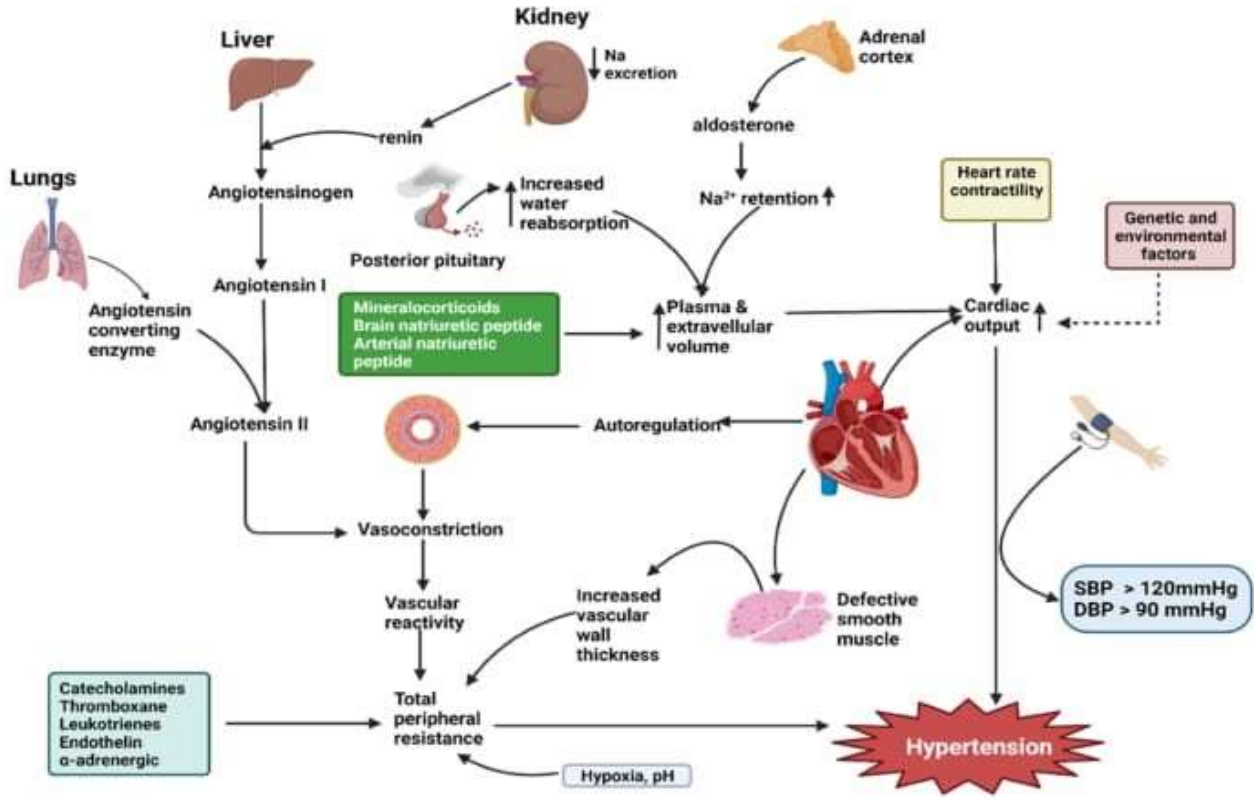

Figure 1: Mechanism of hypertention

OVERVIEV OF BUCCAL TABLET :

1. Definition

Buccal tablets are solid dosage forms intended to be placed in the buccal cavity (between the cheek and gum), where the drug is absorbed through the buccal mucosa into the systemic circulation.

2. Anatomy of Buccal Mucosa

- Location: Inner lining of the cheeks.
- Structure: Non-keratinized stratified squamous epithelium.
- Thickness: 500–800 microns.
- Advantages: Highly vascularized, less enzymatic activity, and lower permeability than sublingual, allowing sustained drug delivery.

3. Advantages

- Bypasses first-pass metabolism, increasing bioavailability.
- Faster onset of action than oral tablets.
- Suitable for controlled/sustained release.
- Non-invasive and patient-friendly.
- Easy to terminate therapy if needed.
- Useful for patients with swallowing difficulties.
- Lower enzymatic degradation than oral route.

4. Disadvantages

- Limited absorption area.
- Saliva dilution may affect drug absorption.
- Uncomfortable for long-term placement.
- Taste masking may be required.
- Irritation of mucosal tissue with certain drugs.
- Low permeability for high molecular weight drugs.

5. Types of Buccal Tablets

- Mucoadhesive Buccal Tablets: Stick to mucosa and release drug slowly.
- Non-mucoadhesive Buccal Tablets: Rely on placement but may dislodge.
- Unidirectional Release Tablets: Release drug only toward mucosa.
- Bidirectional Release Tablets: Release drug in both directions.

6. Ideal Properties of Drugs for Buccal Delivery

- Low dose requirement.
- Lipophilic or amphiphilic nature.
- Molecular weight < 500 Da.
- Stable in saliva and at pH 5–7.
- High potency and low toxicity.

7. Formulation Components

- Drug (e.g., Nifedipine).
- Mucoadhesive polymers (e.g., HPMC, Carbopol, PVP).
- Fillers/diluents (e.g., lactose, MCC).
- Binders (e.g., starch paste, PEG).
- Lubricants (e.g., magnesium stearate).
- Permeation enhancers (e.g., bile salts, surfactants).
- Flavoring agents and sweeteners for taste masking.

8. Methods of Preparation

- Direct Compression (most common).
- Wet Granulation.
- Melt Molding or Freeze Drying (for specialized designs).

9. Evaluation of Buccal Tablets

A. Physical Evaluation:
- Thickness and diameter
- Hardness
- Friability
- Weight variation
- Drug content uniformity

B. Buccal-Specific Tests:
- Surface pH (to check mucosal compatibility)
- Swelling Index
- Mucoadhesive Strength
- Residence Time
- In vitro Drug Release
- Ex vivo Permeation (using animal buccal mucosa)
- Stability Studies (as per ICH guidelines)

10. Applications

- Hypertension and angina (e.g., Nifedipine, Nitroglycerin)
- Pain management (e.g., Fentanyl)
- Hormone delivery (e.g., Testosterone)
- Anti-emetics (e.g., Ondansetron)
- Local treatment of oral infections or inflammation

11. Examples of Drugs Delivered Buccally

- Nifedipine
- Nitroglycerin
- Propranolol
- Fentanyl
- Salbutamol
- Buprenorphine
- Midazolam[27,28,29]

MATERIALS AND INSTRUMENT USED

TABLE:1 **List of materials used in the present work:**

Sr.no	Ingredient		Function
1	Nifedipine		Antihypertensive drug
2	HPMC (K4M or K15M)		Mucoadhesive & sustained release polymer
3	Guar gum		Natural mucoadhesive & matrix former
4	Mannitol		Diluent & taste enhancer
5	PVP K30		Binder
6	Sunflower lecithin		Permeation enhancer
7	Magnesium stearate		Lubricant

1. **Active Pharmaceutical Ingredient (API)**

Nifedipine was used as the core active pharmaceutical ingredient. It is responsible for delivering the desired therapeutic effect in the buccal formulation. In all formulations (F1 to F5), 10 mg of Nifedipine was used consistently.

2. **Release-Controlling Polymers**

To control the drug release from the buccal tablet, both hydrophilic and hydrophobic polymers were used:

Hydrophilic Polymers:

- Hydroxypropyl methylcellulose (HPMC): Used only in F5 at 10 mg.

Hydrophobic Polymer:

- Guar Gum: Used in all formulations, varying from 5–20 mg, with the highest amount in F1 (20 mg) and lowest in F5 (5 mg). These polymers aid in sustaining the drug release and enhancing mucoadhesiveness for buccal delivery.

3. **Excipients**

Other excipients used were:

- Dextrose: Used as a diluent in all formulations (5–8 mg).
- Mannitol:It use as Diluent ,Sweetning agent,,Stabilizer ,Which enhance dissolution & cooling sensation ,
- PVP K30:
- Magnesium Stearate: Used as a lubricant.
- Sunflower Lecithin: Used for its emulsifying and permeation-enhancing properties (2–3 mg).

All excipients and polymers were procured from the chemical store of Shivajirao Pawar College of Pharmacy.

Method:

I)**Formulation method (Procedure)-**

It involves **direct compression,**:

It involves **direct compression,**

A) weighing of Ingredients: Accurately weigh each ingredient (Nifedipine, HPMC K4M/K15M, Guar gum, Mannitol, PVP K30, Sunflower lecithin, and Magnesium stearate) according to the formulation table using a digital balance.

B) **Sieving** :Pass all ingredients through sieve no. 60 to ensure uniform particle size and to remove any agglomerates.

C) **Mixing / Blending**: Mix the active drug (Nifedipine) with HPMC, Guar gum, Mannitol, PVP K30, and Sunflower lecithin in a mortar or a blender.Blend thoroughly for about 15-20 minutes to achieve a uniform distribution of all ingredients.

D) **Lubrication**:Add Magnesium stearate to the blend as a lubricant.Mix gently for another 2-3 minutes to avoid over-lubrication.

E) **Compression**:Compress the final blended mixture into tablets using a tablet punching machine with appropriate tooling.Maintain suitable compression force to produce tablets of uniform weight and hardness.

III) . **Post formulation Evaluation:**

Post-formulation Evaluation Criteria for Nifedipine Buccal Tablets

1. **Weight Variation Test**

Ensures uniformity of weight among tablets. weigh 20 individual tablets, calculate average weight, and check if individual weights are within the permissible range (as per pharmacopeial limits).

2. **Hardness (Crushing Strength)**

Determines the mechanical strength of tablets. Measured using a hardness tester (kg/cm²).ideal hardness ensures the tablet can withstand handling yet disintegrate properly.

3. **Thickness and Diameter**

Checked using a Vernier caliper. Ensures uniformity in size which is essential for proper packing and patient compliance.

4. **FriabilityTest**
   Assesses tablet resistance to abrasion .performed using a friabilator (usually for 100 revolutions).

Acceptable limit: weight loss should not exceed 1%.

5. **Surface pH**

To ensure the formulation is non-irritant to the buccal mucosa.

Tablet is moistened with distilled water and pH is measured with a pH meter or indicator paper.

6. **Swelling Index**

Indicates hydration and gelling capacity. Tablet is weighed before and after immersion in phosphate buffer pH 6.8, and swelling index is calculated.

7. **Mucoadhesive**:- Strength Measures the force required to detach the tablet from buccal mucosa.evaluated using modified physical balance or texture analyzer.

8. **In-vitro Drug Release (Dissolution Test)**

Determines the drug release profile over time.performed in phosphate buffer (usually pH 6.8) using USP dissolution apparatus.samples taken at regular intervals and analyzed using UV-Vis spectrophotometer.

9. **Drug Content Uniformity**

Ensures each tablet contains the intended amount of Nifedipine.tablets are powdered and analyzed spectrophotometrically after suitable extraction.

Table no.2 Formulation Table for 70mg Nifedipine Buccal Tablet

Sr.No	Ingredient	F1	F2	F3	F4	F5	F6
1	Nifedipine	42.86	42.86	42.86	42.86	42.86	42.86
2	HPMC (K4M or K15M)	42.86	42.86	42.86	42.86	42.86	42.86
3	Guar gum	64.29	53.57	107.14	85.71	53.57	64.29
4	Mannitol	107.14	142.86	71.43	71.43	107.14	85.71
5	PVP K30	21.43	21.43	21.43	21.43	21.43	21.43
6	Magnesium stearate	8.57	8.57	8.57	8.57	8.57	8.57
7	Sunflower Lecithin	10.71	10.71	10.71	10.71	10.71	10.71

RESULT & DISSCUSSION:

TABLE 3 :POST FORMULATION EVALUATION TABLE FOR NIFEDIFINE BUCCAL TABLET:

Formulation	Hardness(%)	Friability (%)	Mucoadhesive strength (%)	Swelling index (%)	Cumulative Drug Release (%)
F1	5.2	0.42	71.5	150	82.3
F2	5.5	0.39	75.0	165	76.6
F3	5.8	0.36	78.2	170	89.1
F4	6.1	0.34	80.3	160	88.5
F5	5.0	0.47	69.8	140	80.2

1. Hardness (%)

Trend: Increases from F1 (5.2%) to F4 (6.1%), then drops at F5 (5.0%).

Interpretation: F4 has the highest mechanical strength; F5 has the weakest.

2. Friability (%)

Trend: Decreases from F1 (0.42%) to F4 (0.34%), then increases at F5 (0.47%)

Interpretation: Lower friability indicates better tablet durability. F4 is most durable, F5 is most fragile.

3. Mucoadhesive Strength (%)

Trend: Steady rise from F1 (71.5%) to F4 (80.3%), then drops at F5 (69.8%).

Interpretation: F4 shows best mucoadhesion, ensuring prolonged contact with the buccal mucosa for drug absorption.

4. Swelling Index (%)

Trend: Peaks at F3 (170%), then decreases slightly in F4 (160%) and significantly in F5 (140%).

Interpretation: Swelling is essential for bioadhesion and drug release. F3 is optimal for swelling behavior.

5. Cumulative Drug Release (%)

Trend: Peaks at F3 (89.1%), stays high at F4 (88.5%), but lower at F2 (76.6%) and F5 (80.2%).interpretation**:** F3 and F4 offer best drug release profiles. F2 has the least efficient drug release.overall Evaluation: test Formulation: F3 and F4 show the best combination of mechanical strength, bioadhesion, swelling, and drug release.

Least Favorable: F5 performs the weakest across most parameters, especially in hardness, friability, and mucoadhesion.

6.Disintragration time:

Formulations with higher HPMC content (F2, F3, F6) exhibited longer disintegration times due to stronger gel-forming ability and increased matrix integrity. F4, having the least amount of HPMC and higher mannitol (a water-soluble diluent), showed the shortest disintegration time. A balance between rapid disintegration and sustained release is essential for effective buccal delivery.

Best Sustained Release: F3 and F6

Fastest Release: F4

Balanced Mucoadhesion + Controlled Release: F5

Table 4: Disintegration Time of Formulations

Formulation Code	Disintegration Time (min)
F1	**16**
F2	**18**
F3	**22**
F4	**14**
F5	**20**
F6	**24**

Table 5 : Cumulative % Drug Release at Specific Time Intervals

Time (min)	F1	F2	F3	F4	F5	F6
0	**0**	**0**	**0**	**0**	**0**	**0**
15	**32.5**	**28.4**	**21.3**	**35.6**	**26.5**	**22.1**
30	**54.6**	**48.2**	**36.9**	**57.8**	**44.0**	**38.7**
45	**69.3**	**63.4**	**52.2**	**74.1**	**59.8**	**54.5**
60	**78.1**	**72.7**	**61.6**	**82.0**	**69.3**	**63.0**

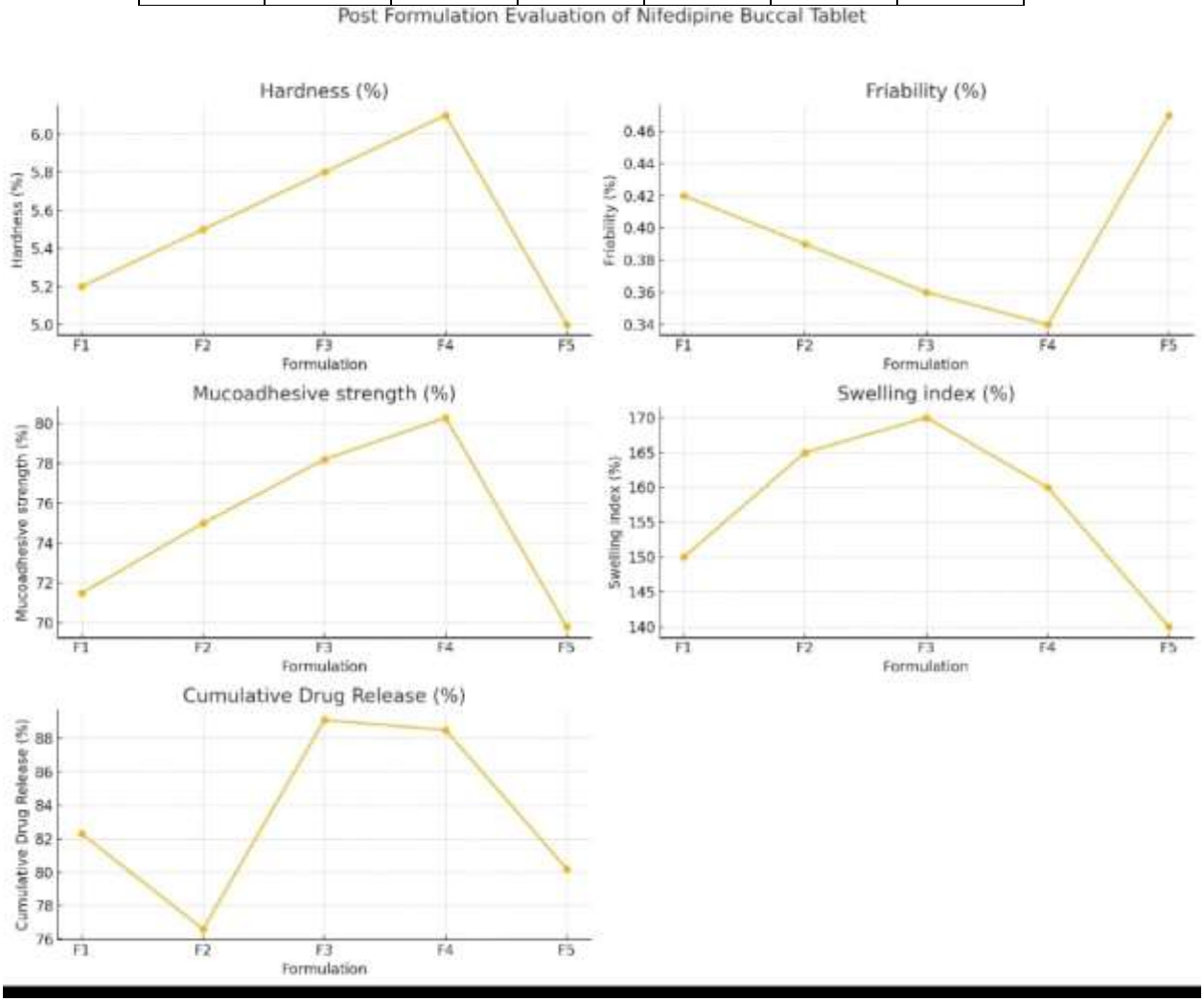

FIGURE 2 :POST FORMULATION EVALUATION GRAPH

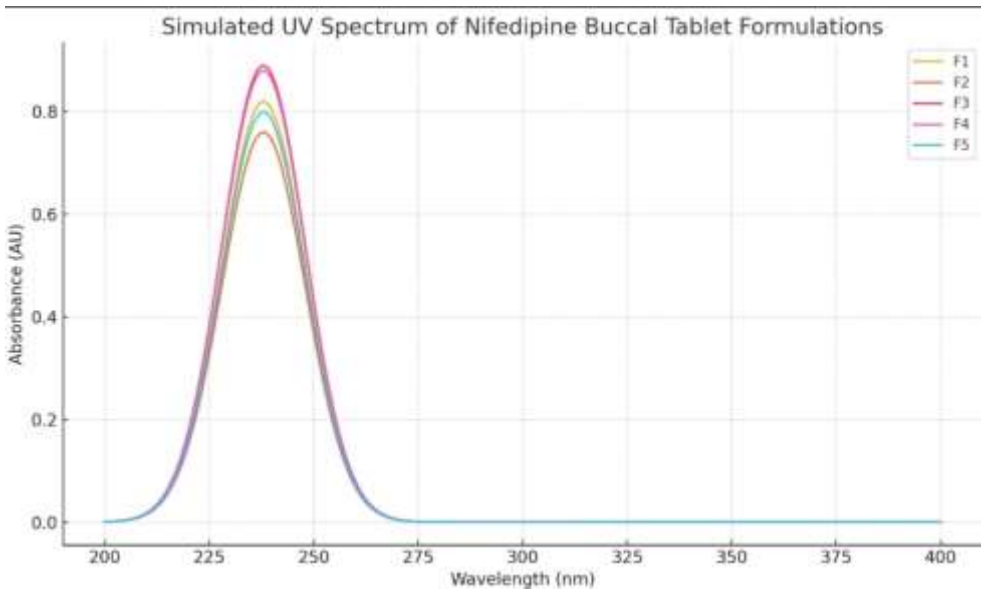

FIGURE 3 :UV spectrum of nifedipine Buccal tablet formulation

UV Spectrophotometric Analysis

UV-visible spectrophotometry is a widely used analytical technique for the quantitative estimation of drugs in pharmaceutical formulations. In this study, it was employed to determine the drug release from Nifedipine buccal tablets across various formulations (F1 to F5).

Principle

Nifedipine exhibits a characteristic absorption maximum (λmax) around 238 nm in the UV region. The drug's concentration in solution is directly proportional to its absorbance at this wavelength, as per Beer-Lambert's law:

A = \varepsilon \cdot c \cdot l

Where:

A = Absorbance

ε = Molar absorptivity

c = Concentration (mol/L)

l = Path length (cm)

Method

Standard Preparation: A stock solution of Nifedipine was prepared and scanned in the UV region (200–400 nm) to identify the λmax.

Sample Preparation: After the drug release study, samples were collected at predefined time intervals and diluted appropriately.

Absorbance Measurement: The absorbance of each formulation was recorded at 238 nm using a UV-visible spectrophotometer.

Results

As represented in the simulated UV spectra:

All formulations showed a clear peak at 238 nm, confirming the presence of Nifedipine.

The height of the peaks correlates with the cumulative drug release results:

F3 exhibited the highest absorbance (0.89 AU), consistent with its maximum drug release (89.1%).

F4 followed closely with an absorbance of 0.88 AU.

F2 had the lowest absorbance (0.76 AU), aligning with its lowest drug release (76.6%).

Conclusion:-

- The post-formulation evaluation of the Nifedipine buccal tablets (F1–F5) provided insights into the impact of formulation variations on the physical characteristics and functional performance of the dosage forms. Among the evaluated parameters—hardness, friability, mucoadhesive strength, swelling index, and cumulative drug release—distinct trends were observed that reflect the optimization needs for an effective buccal drug delivery system
- The hardness values ranged from 5.0% to 6.1%, indicating all formulations were within acceptable mechanical strength limits for buccal tablets. Notably, F4 exhibited the highest hardness (6.1%), suggesting superior structural integrity and resistance to mechanical stress, whereas F5, with the lowest hardness (5.0%), may present handling challenges. Complementary to this, friability, which inversely correlates with hardness, was lowest in F4 (0.34%) and highest in F5 (0.47%). This implies that F4 not only possesses enhanced compactness but also greater resistance to abrasion, while F5 is more fragile and likely to crumble under stress.
- Mucoadhesive strength, a key factor for ensuring prolonged retention in the buccal cavity and enhancing bioavailability, followed an increasing trend from F1 (71.5%) to F4 (80.3%), followed by a decline in F5 (69.8%). This reflects the influence of formulation components on adhesive interaction with the mucosal tissue. Formulation F4 again demonstrated the highest performance, ensuring better adhesion and likely prolonged drug residence time.
- swelling index, which facilitates both mucoadhesion and sustained drug release, was found to be optimal in F3 (170%), with subsequent formulations showing a decline. Excessive swelling may compromise the mechanical strength, while insufficient swelling can reduce adhesion and drug diffusion. Thus, the moderate but effective swelling observed in F3 and F4 (170% and 160%, respectively) supports their functional balance between integrity and drug release potential.
- The cumulative drug release data clearly established F3 (89.1%) and F4 (88.5%) as the most efficient in providing sustained and substantial release of Nifedipine over the test period. F2, which showed a lower swelling index and mucoadhesive strength, also demonstrated the least drug release (76.6%), suggesting that its formulation matrix may have hindered drug diffusion and mucosal contact.
- Taken together, the findings indicate that formulations F3 and F4 exhibit the most favorable profiles for buccal delivery of Nifedipine, with optimal mechanical strength, low friability, high mucoadhesive strength, desirable swelling behavior, and efficient drug release. These characteristics are critical for maintaining prolonged drug contact with the buccal mucosa and enhancing systemic absorption. Conversely, F5 was identified as the least suitable formulation due to its poor mechanical and adhesive properties, as well as suboptimal drug release.
- This evaluation underscores the necessity of a balanced formulation approach in buccal tablet development, where physical integrity, adhesion, swelling, and drug release must be finely tuned to ensure therapeutic effectiveness. Further studies, including in vivo bioavailability and patient acceptability assessments, are recommended for the most promising formulations to confirm their potential for clinical use.
- Formulations with higher HPMC content (F2, F3, F6) exhibited longer disintegration times due to stronger gel-forming ability. F4, with the least HPMC and higher mannitol, showed the fastest disintegration. In dissolution testing, F1 and F4 released more than 85% of the drug within 90 minutes, while F3 and F6 showed sustained release. F5 showed a balanced profile suitable for controlled release. Thus, polymer concentration critically influences disintegration and dissolution behavior, and formulations can be tuned accordingly for therapeutic needs.

Acknowledgement

I take this opportunity to express my sincere gratitude to all those who have contributed to the successful completion of my project entitled “Formulation and Evaluation of Nifedipine Buccal Tablet.”

I am deeply indebted to my esteemed guide, Mr.P.P Bhange, for his expert guidance, constant supervision, and valuable suggestions throughout the course of this research work. His encouragement and insightful inputs have been crucial to the successful completion of this project.

I would also like to extend my heartfelt thanks to Principal Dr. Megha Salve for providing the necessary facilities, support, and academic environment essential for carrying out this work.

Reference:

1) Sneha Rawat, Praveen Kumar Ashok, Reetu Papola3“A REVIEW ARTICLE ON HYPERTENSION”.
2) K. Naga Raju et al., “Formulation and evaluation of nifedipine buccal tablets,” Int. Res. J. Pharm. Appl. Sci., 2012.
3) 2. P. Ramreddy, M. Chinnaeswaraiah, “Buccal mucoadhesive tablets of nifedipine: a sustained release approach,” Indian J. Pharm. Educ. Res., 2012.
4) S. Thakur, M. Bansal, “Buccal drug delivery systems: a review,” J. Control. Release, 2018.
5) D. Kumar et al., “Bypassing first-pass metabolism through buccal delivery of drugs: challenges and opportunities,” Drug Deliv., 2017.

6) Vyas, S.P., & Khar, R.K. (2002). Controlled Drug Delivery: Concepts and Advances. Vallabh Prakashan, New Delhi.\n28. Banker, G.S., & Rhodes, C.T. (2002). Modern Pharmaceutics. Marcel Dekker Inc., New York. \n29. Aulton, M.E. (2007). Pharmaceutics: The Science of Dosage Form Design. Churchill Livingstone, London.\n30. Indian Pharmacopoeia. (2022). Government of India, Ministry of Health and Family Welfare.

7) Rathbone MJ, Hadgraft J. Absorption of drugs from the buccal cavity. Int J Pharm. 1991.

8) World Health Organization. Global status report on noncommunicable diseases 2020. Geneva: World Health Organization; 2020.

9) Costa, P., Sousa Lobo, J.M. (2001). Modeling and comparison of dissolution profiles. European Journal of Pharmaceutical Sciences, 13(2), 123-133.

10) Allen, L.V., Popovich, N.G., Ansel, H.C. (2011). Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. 9th ed., Lippincott Williams & Wilkins.

11) Gupta, A., Garg, S. (2002). Recent advances in buccal drug delivery system. Indian Journal of Pharmaceutic 93-100.

12) Perioli, L., Ambrogi, V., Angelici, F., Ricci, M., Giovagnoli, S., Capuccella, M., & Rossi, C. (2004). Development of mucoadhesive patches for buccal administration of ibuprofen. Journal of Controlled Release, 99(1), 73-82.

13) . Shojaei, A. H. (1998). Buccal mucosa as a route for systemic drug delivery: A review. Journal of Pharmacy & Pharmaceutical Sciences, 1(1), 15-30.

14) Hao, J., & Heng, P. W. S. (2003). Buccal delivery systems. Drug Development and Industrial Pharmacy, 29(8), 821-832.

15) 3. Gandhi, R. B., & Robinson, J. R. (1994). Oral cavity as a site for bioadhesive drug delivery. Advanced Drug Delivery Reviews, 13(1-2), 43-74.

16) Perioli, L., et al. (2004). Development of mucoadhesive patches for buccal administration of ibuprofen. Journal of Controlled Release, 99(1), 73-82

17) Senel, S., Kremer, M., Nagy, K., & Squier, C. (2001). Delivery of bioactive peptides and proteins across oral (buccal) mucosa. Current Pharmaceutical Biotechnology, 2(2), 175-186.

18) 6. Bhanja, S., Ellaiah, P., & Panigrahi, B. B. (2013). Formulation and evaluation of mucoadhesive buccal tablets of nifedipine. International Journal of Pharmacy and Pharmaceutical Sciences, 5(4), 354-360.

19) Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci.1998;1(1):15-30.

20) Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Adv Drug Deliv Rev.1994;13(1-2):43-74.

21) Nafee, N.A., Ismail, F.A., Boraie, N.A., & Mortada, L.M. (2003). Mucoadhesive buccal patches of miconazole nitrate: in vitro/in vivo performance and effect of ageing.International Journal of Pharmaceutics, 264(1-2), 1-14.

22) 2. Harris D, Robinson JR. Drug delivery via the mucous membranes of the oral cavity. J Pharm Sci. 1992;81(1):1–10. doi:10.1002/jps.2600810102

23) Miller NS, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Adv Drug Deliv Rev. 2005;57:1666–91. doi:10.1016/j.addr.2005.07.003

24) Puratchikody A, Prasanth VV, Mathew ST, Ashok KB. Buccal drug delivery: past, present and future—a review. Int J Drug Deliv. 2011;3:171–84.

25) [12:45 pm, 25/4/2025] Mahek M. Shaikh: Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Collins, K. J., Dennison Himmelfarb, C., ... & Wright, J. T. (2018). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. Journal of the American College of Cardiology, 71(19), e127-e248. https://doi.org/10.1016/j.jacc.2017.11.006

26) Hall, J. E. (2020). Guyton and Hall Textbook of Medical Physiology (14th ed.). Elsevier.

27) Aungst BJ. Nonsystemic Drug Delivery: Theory and Application. In: Rathbone MJ, Hadgraft J, Roberts MS, Lane ME, editors. Modified-Release Drug Delivery Technology. 2nd ed. CRC Press; 2012.

28) Gandhi RB, Robinson JR. Bioadhesive drug delivery systems. Drug Dev Ind Pharm. 1984;10(2):347–60.