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Formulation And Evaluation Of Buccal Films For Controlled Delivery Of Enalapril Maleate: Enhancing Bioavailability And Patient Compliance

Dilip Kumar[1], Prof. (Dr.) Sunder Singh[2]
Oriental University, Indore, Madhya Pradesh India(453555)
Oriental University, Indore, Madhya Pradesh India(453555)

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ABSTRACT
The aim of this study was to develop and evaluate buccal films for the controlled delivery of Enalapril Maleate, a widely used antihypertensive drug, with the goal of improving its bioavailability and patient compliance. Enalapril Maleate, due to its first-pass metabolism and low bioavailability when administered orally, has prompted the exploration of alternative drug delivery systems. Buccal films offer several advantages, such as bypassing the gastrointestinal tract and hepatic metabolism, leading to enhanced drug absorption directly through the buccal mucosa. The study involved the formulation of several buccal films using different polymeric compositions and plasticizers, with an emphasis on optimizing parameters such as bioadhesive strength, swelling index, thickness, density, and folding endurance. The results showed that the optimal formulation, BF-3, demonstrated the best balance of physical properties, including high bioadhesive strength (11.90 mg), moderate swelling index (2.150 ± 0.08), and adequate folding endurance (414). BF-3 was also found to have the highest drug release rate, making it the most effective formulation for controlled drug delivery. In contrast, formulations such as BF-8 exhibited excessive swelling, which could compromise film integrity and patient comfort. The findings suggest that buccal films, particularly BF-3, provide a promising delivery system for Enalapril Maleate, offering advantages in terms of enhanced bioavailability, ease of application, and patient adherence. Further studies on long-term stability and clinical evaluation are recommended to validate the potential of buccal films in the therapeutic management of hypertension.

INTRODUCTION:

Enalapril Maleate is an angiotensin-converting enzyme (ACE) inhibitor commonly used in the management of hypertension, heart failure, and chronic kidney disease. As a widely prescribed medication, its pharmacokinetic and pharmacodynamic properties are critical for ensuring its efficacy and patient adherence. The oral bioavailability of Enalapril Maleate is often compromised due to its limited solubility and absorption variability in the gastrointestinal tract[1,2]. To address these challenges and improve therapeutic outcomes, alternative drug delivery systems, such as buccal films, have gained significant attention in recent years[3].

Buccal drug delivery offers several advantages over conventional oral dosage forms, including bypassing the first-pass metabolism in the liver, providing rapid onset of action, and offering a more patient-friendly route of administration[4]. Buccal films are thin, flexible films that adhere to the mucosal surface of the buccal cavity and allow for controlled, sustained drug release, making them an ideal formulation for Enalapril Maleate[5]. The formulation and optimization of these films involve considering factors such as drug solubility, bioadhesive strength, mechanical properties, swelling index, and stability[6].

This study focuses on the preparation, characterization, and optimization of buccal films containing Enalapril Maleate. The key physical properties, including thickness, density, folding endurance, and swelling index, were evaluated to assess their influence on the film's performance. Additionally, the bioadhesive strength and content uniformity were assessed to ensure effective and consistent drug delivery. The findings aim to provide insights into the design of an efficient buccal film formulation for Enalapril Maleate that could enhance patient compliance and therapeutic efficacy.

The buccal drug delivery system has gained widespread attention for its ability to provide rapid absorption and improved bioavailability compared to conventional oral formulations[7]. Buccal films, in particular, have emerged as an effective alternative for drug delivery, offering controlled release, localized action, and avoidance of first-pass metabolism[8]. These films, which adhere to the buccal mucosa, allow for the sustained release of active pharmaceutical ingredients (APIs), making them ideal for drugs like Enalapril Maleate, an ACE inhibitor commonly used to treat hypertension[9].

Enalapril Maleate, a highly soluble antihypertensive drug, has traditionally been administered orally. However, due to its first-pass metabolism and low bioavailability, researchers have been exploring alternative drug delivery systems to improve its therapeutic efficacy[10]. Buccal films, which allow for the direct absorption of drugs into the bloodstream through the buccal mucosa, provide an opportunity to bypass first-pass metabolism and increase bioavailability[11]. Additionally, buccal films are easy to apply, offer precise dosing, and are associated with improved patient compliance due to their non-invasive nature[12].

The formulation of buccal films involves a variety of critical parameters, including thickness, swelling index, bioadhesive strength, and folding endurance, all of which impact the drug release rate and the film's adhesion properties[13]. A study by Patel et al. (2019) highlighted the importance of bioadhesive strength in ensuring the sustained attachment of the film to the buccal mucosa, which is essential for achieving a controlled release profile. Swelling behavior also plays a crucial role in regulating the drug release from the film, as the interaction between the film and saliva influences the rate of hydration and expansion[14].

Further research has also investigated the use of various excipients and polymers such as hydroxypropyl methylcellulose (HPMC), carbopol, and polyvinyl alcohol (PVA) to optimize the mechanical properties and stability of buccal films[15,16]. These polymers not only improve the mechanical strength but also contribute to the controlled drug release, flexibility, and comfort of the buccal film [16]. Moreover, studies on the effect of plasticizers, such as glycerin, have also been reported to improve the film's flexibility and prevent cracking or breaking during use[17,18].

In summary, the formulation of buccal films for drug delivery, particularly for Enalapril Maleate, offers promising advantages, such as enhanced bioavailability, improved patient compliance, and reduced first-pass metabolism. The optimization of physical parameters, such as bioadhesion, swelling index, and mechanical properties, is crucial in developing an effective and reliable buccal drug delivery system.

MATERIAL & METHODS:

The study utilized various analytical grade chemicals, drugs, and reagents, including Enalapril Maleate, Methanol, Ethanol, Sodium Chloride, Phosphate Buffer Saline (PBS, pH 7.4), Distilled Water, Ferric Chloride Solution, Sulphate, Hydrochloric Acid, Sulphuric Acid, Sodium Hydroxide, Chloroform, Dichloromethane, Polyvinyl Alcohol (PVA) Solution, and Sodium Bicarbonate. All materials were of analytical grade and used as received without further purification.

Pre formulation study of Enalapril Maleate:

Physical appearance:

The physical appearance of Enalapril Maleate was evaluated using organoleptic methods—colour, odour, and taste—and compared with standard reference parameters[19,20].

Identification of drug Enalapril Maleate:

Melting point method:

Enalapril Maleate was identified by its melting point (143–144°C) using a calibrated apparatus. The finely ground sample was heated gradually, and the melting range was recorded and compared to standard values. Safety protocols and PPE were followed throughout[19,21].

Solubility:

The solubility of Enalapril Maleate was tested in various solvents (water, ethanol, methanol, chloroform, acetone, and pH-adjusted buffers). A 10 mg sample was added to 10 mL of each solvent and shaken for 15–30 minutes at room temperature. Solubility was assessed visually, with filtration used if undissolved particles remained. pH-dependent solubility was evaluated using buffered solutions.

Loss on Drying:
Loss on drying (LOD) of Enalapril Maleate was determined by drying 1–2 g of sample at 105°C for 3 hours in a pre-weighed dish. After cooling in a desiccator, the final weight was recorded. LOD was calculated as the percentage weight loss, indicating moisture and volatile content. All procedures followed standard safety protocols[22].

"Loss on Drying = [(Initial weight of material – final weight of material) / Initial weight of material] X 100**"**

Determination of flow properties of pure drug
Bulk density:
Bulk density of Enalapril Maleate was determined by gently filling a dry graduated cylinder with the dry sample, without tapping. The sample mass was calculated by subtracting the empty cylinder weight from the filled weight. Bulk density was then calculated as mass divided by volume. All steps were performed using clean equipment and appropriate PPE [23].

Bulk density = Mass of powder/volume of powder

Tapped density:
Tapped density of Enalapril Maleate was determined by filling a dry graduated cylinder with the sample and tapping it using a standard tapping apparatus (100–500 taps). The final volume was recorded, and tapped density calculated as mass divided by tapped volume. Clean equipment and PPE were used throughout to ensure accuracy and safety.

Tapped density = Mass of powder/Tapped volume

Compressibility index and Hausner ratio:
The bulk density of Enalapril Maleate was determined by weighing a clean, dry graduated cylinder (V1) and recording its weight. The cylinder was then filled with the sample, without compacting, until it reached the specified volume mark. The weight of the cylinder with the sample (V1 + M1) was recorded. For the tapped density, the same procedure was followed, but the cylinder containing the sample was tapped using a tapping apparatus for 100–500 taps. The weight of the cylinder with the tapped sample (V2 + M2) was then recorded [24]. Calculate the compressibility index using the formula:

Carr's index = TD-BD/TD×100
Where,
TD=Tapped density
BD=Bulk density
Hausner ratio = TD/BD
Hausner ratio, <=1.25(good flow)

Angle of repose:
The angle of repose of Enalapril Maleate was determined by sieving the sample to ensure it was dry and free-flowing. The sample was poured gently through a funnel onto a flat surface, forming a cone-shaped pile. The height (h) and radius (r) of the pile were measured. The angle of repose (θ) was calculated as the arctangent of the height-to-radius ratio. A lower angle indicates better flow properties, while a higher angle suggests poorer flow. All measurements were recorded, and safety protocols, including PPE, were followed.

$$\tan \theta = h/r$$
$$\theta = \tan\text{-}1h/r$$

Where,
H = height of pile (cm)
r = radius of pile (cm)

Preparation of Buccal Film for Enalapril Maleate:
The polymeric solution for the buccal film is prepared by accurately weighing the polymer, dissolving it in an appropriate solvent (e.g., ethanol or water-ethanol mix), and stirring for 10 minutes. The weighed Enalapril Maleate is then added to the solution and thoroughly mixed to ensure uniform distribution. A plasticizer (e.g., glycerol) is incorporated to adjust the film's flexibility, and the mixture is stirred to ensure even dispersion. The solution is poured into a clean 6 cm Petri dish, tilted for even spreading, and placed on a level surface. A funnel is placed inverted over the dish to allow controlled solvent evaporation, which takes several hours to overnight. Once the solvent has evaporated, the flexible film is carefully peeled from the dish. The film is stored in a desiccator or airtight container to protect it from moisture.

Table 1: Composition Of Different Buccal Film Containing

Formulation Code (BUCCAL FILM-BF)	HPMC (mg)	Ethanol (ml)	Chitosan (mg)	Glycerine (ml)	Propylene glycol (ml)	Drug (mg)
BF -1	30	20	40	10	8	25
BF -2	35	20	60	15	10	25
BF -3	40	20	50	10	8	25
BF -4	45	20	40	15	10	25
BF -5	50	20	60	10	8	25
BF -6	55	20	50	15	10	25
BF -7	60	20	40	10	8	25
BF -8	30	20	60	15	10	25
BF -9	35	20	50	10	8	25

BF-10	40	20	40	15	10	25

Preparation of Backing Membrane:
The backing membrane is prepared by dissolving 200 mg of ethyl cellulose in 10 ml of absolute ethanol, stirring until a homogeneous solution forms. 1 ml of glycerin is then added and mixed to ensure even distribution. The solution is left undisturbed for about an hour to remove any air bubbles. It is then poured into a clean Petri dish and placed on a level surface to dry overnight, allowing complete solvent evaporation. The dried film is carefully peeled from the Petri dish, ensuring it is uniform and free from defects.

Assembly of Buccal film:
The drug-loaded buccal film is prepared using the solvent casting method, ensuring uniform thickness and homogeneity. The backing membrane is cut into slightly larger sections (e.g., 2.5x2.5 cm^2), and the drug-loaded film is carefully placed on its center. Gentle pressure is applied to ensure proper adhesion and eliminate air bubbles. The combined film is then cut into 2x2 cm^2 squares using a sharp blade or scissors. The assembled films are stored in a cool, dry, moisture-proof container to maintain stability until use.

Evaluation of Buccal Film:
Weight variation test:
The weight variation test ensures uniformity in buccal film dosage, crucial for consistent Enalapril Maleate delivery. A sample of 10 films is weighed using an analytical balance. The mean weight is calculated, and deviations from the mean are determined as a percentage. According to pharmacopeial or internal standards, the films pass if no more than two films deviate by more than ±5%, and none deviate by more than ±10%. This test ensures uniform weight, indicating consistent distribution of the active ingredient, and contributes to the film's therapeutic efficacy and safety.

Thickness test:
The thickness test ensures uniformity in buccal film dimensions, which affects drug release, adhesion, and patient comfort. A sample of 10 films is selected, and thickness is measured at multiple points using a calibrated digital micrometer. The average thickness and standard deviation are calculated to assess uniformity. The films should typically have a thickness within ±10% of the mean. Consistent thickness ensures reliable drug release, proper adhesion to the buccal mucosa, and optimal patient comfort. This test is crucial for confirming the quality, safety, and performance of the buccal films.

Folding Endurance:
The folding endurance test evaluates the flexibility and durability of buccal films by measuring their ability to withstand repeated folding at the same location without breaking or cracking. A sample of 10 films is tested, with each patch folded until failure, and the number of folds before damage is recorded. The average folding endurance is calculated. This test ensures the films' durability, preventing breakage during handling or use in the oral cavity. High folding endurance enhances drug delivery, patient comfort, and compliance, ensuring the film remains intact and adheres well for consistent therapeutic effects.

Content uniformity:
To perform potentiometric titration for Enalapril Maleate quantification, prepare accurate solutions of Enalapril Maleate and a standardized NaOH solution. Calibrate the pH meter with standard buffers. Set up the titration apparatus with a magnetic stirrer, burette, and pH electrode. Add NaOH to the Enalapril Maleate solution while monitoring pH. The pH will rise as NaOH neutralizes the acid, and the endpoint is reached when a significant, sustained pH increase occurs. Record the NaOH volume at the endpoint and calculate the Enalapril Maleate concentration based on the NaOH volume and concentration. Validate the method with replicate titrations and standard reference materials.

Density of the film:
Use a calibrated micrometer or digital caliper to measure the length, width, and thickness of the film at multiple locations to account for variations. Record the measurements accurately.

Calculation of Cross-sectional Area: Calculate the cross-sectional area (A) of the film using the formula:
$A=L\times W$
This represents the area of one face of the film and will be used to calculate the volume in the subsequent steps.
Measurement of Film Mass Weigh the film using an analytical balance to determine its mass (M). Ensure that the balance is properly calibrated before use and handle the film carefully to avoid any loss or contamination. Record the mass accurately.

Calculation of Film Volume Calculate the volume (V) of the film using the formula: $V=A\times T$. This calculation combines the cross-sectional area (A) with the thickness (T) of the film to determine the total volume occupied by the film.

Calculation of Film Density: Calculate the density (ρ) of the film using the formula:

$\rho = MV$

This calculation yields the mass per unit volume of the film, representing its density. Ensure that units are consistent throughout the calculation.

Determination of % yield

To determine the percentage yield of Enalapril Maleate, first calculate the theoretical yield based on stoichiometry and the limiting reagent. Then, measure the actual yield after synthesizing and purifying the product. The percentage yield is calculated by comparing the actual yield to the theoretical yield. A higher percentage yield indicates a more efficient process, while lower yields may suggest inefficiencies or losses. Document all relevant data, and perform multiple trials for reproducibility. Safety protocols should be followed to ensure a safe working environment. This procedure provides insights into the efficiency of the production process.

Surface pH study

To measure the pH of Enalapril Maleate, first prepare a series of freshly standardized buffer solutions, such as phosphate, citrate, or acetate, covering a range of pH values. Next, prepare the Enalapril Maleate sample in the desired form (powder, solution, or solid), ensuring the surface is accessible for measurement. Calibrate the pH meter using standard buffer solutions, following the manufacturer's instructions for accuracy. Place the sample on a clean surface, immerse the pH electrode in the buffer solution, and gently touch the electrode to the sample. Allow the reading to stabilize, then record the pH value. For accuracy, repeat the measurement at multiple locations on the sample's surface to account for any variations.

Swelling study

To conduct a swelling study of Enalapril Maleate, prepare the samples (tablets, capsules) and accurately weigh and label them. Select an appropriate swelling medium (e.g., SGF, SIF, PBS) and prepare it according to standards. Place the samples in transparent containers with the medium and record their initial dimensions and weight. Immerse the samples under controlled conditions, periodically measuring their dimensions and weight at set intervals. Calculate the swelling ratio using the formula:

Swelling Ratio (%) = [(Swollen Dimensions - Initial Dimensions) × 100%]

Measurement of bioadhesive strength

To determine the bioadhesive strength of Enalapril Maleate, the sample (e.g., tablet or film) is prepared and placed onto a suitable substrate, such as mucin or tissue-mimicking materials. A texture analyzer or universal testing machine is used to apply controlled force perpendicular to the substrate, mimicking physiological conditions. The maximum force required to detach the sample from the substrate is measured, reflecting its bioadhesive strength. This strength is calculated by dividing the maximum force by the contact area between the sample and the substrate. Multiple measurements are taken to ensure reproducibility, and the average bioadhesive strength is calculated. This test helps evaluate how well the medication adheres to biological surfaces, influencing drug delivery and therapeutic effectiveness.

RESULT & DISCUSSIONS:

Preformulation studies:

Enalapril Maleate was received for the preformulation studies.

Organoleptic properties:

Enalapril Maleate is a white to off-white crystalline powder with no odor. It has a fine, slightly gritty texture and a mildly bitter taste, common to many pharmaceutical compounds..

Table 2: The organoleptic properties of Enalapril Maleate

S.No	Properties	Outcome
1.	Colour	White to off-white
2.	Shape	Crystalline powder
3.	Odour	Odourless
4.	Texture	Fine, slightly gritty powder
5.	Taste	Slightly bitter

Identification of Enalapril Maleate:

Melting point

Enalapril Maleate has a melting point between 143°C and 144°C, which serves as an important indicator of its purity and thermal stability.

Table 3: Melting point of Enalapril Maleate

Crude drug	Melting point
Enalapril Maleate	Within the range of 143°C to 144°C

Solubility of Enalapril Maleate

Enalapril Maleate shows varying solubility across different solvents. It dissolves well in ethanol, methanol, and chloroform, forming clear, colorless solutions. In water, it is slightly soluble, resulting in a cloudy or translucent solution. It is moderately soluble in acetone, producing a clear solution, but is insoluble in petroleum ether, leaving undissolved particles. These solubility properties are essential for its use in pharmaceutical formulations.

Table 4: Solubility of Enalapril Maleate in different solvents

S. No	Parameters (% w/w)	Solubility	Color Obtained
1.	Ethanol	Soluble	Clear, colorless solution
2.	Pet. Ether	Insoluble	Clear with undissolved particles

3.	Water	Slightly soluble	Slightly cloudy or translucent
4.	Methanol	Soluble	Clear, colorless solution
5.	Acetone	Moderately soluble	Clear, colorless solution
6.	Chloroform	Soluble	Clear, colorless solution

Loss on drying of Enalapril Maleate

The loss on drying for Enalapril Maleate is 7.86% w/w. This data indicates that when the substance is subjected to drying, it loses 7.86% of its weight, primarily due to moisture and volatile components.

Table 5: Loss on drying

Crude drug	Loss on drying (% w/w)*
Enalapril Maleate	7.86

Determination of flow properties of pure drug

Bulk density and tapped density

The determination of flow properties for the pure drug reveals that it has a bulk density of 0.87 g/cm³ and a tapped density of 0.97 g/cm³. These values are crucial for assessing the drug's flowability and compaction properties, which are important factors in the formulation and manufacturing processes of pharmaceutical products.

Table 6: Determination of compaction properties of pure drug

Parameters	Values
Bulk density	0.87
Tapped density	0.97

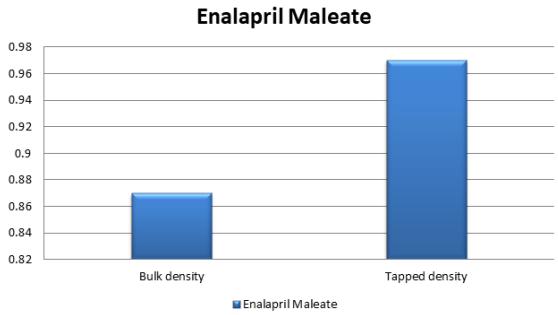

Figure 1: Graph of flow properties of Enalapril Maleate

Compressibility index, hausner ration and angle of repose

Enalapril Maleate powder has moderate compressibility (CI of 10.31%), good flowability (HR of 1.11), and excellent flow properties (Angle of Repose of 26.56°). These characteristics ensure efficient processing and consistent product quality during manufacturing.

Table 7: Determination of flow properties of pure drug

Parameters	Values
Compressibility index (%)	10.31%
Hausner ratio	1.11
Angle of repose	26.56%

Enalapril Maleate standard curve

The standard curve for Enalapril Maleate was constructed using a phosphate buffer at pH 7.2, with absorbance measured at 206 nm. The regression line showed a slope of 0.0468, indicating a direct relationship between concentration and absorbance. The R^2 value was 0.9998, demonstrating a near-perfect linear correlation, confirming the method adheres to Beer's Lambert's law. The method is highly reliable for quantifying Enalapril Maleate in the concentration range of 2-20 µg/ml.

Table 8: Standard Curve for Enalapril Maleate in Phosphate Buffer pH 7.2

Concentration (µg/mL)	Absorbance at 206 nm
0	0.000
2	0.105
4	0.205
6	0.295
8	0.385
10	0.475
12	0.565
14	0.660
16	0.750
18	0.850
20	0.955

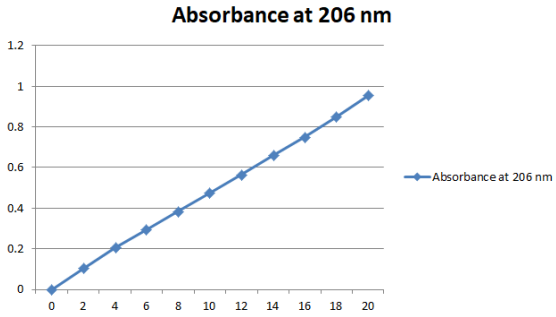

Fig 2: Plot visually represents the linear relationship between concentration and absorbance

FTIR compatibility Analysis:

The FT-IR spectrum of Enalapril Maleate reveals key functional groups in its molecular structure. The peak at 3026.00 cm^{-1} indicates aromatic C-H stretching, confirming aromatic rings. A peak at 1596.50 cm^{-1} corresponds to C-C stretching in the benzene ring. Carbonyl groups are identified by peaks at 1598.00 cm^{-1} and 1728.50 cm^{-1}, while the hydroxyl group is indicated by a peak at 1360.50 cm^{-1}. Tertiary aromatic nitrogen is suggested by peaks at 1360.00 cm^{-1} and 1300.00 cm^{-1}, and secondary aliphatic amine functionality is confirmed by peaks at 1268.00 cm^{-1} and 1360.00 cm^{-1}. These peaks collectively describe the chemical composition of Enalapril Maleate.

Table 9: Functional groups based on their characteristic peak positions

S. No	Functional Group	Peak (cm^{-1})	Description
1	Aromatic C-H Stretching	3026.00	Indicates the presence of aromatic C-H bonds.
2	Benzene Ring	1596.50	Corresponds to C-C stretching vibrations in the benzene ring.
3	Carbonyl Group	1598.00, 1728.50	Shows stretching vibrations of the carbonyl group (C=O).
4	-OH Group	1360.50	Associated with bending vibrations of the -OH group.
5	Tertiary Aromatic Nitrogen	1360.00, 1300.00	Indicates the presence of tertiary aromatic nitrogen (N-H bending or C-N stretching).
6	Secondary Aliphatic Amine	1268.00, 1360.00	Corresponds to C-N stretching and N-H bending vibrations of a secondary aliphatic amine.

EVALUATION TESTS FOR BUCCAL FILM:

Physical Characteristic Studies:

The physical parameters of the buccal films were evaluated, focusing on weight variation and bioadhesive strength. Weight variation ranged from 161 mg to 166 mg, with most formulations (BF-1, BF-3, BF-6, BF-8, and BF-9) around 164 mg. BF-9 and BF-10 had slightly higher weights, while BF-4 had the lowest at 161 mg. Bioadhesive strength varied from 11.02 mg to 12.62 mg, with BF-4 showing the highest value at 12.62 mg, followed by BF-10 and BF-6. The lowest bioadhesive strength was observed in BF-7 (11.02 mg). Overall, BF-4 exhibited the best performance due to its highest bioadhesive strength, making it ideal for sustained attachment to the buccal mucosa. Despite a lower weight variation, BF-3 showed promising bioadhesive strength, making it a strong candidate for effective drug delivery.

Table 10: Physical Parameters of Buccal Film (Weight Variation & Bioadhesive Strength)

Formulations (Buccal Film - BF)	Weight Variation (mg)	Bioadhesive Strength (mg)
BF -1	164 ± 0.02	11.57 ± 1.11
BF -2	162 ± 0.03	11.07 ± 1.12
BF -3	164 ± 0.02	11.90 ± 1.15
BF -4	161 ± 0.02	12.62 ± 1.04
BF -5	163 ± 0.03	12.22 ± 1.08
BF -6	164 ± 0.02	12.25 ± 1.10
BF -7	163 ± 0.04	11.02 ± 1.24
BF -8	164 ± 0.03	12.10 ± 1.49
BF -9	165 ± 0.01	11.20 ± 1.03
BF -10	166 ± 0.02	12.30 ± 1.14

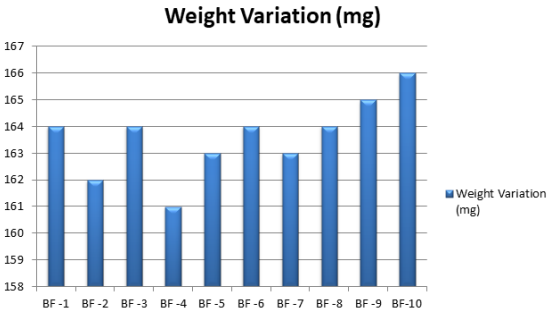

Figure 3: Evaluation of different formulations for Weight Variation

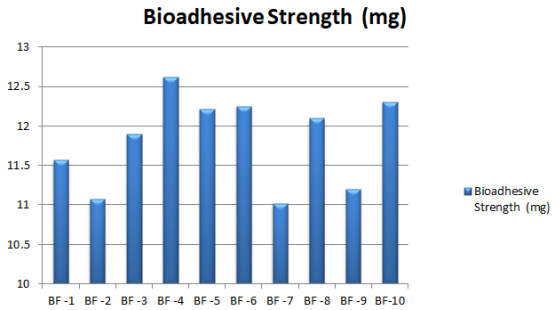

Figure 4: Evaluation of different formulations for Bioadhesive Strength (mg)

Physical characteristic studies:

The physical parameters of the buccal films highlight differences in content uniformity and yield. BF-5 offers the highest content uniformity at 95.3 ± 0.19%, but with the lowest yield at 88 ± 1.2%, indicating a trade-off between uniformity and production efficiency. BF-2 provides a balanced profile with good content uniformity (92.6 ± 0.16%) and the highest yield (97 ± 1.5%), making it the most consistent formulation. BF-3, with the lowest content uniformity (89.4 ± 0.15%), compensates with a high yield of 97 ± 1.3%, making it suitable for high-output scenarios. BF-4 strikes a middle ground with moderate content uniformity (92.1 ± 0.17%) and yield (93 ± 1.4%). In conclusion, while BF-5 excels in content uniformity, its low yield may limit its large-scale feasibility. BF-2 stands out as the most well-rounded formulation, offering a good balance of content uniformity and high yield, making it the most suitable for further development and commercialization.

Table 11: Physical Parameters of Buccal Film(Content Uniformity & %yield)

Formulations (BUCCAL FILM -BF)	Content Uniformity (%)	Yield (%)
BF -1	**93.8 ± 0.14**	**95 ± 1.3**
BF -2	**92.6 ± 0.16**	**97 ± 1.5**
BF -3	**89.4 ± 0.15**	**97 ± 1.3**
BF -4	**92.1 ± 0.17**	**93 ± 1.4**
BF -5	**95.3 ± 0.19**	**88 ± 1.2**
BF -6	**87.8 ± 0.18**	**91 ± 1.2**
BF -7	**90.7 ± 0.18**	**93 ± 1.3**
BF -8	**90.1 ± 0.13**	**92 ± 1.3**
BF -9	**93.4 ± 0.18**	**91 ± 1.3**
BF-10	**89.2 ± 0.19**	**92 ± 1.4**

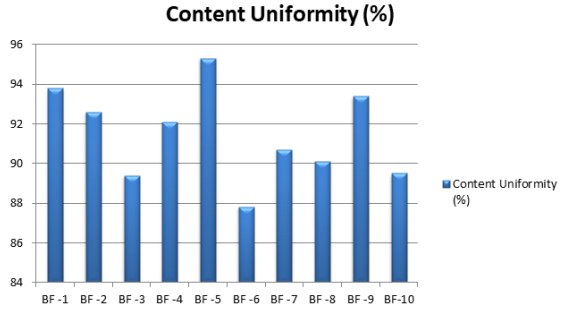

Figure 5: Evaluation of different formulations for Content Uniformity (%)

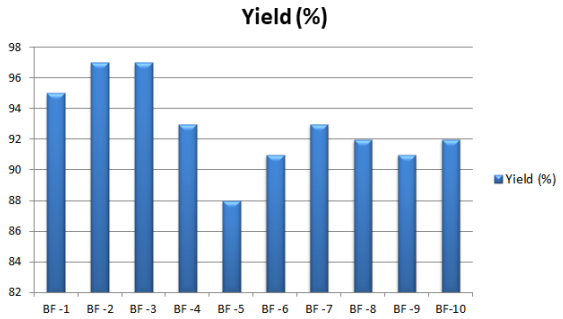

Figure 6: Evaluation of different formulations for yield (%)

Physical characteristic studies:

The physical parameters of the buccal films, including thickness, density, and folding endurance, provide essential insights into their structural integrity and handling characteristics. The thickness of the films ranges from 0.30 ± 0.01 mm (BF-3) to 0.35 ± 0.01 mm (BF-10). Thinner films, like BF-3, are more comfortable for users but may have reduced mechanical strength, while thicker films, such as BF-10, offer better stability but could be less comfortable. The density of the films is consistent, ranging from 0.47 ± 0.02 mg/CC to 0.49 ± 0.03 mg/CC, with higher-density formulations like BF-3, BF-6, and BF-8 suggesting consistent drug release and mechanical properties. Folding endurance, which measures the film's durability during handling and application, varies significantly, with BF-1 demonstrating the highest endurance (480 ± 5) and BF-2 the lowest (360 ± 8). Overall, these parameters provide a comprehensive understanding of the films' performance, with BF-3 being well-balanced for its thin profile, high density, and sufficient folding endurance.

Table 12: Structural Integrity Parameters of Buccal Film

Formulations (BUCCAL FILM -BF)	Thickness (mm)	Density (mg/CC)	Folding Endurance
BF -1	**0.32 ± 0.01**	**0.48 ± 0.02**	**480 ± 6**
BF -2	**0.34 ± 0.02**	**0.47 ± 0.02**	**360 ± 8**
BF -3	**0.30 ± 0.01**	**0.49 ± 0.02**	**414 ± 7**
BF -4	**0.34 ± 0.03**	**0.48 ± 0.02**	**375 ± 6**
BF -5	**0.31 ± 0.01**	**0.47 ± 0.03**	**400 ± 5**
BF -6	**0.33 ± 0.02**	**0.49 ± 0.03**	**395 ± 8**
BF -7	**0.32 ± 0.03**	**0.48 ± 0.03**	**430 ± 6**
BF -8	**0.31 ± 0.02**	**0.49 ± 0.02**	**460 ± 7**
BF -9	**0.34 ± 0.01**	**0.47 ± 0.03**	**450 ± 5**
BF-10	**0.35 ± 0.01**	**0.48 ± 0.02**	**440 ± 5**

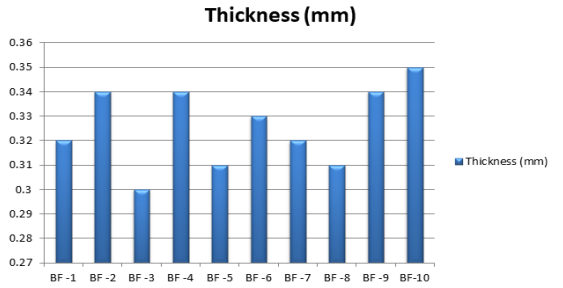

Figure 7: Evaluation of different formulations for Thickness (mm)

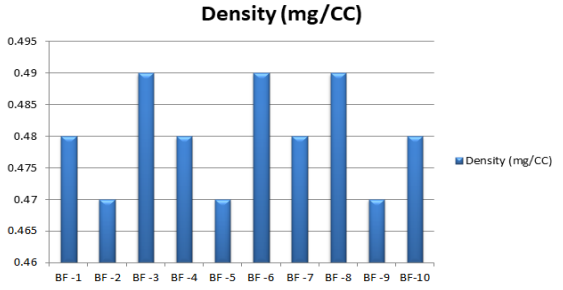

Figure 8: Evaluation of different formulations for Density (mg/CC)

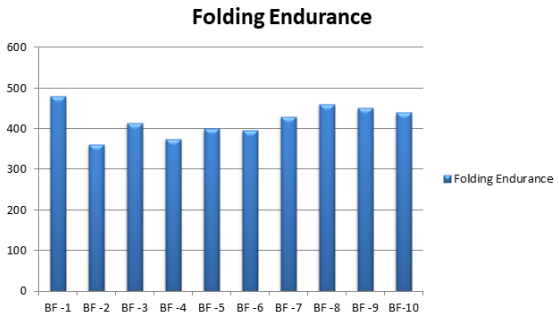

Figure 9: Evaluation of different formulations for Folding Endurance

Evaluation of different formulations of Buccal Film:

The physical characteristic studies of the buccal films reveal significant differences in their swelling indices, which directly affect their drug release profiles and adhesive properties. Among the formulations, BF-3 stands out with a swelling index of 2.150 ± 0.08, indicating a notable ability to absorb moisture. This characteristic helps achieve

more controlled drug release and enhances adhesion to the buccal mucosa, making BF-3 an effective formulation. Although BF-8 shows the highest swelling index at 2.750 ± 0.08, suggesting greater moisture absorption and potentially more extensive drug release, excessive swelling could compromise the film's structural integrity and cause discomfort. In contrast, films like BF-5 and BF-6, with swelling indices of 1.700 ± 0.05 and 1.650 ± 0.07, respectively, exhibit lower swelling capacities, which may lead to slower drug release and weaker adhesion. Overall, BF-3 offers an optimal balance between swelling index, drug delivery, adhesion, and user comfort.

Table 13: Physical characteristic studies of Buccal Film

Formulations (BUCCAL FILM - BF)	Swelling Index
BF -1	1.920 ± 0.05
BF -2	2.010 ± 0.07
BF -3	2.150 ± 0.08
BF -4	1.800 ± 0.06
BF -5	1.700 ± 0.05
BF -6	1.650 ± 0.07
BF -7	2.100 ± 0.06
BF -8	2.750 ± 0.08
BF -9	2.050 ± 0.05
BF-10	1.800 ± 0.06

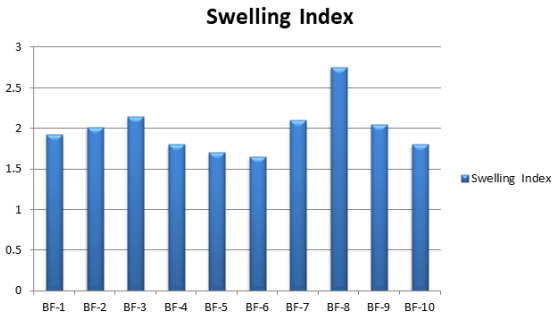

Figure 10: Evaluation of different formulations for (Swelling Index)

CONCLUSION:

Enalapril Maleate exhibits key physical properties that influence its formulation and performance in pharmaceutical applications. Its crystalline nature, melting point range of 143°C to 144°C, and varied solubility in different solvents highlight its versatility and importance in drug development. The compound's flow properties, including a moderate Compressibility Index (CI) of 10.31% and excellent flowability as indicated by its Hausner Ratio (HR) of 1.11, support efficient manufacturing processes. The standard curve analysis confirms the reliability of the analytical method for quantifying Enalapril Maleate, ensuring accurate drug concentration measurements. The evaluation of buccal film formulations further underscores the versatility of Enalapril Maleate in drug delivery systems, particularly in the buccal route. Among the tested formulations, BF-3 emerges as the optimal choice due to its balanced combination of weight, bioadhesive strength, density, and swelling index. Despite BF-4's slightly higher bioadhesive strength, BF-3 provides a more user-friendly and effective option for sustained drug release and mucosal adhesion. In terms of content uniformity and yield, BF-2 strikes the best balance for production efficiency, with a high yield and acceptable uniformity. Additionally, the swelling index of BF-3 further complements its overall profile, offering effective drug release without compromising structural integrity. Therefore, BF-3 is the most suitable formulation for buccal delivery, with its combination of comfort, consistency, and performance making it the most promising candidate for further development and clinical use.

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CONFLICT OF INTEREST:

The author declares that there is no conflict of interest regarding the publication of this research.

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