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# Formulation and In-vitro evaluation of of bilayered mucoadhesive buccal tablets of Meclizine HCl

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## ABSTRACT

**The primary objective of this study was to create bilayered mucoadhesive buccal tablets containing Meclizine hydrochloride in order to enhance the duration of drug residency in the buccal mucosa and the rate of drug dissolution, circumvent first-pass metabolism, and expedite the entry of the medication into the systemic circulation. Using the direct compression approach, twenty bilayered formulations of mucoadhesive buccal tablets containing meclizine HCl were synthesized by using various bioadhesive polymers which included HPMC 15cps, HPMC 50cps, HPMC 100cps, and HPMC K4M in different ratios and ethylcellulose as the backing layer. The prepared buccal tablets were characterized for a number of parameters like hardness, friability, uniformity of weight, thickness, swelling index, mucoadhesive strength, surface pH, *in-vitro* drug release studies and compatibility studies of drugs and excipients by FT-IR spectroscopy. Among all the twenty formulations, formulation ($AH_1$) containing HPMC 15cps showed swelling index 92.36±4.51%, mucoadhesive strength 6.16±0.08g, and *in-vitro* drug release 88.43±1.73% within 8 hrs.The outcomes revealed that Meclizine HCl bilayered mucoadhesive buccal tablets would be an effective strategy for avoiding severe hepatic first-pass metabolism while enhancing the bioavailability of drug through the buccal mucosa.**

**Keywords: Buccal tablets, Meclizine HCl, mucoadhesive, drug release, HPMC.**

## INTRODUCTION

The oral route of drug administration is the most prevalent and recommended route for drug delivery since it allows for easy ingestion, self-medication, exact dosage, a flexible and controlled dosing schedule, patient compliance, and a minimal probability of administration problem.[1] Oral administration has several advantages, such as correct dosing, drug stability, affordability, and ease of use. Despite its benefits, its usage is restricted by hepatic first-pass metabolism, which is the elimination of drug by the liver before reaching the systemic circulation and enzyme degradation within the GIT, serves as limiting factors for its use.[2] The buccal mucosa has sufficient vascular and lymphatic drainage, which prevents first-pass metabolism in the liver and pre-systemic clearance in the gastrointestinal tract.[3]

Buccal drug delivery systems present a viable way to administer drugs to the buccal mucosa for the treatment of oral disorders, as well as to the systemic circulation through mucosal absorption at a predetermined and regulated rate.Furthermore, unlike the sublingual route, the buccalmucosa allows for extended retention of a dose form without significantly interfering with speech or mastication, especially when mucoadhesive polymers are used.Buccal medication administration permits stops whenever toxicity or unfavorable effects occur. Drug administration is an additional option for people who have trouble swallowing.[4]

Mucoadhesive drug delivery systems utilize the properties of the bioadhesion of certain polymers. The term "bioadhesion" refers to a material's capacity to stick to a specific area of the body for a prolonged amount of time. This property is useful

for both local drug targeting and improved systemic delivery control. The interaction of a mucin surface with a synthetic or natural polymer is known as mucoadhesion. [5]Meclizine HCl is a tasteless, crystalline powder that is white and slightly yellowish with a slight odor. Meclizine acts as an antagonist at H1 receptors, but it also has depressive and local anesthetic effects on the central nervous system. Meclizine may have an impact on the medullary chemoreceptor trigger zone and decreases vestibular stimulation and labyrinth excitability.
Additionally, it is used to treat vertigo symptoms and prevent nausea, vomiting, and dizziness brought on by a number of illnesses, including motion sickness. Additionally, it has been used to treat pruritic skin diseases and hypersensitivity reactions symptomatically.

Meclizine hydrochloride is readily absorbed when used orally. The bioavailability in its entirety is between 40 and 45 percent. Meclizine HCl's physicochemical characteristics, appropriate half-life of six hours, and molecular weight of 390.948 g/mol make it appropriate for oral administration. [6,7]

By retaining the drug dosage form in contact with the absorption site, such as the buccal cavity, and at the site of intended action, mucoadhesion enhances the localization of drug delivery systems.[8]

In the present study, mucoadhesive tablets were developed using hydrophilic polymers (Carbopol 934P and different grades of HPMC) to provide zero-order controlled drug release. The objective of this study was to design, develop, optimize, and characterize a controlled-release Meclizine HCl buccoadhesive tablet using some selective polymers such as carbopol 934P (CP) and various grades of hydroxypropyl methylcellulose (HPMC). [9]

Hydrophilic matrices are compressed powder mixtures of a drug and fillers, including one or more hydrophilic polymers that swell in water. Matrices are usually compressed. Such matrices are commonly used because of the advantages associated with their production, including ease of formulation, use of existing tabletting technologies, and the low cost of polymers that are generally considered safe (GRAS) excipients.

Because of its capacity to absorb water, HPMC is hydrophilic, non-toxic, biocompatible, and biodegradable. It may also expand quickly. By creating an adhesive connection between the oral mucosa and the delivery mechanism, HPMC extends the duration of drug residency at the absorption site. This enables peptide drugs to be sustained for the necessary amount of time.[10]

In the current investigation, different grades of HPMC were used in an effort to create effective, prolonged-release mucoadhesive buccal tablets of meclizine HCl that would minimize first-pass metabolism, lower dosage frequency, and increase patient compliance while maintaining better bioavailability.

## MATERIALS AND METHODS

**Material**
Meclizine HCl was gifted by Symed Labs Ltd., Hyderabad. Ethyl cellulose was gifted by Loba Chemie Pvt. Ltd., Mumbai, India. Carbopol 934P was gifted by Alkem Labs Pvt. Ltd., Mumbai. All other materials were of analytical or pharmacopoeial grade and used as received.

**Preparation of Standard Calibration Curve of Meclizine hydrochloride in methanol:**
Accurately weighed 100mg of Meclizine hydrochloride dissolved in 100ml of methanol to give a concentration of 1000 µg/ml.

From stock solution working standard was prepared to give a concentration of 100µg/ml. Aliquots of working standard solution were suitably diluted with methanol to get a final concentration range of 2-10 µg/ml. The absorbance of prepared aliquots measured at 232 nm in UV spectrophotometer (Shimadzu 1800) against appropriate blanks**.**

**Preparation of Standard Calibration Curve of Meclizine hydrochloride in pH 6.8 Phosphate Buffer:**
100 mg of drug was dissolved in 100 ml of methanol by slight shaking (1000 mcg/ml). 1 ml of this solution was taken and made up to 50 ml with methanol, which gives 20 mcg/ ml concentration (stock solution).

From the stock solution, concentrations of 2, 4, 6, 8 and 10 µg/ml in pH 6.8 phosphate buffer were prepared. The absorbance of diluted solutions was measured at 272 nm and a standard plot was drawn using the data.

**Formulation of mucoadhessivebuccal tablets of Meclizine HCl**

**Preparation**

In the current investigation, preliminary trial formulations of Meclizine HCl buccal tablets were prepared by the direct compression method using synthetic polymers like HPMC 15cps, HPMC 50cps, HPMC 100cps, and HPMC K4M, along with Carbopol 934P in different ratios.

**Procedure**

All the ingredients, including drugs, polymers, and excipients, were weighed accurately according to the batch formulae.In the beginning the drug and mannitol were thoroughly mixed on a piece of butter paper using a stainless steel spatula. After that, all the ingredients were mixed in ascending weight order and blended for 10 minutes in an inflated polyethylene pouch. Finally, the lubricant was added and mixed for an additional 2 minutes.

To create a single-layered, flat-faced tablet with an 8 mm diameter, the prepared mix of each formulation was pre-compressed on a 10-station rotary tablet punching machine (Clit, Ahmedabad) at a pressure of 0.5 tons and turret speed of 2 rpm.

After that, 50 mg of ethyl cellulose powder was added, and the mixture was finally compressed at 3.5 tons of pressure and 2 rpm turret speed to produce buccal tablets containing meclizine hydrochloride.[11] The composition of buccal tablets of Meclizine HCl tablets is mentioned in Table 1.

**Table 1. Composition of Buccal Tablets of Meclizine HCl**

| Ingredients* (mg/tablet) | Formulation code | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $AH_0$ | $AH_1$ | $AH_2$ | $AH_3$ | $AH_4$ | $BH_0$ | $BH_1$ | $BH_2$ | $BH_3$ | $BH_4$ | $CH_0$ | $CH_1$ | $CH_2$ | $CH_3$ | $CH_4$ | $DH_0$ | $DH_1$ | $DH_2$ | $DH_3$ | $DH_4$ |
| **Meclizine Hcl** | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| **Carbopol 934p** | --- | 2 | 4 | 6 | 8 | --- | 2 | 4 | 6 | 8 | --- | 2 | 4 | 6 | 8 | --- | 2 | 4 | 6 | 8 |
| **HPMC 15cps** | 10 | 15 | 20 | 25 | 30 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **HPMC 50cps** | --- | --- | --- | --- | --- | 10 | 15 | 20 | 25 | 30 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **HPMC 100cps** | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | 10 | 15 | 20 | 25 | 30 | --- | --- | --- | --- | --- |
| **HPMC K4M** | --- | --- | --- | -- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | 10 | 15 | 20 | 25 | 30 |
| **Mannitol** | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| **Aspartame** | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| **SSF** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| **Flavour** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| **MCC** | 43 | 36 | 29 | 22 | 15 | 43 | 36 | 29 | 22 | 15 | 43 | 36 | 29 | 22 | 15 | 43 | 36 | 29 | 22 | 15 |
| **Ethyl cellulose** | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| **Total weight** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** |

*Weights expressed as mg per tablet;

AH- Formulation containing HPMC 15 cps as polymer BH-formulation containing HPMC 50 cps as polymer

CH-formulation containing HPMC 100 cps as polymer DH-formulation containing HPMC K4M as polymer

**Pre-formulation study of Pre-compression parameters**

**Tapped Density**

A predetermined amount of time was spent tapping the measuring cylinder holding a defined mass of blend.The weight (M) of the blend and the minimal volume (Vt) it occupied in the cylinder were measured. The tapped density ($\rho_t$) was calculated using the formula,[12]

$$\rho_t = M / V_t$$

**Bulk Density**

Apparent bulk density $\rho_b$was determined by pouring the blend into a graduated cylinder. The bulk volume ($V_b$) and weight of powder (M) wasdetermined.The bulk density ($\rho_b$) was calculated using the formula[13]

$$\rho_b = M / V_b$$

**Compressibility Index**

Compressibility is the most simplest method for measuring powder flow; the compressibility index (I) indicates how easily a material may be made to flow. [13]

$$C.I. = (\rho_t - \rho_b) / \rho_t \times 100$$

Where,

$\rho_t$ = Tapped density
$\rho_b$ = Bulk density

The value below 15% indicates a powder with usually give good flow characteristics; where above 25% indicates poor flowability.

**Hausner's ratio**

Hausner's ratiois an indirect index of ease of powder flow. It is calculated by the following formula,[14]

$$\text{Hausner's ratio} = \rho_t / \rho_b$$

Where,

$\rho_{tis}$ tapped density
$\rho_b$ is bulk density

Lower Hausner ratio (< 1.25) indicates better flow properties than higher one(> 1.25).

**Angle of Repose**

Angle of Repose was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a specified cone height (h) wasobtained.Radius of the heap (r) was measured and angle of repose (θ) was calculated by the formula:[15]

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

Where,

θ = Angle of repose,
H = Height of cone,
R = Radius of cone

**Evaluation of buccal tablets**

The prepared batches of tablets were evaluated for weight variation, hardness, friability, drug content uniformity, swelling index, surface pH, *ex-vivo*mucoadhesive strength, *in-vitro* drug release, short-term stability (IR spectroscopy) and drug-excipient interaction.

**Hardness test**

The hardness of a tablet is an indication of its strength. During handling and transit, the tablet should be stable under mechanical stress. The crushing strength ($kg/cm^2$) of tablets was determined by using Monsanto hardness tester.[12,13,14,15]

**Friability test**

This was determined by weighing 20 tablets after dusting, placing them in the friabilator and rotating the plastic cylinder vertically at 25rpm for 4 min. After dusting, the total remaining weight of the tablets was recorded and the percent friability was calculated (% loss in weight).[15,17,19,20]

**Thickness**

Three tablets from each batchof formulation were collected and the thickness of the tablets was measured with the help of venires caliper.[15,16,17,21] The average thickness was calculated.

**Weight variation**
The weight (mg) of each of 20 individual tablets was determined by dusting each tablet off and placing it in an electronic balance. The weight data from the tablets were analyzed for sample mean and percent deviation from the mean.[22]

**Uniformity of drug content**
Five tablets were powdered in a glass mortar and the powder equivalent to 1 mg of drug was placed in a stoppard 100 ml conical flask. The drug is extracted with 25 ml methanol with vigorous shaking on a mechanical gyratory shaker (100 rpm) for 2 h and filtered into 50 ml volumetric flask through Whatman No.1 filter paper (Mean pore diameter 1.5 µm) and more solvent is passed through the filter to 50 ml to produce concentration of 20 µg/ml of Meclizine HCl and analyzed for drug content by measuring the absorbance at 232 nm against solvent blank.[22]

**Surface pH study**
The surface pH of the tablet was determined in order to investigate the possible side effects due to change in pH, since an acidic or alkaline pH may cause irritation to the buccal mucosa. The tablet to be tested was placed in a petridish and was moistened with 0.5 ml of distilled water and kept for 1 hr. The pH was noted afterbringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibrating for 1 min.[23]

**Swelling Index**
The swelling rate of the buccal tablet is evaluated by using of pH 6.8 phosphate buffer. The initial weight of the tablet is determined ($w_1$). The tablets is placed in pH 6.8 phosphate buffer (6 ml) in a petridish placed in an incubator at 37 ± 1° C and tablet is removed at different time intervals (0.0, 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0 and 8.0), blotted with filter paper and reweighed ($w_2$).[24-25]The swelling index is calculated by the formula:

$$\textbf{Swelling index} = 100\ (w_2 - w_1) / w_1.$$

**Mucoadhesion strength**
The apparatus used for testing bioadhesion was assembled in the laboratory (figure-3). Mucoadhesion strength of the tablet was measured on a modified physical balance employing the method described by Gupta *et al* using bovine cheek pouch as model mucosal membrane.

A double beam physical balance was taken, the left pan was removed. To left arm of balance a thick thread of suitable length was hanged. To the bottom side of thread a glass stopper with uniform surface was tied. A clean glass mortar was placed below hanging glass stopper. In this mortar was placed a clean 500 ml glass beaker, within which was placed another glass beaker of 50 ml capacity in inverted position and weighted with 50 g to prevent floating. The temperature control system involves placing thermometer in 500 ml beaker and intermittently adding hot water in outer mortar filledwith water. The balance was so adjusted that right hand-side was exactly 5 g heavier than the left.[26-29]

**METHOD**

The balance adjusted as described above was used for the study. The bovine cheek pouch, excised and washed was tied tightly with mucosal side upward using thread over the base of inverted 50 ml glass beaker. This beaker suitably weighted was lowered into 500 ml beaker, which was then filled with isotonic phosphate buffer (pH 6.8) kept at 37°C such that the buffer reaches the surface of mucosal membrane and keeps it moist. This was then kept below left hand side of balance. The buccal tablet was then stuck to glass stopper through its backing membrane using an adhesive (Feviquick). The 5g on right hand side is removed; this causes application of 5 g of pressure on buccaltablet overlying moist mucosa. The balance was kept in this position for 3 minutes and then slowly weights were increased on the right pan, till tablet separates from mucosal membrane. The total weight on right pan minus 5 g gives the force required to separate tablet from mucosa. This gives bioadhesive strength in grams. The mean value of three trials was taken for each set of formulations. After each measurement, the tissue was gently and thoroughly washed with isotonic phosphate buffer and left for 5 minutes before reading a new tablet of same formulation to get reproducible multiple results for the formulation.

**Fig 1. Bioadhesion Testing Apparatus**

***In-vitro* drug release study**

This is carried out in USP XXIII tablet dissolution test apparatus-II (Electrolab TDT-06N), employing paddle stirrer at 50 rpm and 900 ml of pH 6.8 phosphate buffers as dissolution medium. The release study is performed at 37±0.5ºC. The backing layer of the buccal tablet is attached to glass disk with cyanoacrylate adhesive. The disk is placed at the bottom of the dissolution vessel. Samples of 5 ml are withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through 0.25 µm membrane filter disc (Millipore Corporation) and analysed for Meclizine HCl after appropriate dilution by measuring the absorbance at 272 nm.[30,31]


**Fig 2. Dissolution Testing Apparatus**

**Stability Studies**

Accelerated stability studies were performed at a temperature of 40±2ºC/75±% RH over a period of three months (90 days) on the promising buccal tablets of Meclizine HCl (Optmized formulation OFM). Sufficient number of tablets

(15) were packed in amber coloured rubber stoppered vials and kept in stability chamber maintained at 40±2ºC/75±% RH. Samples were taken at one month interval for drug content estimation. At the end of three month period, dissolution test was performed to determine the drug release profile.

**Fourier transform infrared (FTIR)**

FTIR spectra of pure drug (Meclizine HCl),along with carbopol 934P and HPMC 15cps were obtained by usingBruker FTIR-Tensor 27spectrophotometer, using the potassium bromide (KBr) pellet disk technique. The discwas placed in IR spectrophotometer using sample holder andspectrum was recorded from 4000 to 400 $cm^{-1}$.

## RESULTS AND DISCUSSION

**Calibration Curve of Meclizine HCl**

**Preparation of standard curve of Meclizine HCl in Methanol**

The Meclizine HCl standard calibration curve was prepared in Methanol. The straight line standard calibration curve indicates that the drug complies with Beer's Lambert's law in the concentration range of 2- 10 mcg/ml and the 'r' value was found to be 0.999.

**Table 2. Standard Calibration Curve of Meclizine hydrochloride in Methanol (λmax=232 nm)**

| Concentrations (mcg/ml) | Absorbance | | | Mean ± SD |
|---|---|---|---|---|
| | I | II | III | |
| 0 | 0.000 | 0.000 | 0.000 | 0.000±0.000 |
| 2 | 0.214 | 0.219 | 0.229 | 0.220±0.007 |
| 4 | 0.423 | 0.435 | 0.442 | 0.433±0.009 |
| 6 | 0.631 | 0.642 | 0.652 | 0.641±0.010 |
| 8 | 0.840 | 0.845 | 0.852 | 0.845±0.006 |
| 10 | 1.094 | 1.101 | 1.109 | 1.101±0.007 |

A=0.001 B=0.108x $r^2$=0.999

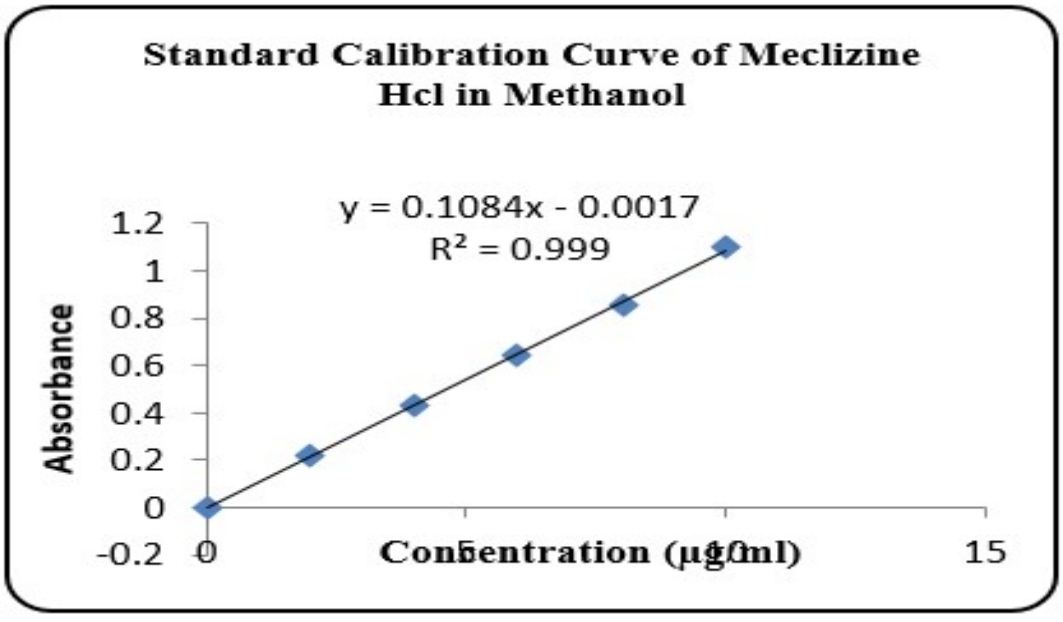


**Fig 3. Standard Calibration Curve of Meclizine hydrochloride in Methanol (λmax= 232 nm)**

**Preparation of standard curve of Meclizine HCl in pH 6.8 Phosphate Buffer**

The Meclizine HCl standard calibration curve was prepared in pH 6.8 Phosphate buffer. The straight line standard calibration curve indicates that the drug complies with Beer's Lambert's law in the concentration range of 2- 10 mcg/ml and the 'r' value was found to be 0.999.

**Table 3. Standard Calibration Curve of Meclizine hydrochloride in pH 6.8 phosphate buffer (λmax= 272 nm)**

| Concentrations (mcg/ml) | Absorbance | | | Mean ± SD |
|---|---|---|---|---|
| | I | II | III | |
| 0 | 0.000 | 0.000 | 0.000 | 0.000±0.000 |
| 2 | 0.126 | 0.132 | 0.128 | 0.128±0.003 |
| 4 | 0.265 | 0.276 | 0.256 | 0.265±0.010 |
| 6 | 0.404 | 0.372 | 0.381 | 0.385±0.016 |
| 8 | 0.512 | 0.506 | 0.502 | 0.506±0.005 |
| 10 | 0.640 | 0.662 | 0.646 | 0.649±0.011 |

A= 0.0012 B= 0.0643 $r^2$= 0.999

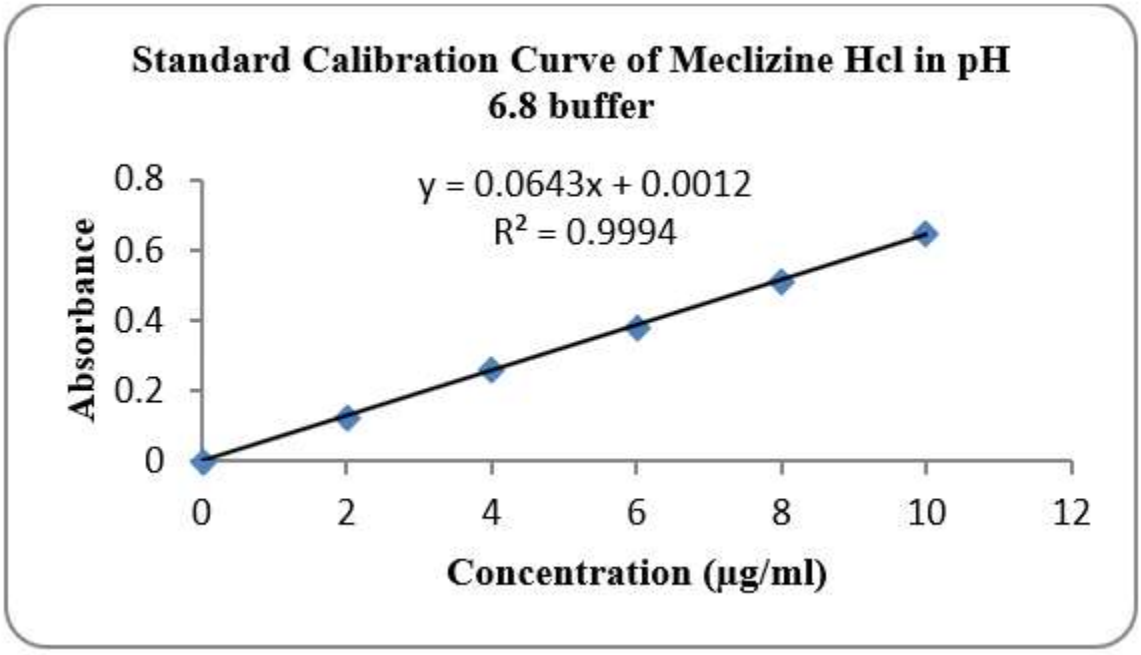


**Fig 4. Standard Calibration Curve of Meclizine hydrochloride in pH 6.8 phosphate buffer (λmax= 272 nm)**

**Infrared Spectrum Analysis**

After examining the infrared spectra of the pure medication meclizine HCl, it was discovered that all significant peaks, which correlate to the different functional groups contained in the structure of meclizine HCl, were present. It exhibits distinctive peaks at 3385.60cm-1, 1493.92cm-1, 3005.53cm-1, and 698.90cm-1, which correspond to the stretching of aromatic C-H, aliphatic C-C, N-H, and C-CL, respectively. It was noted that Meclizine HCl and the employed excipients did not interact.

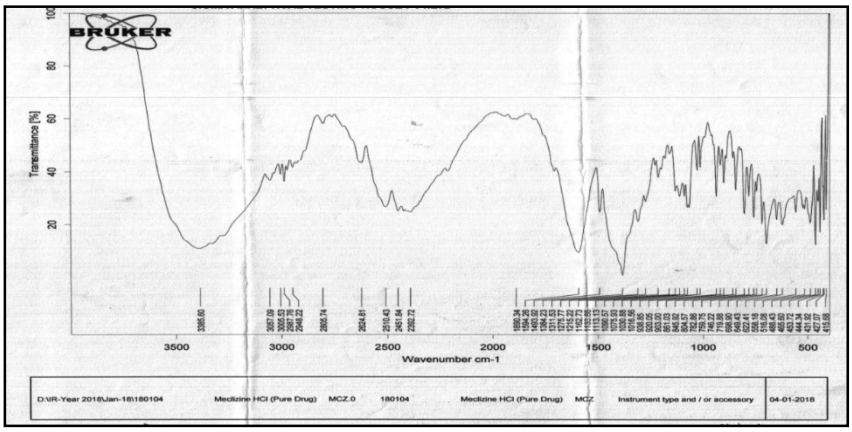


**Fig 5. IR spectrum of Meclizine HCl (Pure Drug)**

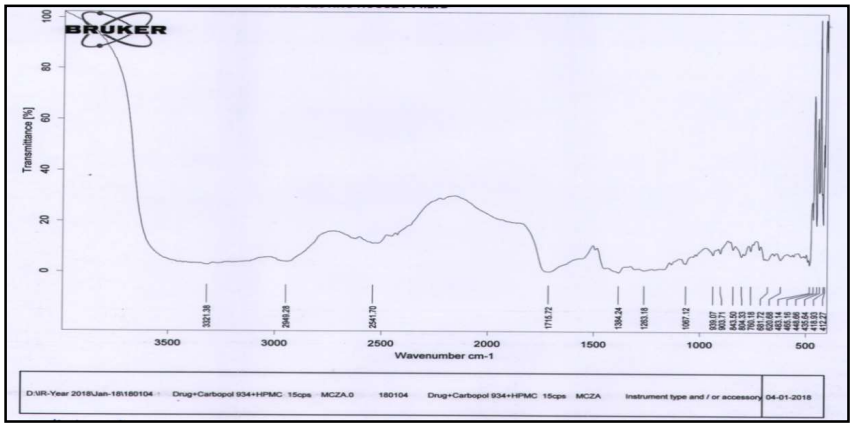


**Fig 6. IR spectrum of Drug + Carbopol + HPMC 15cps**

**Evaluation of Buccal Tablets**

Meclizine HCl buccal tablets that were manufactured were found to have a hardness ranging from 3.35±0.09 to 5.23±0.11 kg/cm2. The produced buccal tablets were found to have thicknesses and weights within the range of 2.86±0.13 to 3.32±0.10mm and 148.80±0.57 to 150.57±0.11mg, respectively.

Less than 1% of friability indicates strong mechanical resistance to handling and transportation difficulties.The produced buccal tablets had an average drug content ranging from 94.95±1.40 to 104.47±1.82%. The low standard deviation values suggest that the medication was distributed uniformly throughout the tablets.

Since an acidic or alkaline pH is certain to irritate the buccal mucosa, the surface pH was measured to look into any potential adverse effects in the oral cavity. It was discovered that the surface pH of every formulation fell between 6.35±0.08 and 8.15±0.24. It follows that these formulations are thought to be non-irritating to the oral cavity.

All formulations had a swelling index between 28.10±1.56 and 92.36± 4.51%. After testing the mucoadhesion of all the buccal tablets with different polymer ratios, it was discovered that the tablets' mucoadhesivity ranged from 3.84±0.06 to 7.11±0.11%.

**Table 3. *In-Vitro* Drug Release Data of Formulations of Meclizine HCl $AH_0$, $AH_1$ and $AH_2$**

| Time | Square root of time | log time | Cumulative Percent Drug Released* | | | Log Cumulative Percent Drug Released | | | Cumulative Percent Drug Remaining | | | log Cumulative Percent Drug Remaining | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | $AH_0$ | $AH_1$ | $AH_2$ | $AH_0$ | $AH_1$ | $AH_2$ | $AH_0$ | $AH_1$ | $AH_2$ | $AH_0$ | $AH_1$ | $AH_2$ |
| 0 | 0.000 | -- | 0±0.00 | 0±0.00 | 0±0.00 | -- | -- | -- | 100 | 100 | 100 | 2 | 2 | 2 |
| 0.5 | 0.7071 | -- | 32.54±0.91 | 29.53±0.61 | 26.31±1.37 | 1.512 | 1.470 | 1.420 | 67.46 | 70.46 | 73.68 | 1.829 | 1.847 | 1.867 |
| 1 | 1.000 | 0.0000 | 37.76±1.29 | 35.98±1.47 | 32.03±1.55 | 1.577 | 1.556 | 1.505 | 62.23 | 64.01 | 67.97 | 1.794 | 1.806 | 1.832 |
| 2 | 1.414 | 0.3010 | 57.67±1.09 | 48.69±1.73 | 42.03±2.31 | 1.760 | 1.687 | 1.623 | 42.32 | 51.30 | 57.96 | 1.626 | 1.710 | 1.763 |
| 3 | 1.732 | 0.4771 | 66.99±0.40 | 56.63±0.61 | 53.35±1.08 | 1.826 | 1.753 | 1.727 | 33.00 | 43.36 | 46.64 | 1.518 | 1.637 | 1.668 |
| 4 | 2.000 | 0.6020 | 70.01±0.45 | 64.88±1.53 | 59.85±1.35 | 1.845 | 1.812 | 1.777 | 29.98 | 35.11 | 40.14 | 1.476 | 1.545 | 1.603 |
| 5 | 2.236 | 0.6989 | 76.32±0.45 | 68.28±1.63 | 61.86±1.20 | 1.882 | 1.834 | 1.791 | 23.68 | 31.71 | 38.13 | 1.374 | 1.501 | 1.581 |
| 6 | 2.449 | 0.7781 | 87.05±0.39 | 77.20±1.35 | 67.91±1.80 | 1.939 | 1.887 | 1.831 | 12.94 | 22.79 | 32.09 | 1.112 | 1.357 | 1.506 |
| 7 | 2.645 | 0.8450 | 90.20±1.40 | 83.74±2.20 | 72.34±2.90 | 1.955 | 1.922 | 1.859 | 9.79 | 16.26 | 27.65 | 0.991 | 1.211 | 1.441 |
| 8 | 2.828 | 0.9030 | 94.14±1.83 | 88.43±1.73 | 78.01±2.34 | 1.973 | 1.946 | 1.892 | 5.85 | 11.56 | 21.99 | 0.767 | 1.06 | 1.342 |

***Average of three determinations**

**Table 4. *In-Vitro* Drug Release Data of Formulations of Meclizine HCl$AH_3$ and $AH_4$**

| Time | Square root of time | log time | Cumulative Percent Drug Released*±SD | | Log Cumulative Percent Drug Released | | Cumulative Percent Drug Remaining | | log Cumulative Percent Drug Remaining | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | $AH_3$ | $AH_4$ | $AH_3$ | $AH_4$ | $AH_3$ | $AH_4$ | $AH_3$ | $AH_4$ |
| 0 | 0 | -- | 0±0.00 | 0±0.00 | -- | -- | 100 | 100 | 2 | 2 |
| 0.5 | 0.7071 | -- | 22.96±2.63 | 19.31±1.46 | 1.36 | 1.285 | 77.04 | 80.68 | 1.886 | 1.906 |
| 1 | 1 | 0 | 27.00±1.67 | 22.51±1.05 | 1.431 | 1.352 | 73 | 77.48 | 1.863 | 1.889 |
| 2 | 1.414 | 0.301 | 36.72±2.60 | 30.62±2.63 | 1.564 | 1.486 | 63.27 | 69.38 | 1.801 | 1.841 |
| 3 | 1.732 | 0.4771 | 43.20±1.85 | 38.39±1.84 | 1.635 | 1.584 | 56.8 | 61.6 | 1.754 | 1.789 |
| 4 | 2 | 0.602 | 50.59±1.94 | 44.31±1.96 | 1.704 | 1.646 | 49.4 | 55.69 | 1.693 | 1.745 |
| 5 | 2.236 | 0.6989 | 55.85±1.57 | 49.33±1.89 | 1.747 | 1.693 | 44.14 | 50.67 | 1.644 | 1.704 |
| 6 | 2.449 | 0.7781 | 58.64±1.93 | 53.86±2.49 | 1.768 | 1.731 | 41.35 | 46.13 | 1.616 | 1.664 |
| 7 | 2.645 | 0.845 | 60.78±1.17 | 56.67±2.24 | 1.783 | 1.753 | 39.21 | 43.33 | 1.593 | 1.636 |
| 8 | 2.828 | 0.903 | 64.38±1.02 | 59.64±1.90 | 1.808 | 1.775 | 35.61 | 40.36 | 1.551 | 1.605 |

***Average of three determinations**

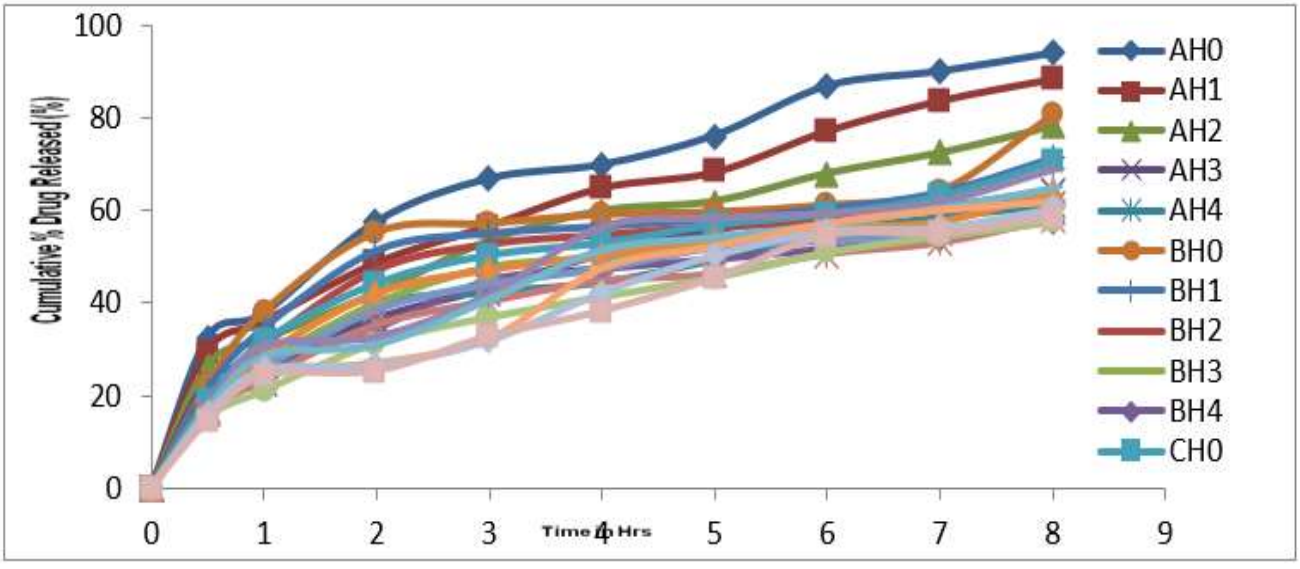


**Fig 5. *In-Vitro* dissolution profile of all 20 formulations**

For a range of formulations (AH0-DH4), an in vitro drug release investigation was conducted in phosphate buffer pH 6.8. The manufactured buccal tablets had varying ratios of polymers. Carbopol 934P was the principal polymer in all twenty batches due to its superior swelling and mucosal surface adhesion properties.

As the concentration of secondary polymers increased, the release of the drug decreased. The $AH_0$-$AH_4$ formulations released 94.14±1.83%, 88.43±1.73%, 78.01±2.34, 64.38±1.02%, and 59.64±1.90% drug release, $BH_0$-$BH_4$ formulations released80.47±0.95%, 71.27±1.04%, 62.38±1.79%, 58.24±3.97% and 57.73±0.88%, $CH_0$-$CH_4$ formulations released 70.55±0.85%,64.06±0.73%, 59.49±1.60%, 58.23±2.98% and 57.40±1.40%, whereas$DH_0$-$DH_4$ showed 68.79±2.40%, 64.60±0.77%, 61.77±0.59%, 60.43±2.00% and 58.62±0.93% drug release in 8 hrs, respectively. (Results are shown in Figure 7). This could be the result of the polymer expanding due to diffusion.

The most promising formulation among the twenty trial formulations was formulation $AH_1$, which comprises 15 mg of HPMC 15Cps and 2 mg of carbopol 934P. The findings of the swelling index were 92.36±4.51%, the mucoadhesive strength was 6.16±0.08g, and the *in-vitro* drug release was 88.43±1.73% in 8 hours.

## CONCLUSION

The goal of this investigation was to create and evaluate mucoadhesive buccal tablets containing Meclizine hydrochloride to increase patient compliance when treating a range of pain disorders. The bilayered buccal tablets that were designed achieved the intended outcomes when it came to dissolving, bioavailability, and physiochemical characteristics.

The goal of the current study was to create mucoadhesive buccal tablets of meclizine HCl by employing various grades of HPMC as polymers. The direct compression approach is used to prepare them. It was discovered that every prepared tablet was intact and had neither chips nor caps. According to pharmacopeial requirements, all of the preparations weight variation, hardness, thickness, friability, and drug content fell within acceptable bounds.

Based on the results of the swelling index (92.36±4.51%), mucoadhesive strength (6.16±0.08g), and in-vitro drug release (88.43±1.73% within 8 hours), it can be concluded that, out of the twenty experimental formulations, formulation $AH_1$ was the most promising formulation. The outcomes demonstrated that carbopol is important in boosting mucoadhesive strength. In order to monitor the rate of drug release and swelling behavior, HPMC can be quite helpful. The weak and inconsistent oral bioavailability of Meclizine HCl linked to commercial formulations may be mitigated, nevertheless, by newly developed bilayered buccal tablets.

The results of the study show that therapeutic levels of Meclizine HCl can be delivered through buccal cavity.

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