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Research Article

Formulation and Evaluation Immediate Release Mucoadhesive Buccal Tablet of Midodrine HCL

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A B S T R A C T

This study aimed to develop and optimize immediate-release mucoadhesive buccal tablets of Midodrine Hydrochloride, intended for rapid onset of action in treating hypotensive states. The tablets were prepared using a direct compression method, with various formulations optimized through a 3^2 randomized full factorial design, focusing on Crospovidone and Carbopol 934P as independent variables affecting diffusion time and mucoadhesive strength. The optimized batch F3 demonstrated superior performance, with a disintegration time of 20 seconds and an in vitro release of 98.25% within 5 minutes, meeting the criteria for immediate release. Additionally, F3 exhibited strong mucoadhesive strength, ensuring prolonged retention in the buccal cavity, and an appropriate surface pH of 6.8, compatible with the buccal environment. Stability studies conducted according to ICH guidelines confirmed that the optimized formulation maintained its integrity and efficacy under accelerated conditions. The findings suggest that the optimized F3 formulation is highly effective for buccal delivery of Midodrine Hydrochloride, offering a promising therapeutic option for patients requiring rapid antihypotensive action. The tablets exhibited efficient mucoadhesive strength, appropriate surface pH, and rapid drug release, making them promising for effective buccal drug delivery of Midodrine Hydrochloride.

Keywords: Midodrine Hydrochloride, mucoadhesive buccal tablet, immediate release, Crospovidone, Carbopol 934P.

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INTRODUCTION

Among the various routes of drug delivery, the oral route is the most suitable and widely accepted by patients for the delivery of therapeutically active drugs. However, many drugs are subjected to pre-systemic clearance in the liver, acid degradation, which often leads to a lack of correlation between membrane permeability, absorption, and bioavailability[1-3].Mucoadhesive drug delivery systems are those which utilize the advantage of the bioadhesion of certain polymers in drug delivery. [4][5].The buccal mucosa is used to give medications because it has a lot of blood flow and is easy for medicines to pass through. Because the buccal mucosa also makes it hard for drugs to be absorbed, penetration enhancers are used to help the drug get through the mucosa and make the drug more bioavailable[6].

Midodrine is an aromatic ether that is 1, 4-dimethoxybenzene which is substituted at position 2 by a 2-(glycylamino)-1-hydroxyethylgroup.

A direct-acting sympathomimetic with selective alpha-adrenergic agonist activity, it is used (generally as its hydrochloride salt) as a peripheral vasoconstrictor in the treatment of certain hypotensive states. Many patients require quick onset of action in particular therapeutic condition and consequently immediate release of medicament is required[7][8].

MATERIALS AND METHODS

Drug and Chemicals

Midodrine HCl received as a gift sample from Actavis Pharma Manufacturing Pvt. Ltd. Alathur. Microcrystalline Cellulose, Magnesium Stearate and Lactose, Spray Dried obtained From Glenmark Pharmaceuticals Ltd, Goa. Crospovidone, Croscarmellose Sodium, Dextrose Monohydrate obtained from Signet Excipients Pvt. Ltd., Mumbai. Sodium Citrate and Carbopol934P obtained from S.D.Fine Chemicals, Mumbai. All the reagents and Chemicals used were of analytical grade.

Instruments

Digital weighing balance (Shimadzu AX200, Japan), UV visible Spectrophotometer (UV-1800 PC Shimadzu Corporation, Japan), Rotary Tablet Punching Machine (Pilot Press, Gujrat),FTIR Spectrophotometer (Shimadzu Corporation, Japan), Friability Tester (Roche Friabilator), Pfizer Hardness Tester (Electro Lab Pvt. Ltd., Goregaon),Franz Diffusion Cell Apparatus (Orchid Scientifics, FDC 06, Mumbai), Disintegration Apparatus (Electro Lab Pvt. Ltd., Goregaon, Mumbai), Thickness Tester (Mitutoyo Vernier Caliper, Japan), Stability Chamber (Skylab, Mumbai).

Methods

Preparation of Immediate Release Mucoadhesive Buccal Tablet of Midodrine HCl

Immediate Release Mucoadhesive Buccal tablets of Midodrine Hydrochloride were prepared by a direct compression method. Before going to direct compression, all the ingredients (drug, polymers, and excipients) were screened through sieve no.60. All the ingredients were thoroughly blended in a glass mortar with a pestle for 15 minutes. After sufficient mixing magnesium stearate was added and again mixed for additional 2-3 minutes. The mixture is compressed using a 9 mm punch on a rotary tablet punching machine. The Formulation of tablets were presented in Table 1.

Table 1: Formulation of Midodrine HCl Trial Batches

Sr. No.	Ingredients (mg)	B1	B2	B3	B4	B5	B6
1	**Midodrine HCl**	10	10	10	10	10	10
2	**Microcrystalline Cellulose**	150	150	150	150	150	150
3	**Croscarmellose Sodium**	8	10	12	-	-	-
4	**Crospovidone**	-	-	-	8	10	12
5	**Dextrose Monohydrate**	2	2	2	2	2	2
6	**Sodium Citrate**	1	1	1	1	1	1
7	**Magnesium Stearate**	2	2	2	2	2	2
8	**Carbopol 934 P**	4	6	8	4	6	8
9	**Lactose**	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
	Total Wt. of Each Tablet (mg)	200	200	200	200	200	200

Optimization of trial batch (B6) by full factorial design

In order to obtain "best" or an "optimized product" nine different formulations were generated using a 3^2 randomized full factorial design.Based on preformulation study the amounts of Crospovidone (X1) and Carbopol 934P (X2) were selected as the independent factors, studied at 3 levels each (-1, 0, +1). The Diffusion Time (Y1) and Mucoadhesive Strength (Y2) were taken as dependent factors. Experimental trials were performed at all 9 possible combinations of X1 and X2. The formulations of all batches for factorial design are shown in Table 2.The formulation of optimized trial batches was presented in Table 4[9][10].

Table 2: Formulation trials as per experimental design

Formulation Code	Coded value	
	X1	X2
F1	-1	-1
F2	0	-1
F3	+1	-1
F4	-1	0
F5	0	0
F6	+1	0
F7	-1	+1
F8	0	+1
F9	+1	+1

Table 3: Translation of coded levels in actual units

Coded value	Actual value	
	X1	X2
-1	12	8
0	14	11
+1	16	14

Table 4: Formulation of optimized batches

Sr. No.	Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	MidodrineHCl	10	10	10	10	10	10	10	10	10
2	Microcrystalline Cellulose	150	150	150	150	150	150	150	150	150
3	Crospovidone	12	14	16	12	14	16	12	14	16
4	Dextrose Monohydrate	2	2	2	2	2	2	2	2	2
5	SodiumCitrate	1	1	1	1	1	1	1	1	1
6	Magnesium Stearate	2	2	2	2	2	2	2	2	2
7	Carbopol 934P	8	8	8	11	11	11	14	14	14
8	Lactose	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
	Total Weight of Each Tablet (mg)	200	200	200	200	200	200	200	200	200

Chemical compatibility studies by FT-IR

The crude drug sample and drug-excipient mixtures from the formulation were chosen for the purpose of study. Disk was created by compressing the samples using potassium chloride. The disk was scanned between 4000-400 cm-1 in a SHIMADZU FT-IR (IR Affinity1) spectrophotometer[11].

Standard Calibration Curve for Midodrine HCl in Phosphate Buffer (pH6.8)

10 mg was dissolved in a 10ml of phosphate buffer (pH 6.8) and volume was made up to 100ml using the same. From the stock solution, serial dilutions were done to obtain solutions in the concentration Ranging from 2 to 10 µg/ml. The absorbance of the solution was measured at 289 nm using a UV-visible spectrophotometer[12].

Pre-compression parameters

The powder was evaluated for pre compression parameters like angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The angle of repose was determined by funnel method. Bulk and tapped density were determined using digital bulk density apparatus. The compressibility index of the powder was determined by Carr's compressibility index and the Hausner's ratio was calculated by using the formula[13-15]:

Hausner's Ratio = Tapped density/ Bulk density.

Carr's index (%) = [(TD-BD) / TD] ×100.

TD = Tapped density, BD = bulk density.

Tan θ = h/r

Post Compression Parameters

a. **Weight Variation:** Twenty tablets were weighed together and separately using analytical balance. The average weight and percent variation of the tablet were calculated. The weight uniformity was determined according to USP specification[16].

b. **Hardness:** The Pfizer hardness tester was used to determine the hardness of the tablet. The tablet was held between a fixed and moving jaw. The scale was adjusted to zero; the load was gradually increased until the tablets fractured. The value of the load at that point gives a measure of the hardness of the tablet. Tablet requiresa certain amount of strength or hardness and resistance to friability to withstand mechanical shocks of handling in manufacture, packing, and shipping. Three tablets from each batch are used for the hardness test and the results are expressed in Kg/cm^2[16].

c. **Thickness:** The thickness of three randomly selected tablets from each formulation was determined in mm using a Vernier Caliper thickness tester. The average values were calculated[17].

d. **Friability:** Friability is the measure of tablet strength. Roche-type friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min, the tablets were weighed and the percentage loss was determined [18].

$$\% \text{ Friability} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Final Weight}} \times 100$$

e. **Drug Content Uniformity:** Ten tablets from each formulation were taken, crushed, and mixed. From the mixture 10 mg of Midodrine hydrochloride equivalent of the mixture was extracted thoroughly with100ml of pH6.8 phosphate buffer. The amount of drug present in each extract was determined using a UV spectrophotometer at 289 nm. This procedure was repeated thrice and this average was chosen[19].

$$\% \text{ Drug Content} = \frac{\text{Absorbance}}{\text{Weight Taken}} \times 100$$

f. **In vitro Disintegration test:** A 1000 mL beaker was filled with 900 ml of distilled water and was maintained at a temperature of 37 ± 0.5 ºC. Six tablets were placed in each of the cylindrical tubes of the basket. To avoid floating of the tablets, discs were used. The time taken to break the tablets into small particles was recorded[19].

Bio adhesive Parameters:

1. Surface pH: The microenvironment pH (surface pH) of the buccal tablets was determined to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may irritate the buccal mucosa, it was determined to keep the surface pH as close to neutral as possible. A combined glass electrode was used for this purpose. The tablet was allowed to swell by keep in git in contact with 2ml of distilled water (pH 6.5±0.05) for 10 min at room temperature. The pH was measured by bringing the electrode in contact with the surface of the tablets and allowing it to equilibrate for 1 min[20].

2. Mucoadhesive Strength: Mucoadhesive strength of the tablet was measured on a modified physical balance. The Dialysis membrane (pore size 2.4 nm purchased from HIMEDIA) was used. Cut into a piece of 4 cm and then boiled in water for 20-25 mins then separated membrane was cut into 4x2cm was hed with phosphate buffer pH 6.8. A piece of dialysis membrane was stuck to the inverted 50 ml beaker which is placed in the centre of a250 ml beaker containing phosphate buffer (pH 6.8). The tablet was stuck to the lower side of the glass vial with cyanoacrylate adhesive. Two pans of the balance were balanced with 5gm weight on the right-hand side pan. A weight of 5 gm was removed from the right-handside pan, which lowered the pan along with the tablet over the membrane. The balance waskept in this position for 5 minutes contact time. The water was added slowly by hand (1drop/min.) to the right-hand side pan until the tablet detached from the membrane surface. The weight in grams required to detach the tablet from the membrane surfaces gave theme a sure of mucoadhesive strength. The weight, in grams, needed to detach the tablet from the dialysis membrane surface results in the measure of mucoadhesive strength. The following parameters were calculated from the mucoadhesive strength[20].

$$\textit{Force of adhesion (N)} = \textit{(Bioadhesivestrength/1000)} \times 9.81 \times \textit{SurfaceArea}$$

3. Mucoadhesion Time: Mucoadhesion Time of the tablet was measured by using Dialysis membrane (Dialysis Membrane-150; LA401-5MT; average diameter 25.4mm and average flat width 42.44mm, poresize2.4nm purchased from HIMEDIA). Dialysis membrane was cut into a piece of 4 cm and then boiled in water for 20-25 mins for activating then separated membrane was cut into 4 x 2 cm washed with phosphate buffer pH 6.8. A piece of dialysis membrane was sticked on glass slide with cyanoacrylate adhesive. Tablet was wetted with phosphate buffer (pH 6.8) and pasted to the Dialysis membrane by applying a light force with fingertip for 20 seconds [20]. The slide was kept inclined and phosphate buffer (pH 6.8) was added 0.4 ml/min, as the tablet start sliding from dialysis membrane that time was noted as adhesion time of the tablet.

In Vitro Drug Diffusion Study:

In Vitro drug diffusion of Midodrine Hydrochloride was studied using synthetic dialysis membrane (Dialysis Membrane - 150; LA401 - 5MT; average diameter 25.4 mm and average flat width 42.44 mm, pore size 2.4 nm purchased from HIMEDIA) as a barrier membrane. Cut into a piece of 4 cm and then boiled in water for 20-25 mins for activating membrane then separated membrane was cutted into 4 x 2 cm. The membrane was washed with distilled water and then with phosphate buffer pH 6.8. The in vitro diffusion study was carried out using the modified Franz diffusion cell at 37°C ± 12°C. The dialysis membrane (4x2 cm diameter) was tied to one end of the Franz diffusion cell, which acted as donor compartment. The buccal tablet containing 10 mg of Midodrine hydrochloride was kept on the dialysis membrane, in such a way that the lower surface of the ablet was in contact with the dialysis membrane then the donor compartment was fixed, so that dialysis membrane was in contact with the receptor medium, 25 ml of phosphate buffer, pH 6.8 in the receptor compartment. Samples of (1ml) were withdrawn at predetermined time intervals (l0,20,30,40,60 and 100 mins) and volume was replaced with the fresh medium. The samples were filtered through Whatman filter paper and analysed after appropriate dilution by UV spectrophotometry #289 nm (Shimadzu Corporation, Japan). The experiments for all formulations were conducted implicate and average values were recorded [21].

Stability Study:

As per ICH guidelines, a stability study was carried out at 40°C ± 2°C / 75 RH ± 5% for 28 days (4 weeks) for the optimized formulation. The optimized formulation was analyzed for the % Drugcontent, Disintegration time ucoadhesive Strength, Surfacep Hand Invitro % Cumulative Drug Diffusion Study [22].

Results And Discussion:

Chemical compatibility studies by FT-IR

Based on the FTIR interpretation results, all the major drug peaks were identified when compared with the physical mixture of drug and polymer, which ensures that there was no any chemical interaction between them.

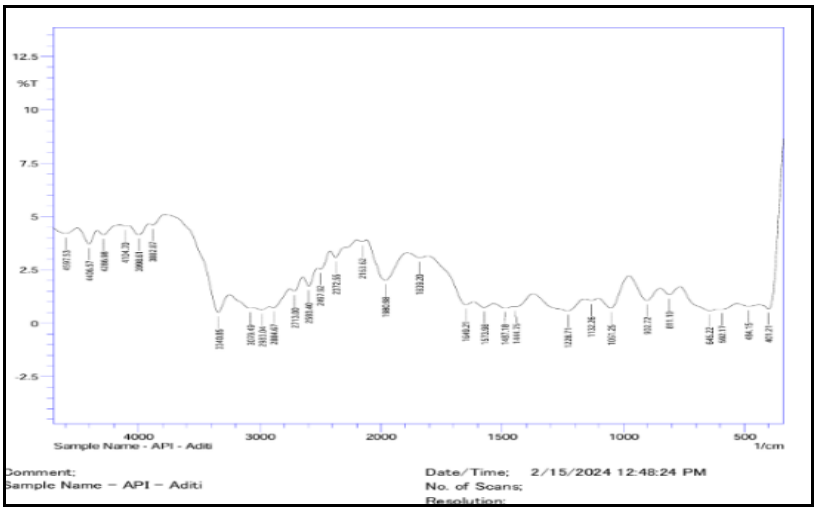

Figure 1: FTIR spectrum of Midodrine Hydrochloride

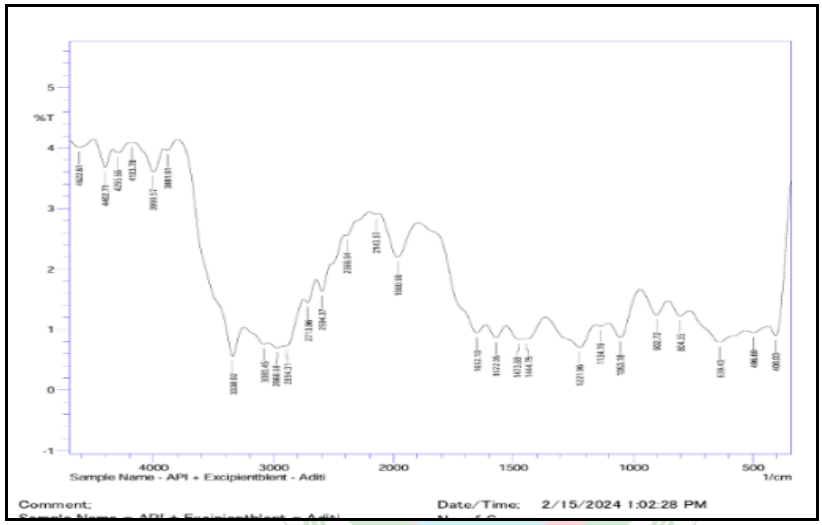

Figure 2: FTIR spectrum of Drug + Excipients

II. Standard Calibration Curve for Midodrine HCl in Phosphate Buffer (pH6.8)

Table 5: Standard Calibration Curve of Midodrine HCl in pH 6.8 Phosphate Buffer

Sr. No	Concentration(µg/ml)	Absorbance
1	0	0
2	2	0.04 ± 0.01
3	4	0.078 ± 0.05
4	6	0.11 ± 0.01
5	8	0.15 ± 0.01
6	10	0.19 ± 0.02

n=3

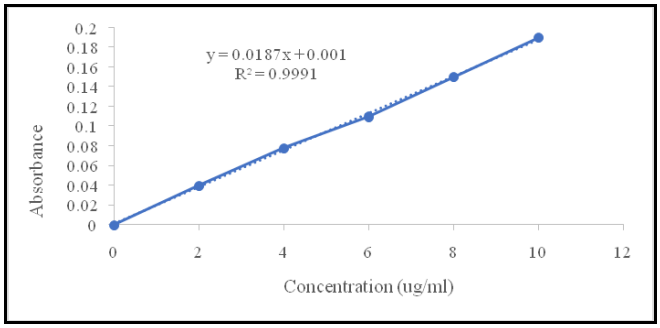

Figure 3: Standard Calibration Curve of Midodrine HCl in pH 6.8 Phosphate Buffer at 289 nm

III. Pre-compression Study of Factorial Batches:

Table 6: Pre-compression Study of Factorial Batches

Batch Code	Bulk Density (g/cm^3±SD)	Tapped Density (g/cm^3± SD)	Carr's Index (%±SD)	Hausner's Ratio (± SD)	Angle of Repose (θ±SD)
F1	0.381 ± 0.146	0.440 ± 1.53	13.40 ± 2.81	1.15 ± 0.39	30.42 ± 1.32
F2	0.366 ± 0.240	0.427 ± 1.43	14.28 ± 1.17	1.16 ± 1.20	30.85 ± 0.49
F3	0.390 ± 0.562	0.441 ± 1.25	11.56 ± 2.43	1.13 ± 1.45	32.75 ± 0.89
F4	0.391 ± 0.621	0.451 ± 1.76	13.30 ± 2.41	1.15 ± 1.40	33.45 ± 0.57
F5	0.342 ± 0.425	0.403 ± 1.65	15.13 ± 1.64	1.17 ± 1.29	34.45 ± 2.06
F6	0.359 ± 0.842	0.420 ± 1.47	14.52 ± 2.53	1.16 ± 1.20	33.44 ± 2.82
F7	0.356 ± 0.238	0.416 ± 1.24	14.42 ± 1.63	1.14 ± 1.20	33.19 ± 1.61
F8	0.371 ± 0.825	0.431 ± 1.79	13.92 ± 1.50	1.16 ± 1.30	33.69 ± 2.52
F9	0.351 ± 0.973	0.406 ± 0.23	13.54 ± 1.42	1.15 ± 1.18	32.85± 0.48

n=3

- **Bulk and Tapped Density:**

The**Bulk and Tapped Density** of formulations from F1 to F9 was in the range **0.342 ± 0.425- 0.391 ± 0.621 gm/cm^{3}and 0.403 ± 1.65 - 0.451 ± 1.76 gm/cm^3** respectively. It indicates small difference between bulk density and tapped density which suggests good compressibility while particles can rearrange efficiently under mechanical stress.

- **Carr's Index**:

Carr's Index of formulations from F1 to F9 was found up to 15 % for all formulations in the range of **11.56 ± 2.43 - 15.13 ± 1.64 %** indicating that the powder bed is compressible.

- **Hausner's Ratio:**

Hausner's Ratio of formulations from F1 to F9 was in the range of **1.13 ± 1.45 - 1.17 ± 1.29**.Thus, it indicates minimal volume change upon tapping indicating good flowability and compressibility.

- **Angle of Repose:**

Angle of Repose of formulations from F1 to F9 was determined after addition of lubricant it found in the range of **30.42 ± 1.32 - 34.45 ± 2.06 *θ***. The results indicates that the powder beds of all formulations are freely flowable and easily compressible.

IV. Post-compression Study of Factorial Batches:

Table 7: Post-compression Study of Factorial Batches

Batch Code	Wt. Variation (±SD)	Hardness (±SD)	Thickness (±SD) mm	Friability (% ± SD)	% Drug Content	Disintegration time (mins)
F1	199.8 ± 2.356	4.4 ± 0.1	3.14 ±0.02	0.47 ±0.22	98.17 ±1.57	3.78 ± 0.12
F2	200.08 ±1.560	4.6 ± 0.4	3.19 ±0.01	0.45 ±0.11	98.35 ±1.74	3.62 ± 0.8
F3	199.20 ±1.564	3.9 ± 0.3	3.25 ±0.03	0.55 ±0.15	99.81 ±2.68	3.50 ± 0.08
F4	199.6 ±2.141	4.5 ± 0.5	3.17 ±0.01	0.41 ±0.19	99.75 ±3.11	4.10 ± 0.15
F5	200.5 ±1.803	4.7 ± 0.5	3.21 ±0.02	0.50 ±0.13	98.84 ±0.64	4.09 ± 0.72
F6	198.4 ±1.216	4.6 ± 0.6	3.18 ±0.02	0.48 ±0.15	99.1 ±1.033	4.03 ± 0.29
F7	200.05 ±0.548	4.8 ± 0.2	3.21 ±0.11	0.51 ±0.19	99.02 ±2.51	4.40 ± 0.11
F8	198.43 ±1.53	4.8 ± 0.5	3.21 ±0.03	0.49 ±0.54	99.19 ±1.76	4.36 ± 0.27
F9	200.08 ±0.628	4.5 ± 0.4	3.16 ±0.05	0.43 ±0.33	98.38 ± 2.78	4.30 ± 0.09

n=3

- **Weight Variation:**

Average Weight of all Tablets within formulation was found to be uniform. This indicates uniform filling of the die cavity during tablet compression. Since the average weight of all tablets was almost **200 mg**, the test requirements are met if none of the individual tablet weights is less than 95% or more than 105% of the average weight.

- **Hardness and Thickness:**

- **Hardness** of Tablets was determined with hardness tester and the hardness was found to be in the range of **3.9 ± 0.3**

to 4.8 ± 0.5 kg/cm^2 this is ensures right compression force indicating desired range of tablet Hardness and All the tablets are within the acceptable range for tablet thickness with values ranging from **3.14 ± 0.02 to 3.25 ± 0.03 mm.**

- **Friability:**

The **Friability** of all Mucoadhesive Buccal Tablets was found to be in the range of **0.41 ± 0.19 to 0.55 ± 0.15 %**. It indicates desired friability of formulations due to appropriate binders, fillers and other excipients that leads to good tablet cohesion and strength.

- **Drug Content:**

Drug Content of all formulations was found to be between **98.17 ± 1.57to 99.81 ± 2.68%**. The values ensure good uniformity of drug content in the tablet.

- **Disintegration Time:**

Disintegration time of all Mucoadhesive Buccal Tablets was found to be in the range of **3.50 ± 0.08 to 4.40 ± 0.11 mins**. This ensures immediate release onset of action because of the addition of super disintegrants.

V. Bioadhesive Parameters of Factorial Batches:

Table 8: Surface pH, Mucoadhesive strength, Force of adhesion and Mucoadhesion time of Factorial Batches

Batch Code	Surface pH	Mucoadhesive Strength (gm)	Force of Adhesion (N)	Mucoadhesion Time (mins)
F1	6.67 ± 0.10	08.56 ± 0.35	0.088 ± 0.93	54.50 ± 0.54
F2	6.56 ± 0.31	08.61 ± 0.14	0.089 ± 0.31	54.45 ± 0.25
F3	6.48 ± 0.31	07.56 ± 0.65	0.085 ± 0.70	54.06 ± 0.58
F4	6.42 ± 0.23	09.64 ± 0.48	0.097 ± 0.23	56.59 ± 0.45
F5	6.76 ± 0.45	09.70 ± 0.48	0.097 ± 0.07	55.48 ± 0.55
F6	7.33 ± 0.12	09.26 ± 0.30	0.094 ± 0.31	55.41 ± 0.6
F7	6.44 ± 0.13	09.55 ± 0.48	0.096 ± 0.54	58.36 ± 0.35
F8	6.34 ± 0.18	09.30 ± 0.23	0.094 ± 0.64	58.58 ± 0.24
F9	7.07 ± 0.19	09.16 ± 0.25	0.093 ± 0.68	57.24 ± 0.51

n=3

- **Surface pH:**

Surface pH of all Mucoadhesive Buccal Tablets was found to be in the range of **6.34 ± 0.18 to 7.33 ± 0.12** This ensures that all formulated tablets was in orally acceptable range.

- **Mucoadhesive Strength and Force of adhesion:**

Mucoadhesive Strength of all Mucoadhesive Buccal Tablets was found to be in the range of **07.56 ± 0.65 to 09.70 ± 0.48 g**. This ensures good mucoadhesive strength because of the addition of mucoadhesive polymer Carbopol 934P and **Force of adhesion** of all Mucoadhesive Buccal Tablets was found to be in the range of **0.088 ± 0.93 to 0.097 ± 0.23 N**. This ensures a desired force of adhesion.

- **Mucoadhesion Time:**

Mucoadhesion Time of all Mucoadhesive Buccal Tablets was to be in range of **54.06 ± 0.58 to 58.36 ± 0.35 minutes** because of the Varying Concentration of Mucoadhesive Polymer.

VI. In Vitro Drug Diffusion Study of Factorial Batches:

% Cumulative Drug Diffusion of Mucoadhesive BuccalTablets (F1-F9) was found in the range of **92.11 ± 0.51 to 94.4 ± 0.98 %** within 80-100 min. It was observed that %Cumulative Drug Diffusion of Mucoadhesive Buccal Tablets depend on the concentrations of Crospovidone and Carbopol 934P. Maximum % Cumulative Drug Diffusion was found 94.4 ± 0.98% within 80 mins for F3 and prolong %Cumulative Drug Diffusion was found 94.07 ±0.27 within 100 mins for F4. From the obtained results F3 was found to be optimized batch.

Table 9: Invitro Drug Diffusion Study of Factorial Batches

Batch Code	% Cumulative Drug Diffused (in mins)							
	0	**10**	**20**	**30**	**40**	**60**	**80**	**100**
F1	0	5.17 ± 0.54	8.81 ± 0.62	13.49 ±0.59	27.97 ±0.34	68.68 ±0.35	85.09 ±0.56	93.95 ±0.36
F2	0	6.96 ± 0.59	9.36 ± 0.23	13.98 ±0.86	29.30 ±0.48	70.07 ±0.32	88.53 ±0.69	94.07 ±0.27
F3	0	7.85 ± 0.74	11.83 ± 0.41	15.13 ±0.52	30.36 ±0.77	72.52 ±0.48	94.4 ±0.98	-
F4	0	6.63 ±0.13	9.78 ± 0.49	13.15 ±0.33	28.18 ±0.54	67.11 ±0.12	86.79 ±0.38	92.11 ±0.51
F5	0	7.66 ±0.78	9.86 ±0.32	14.26 ±0.21	30.05 ±0.54	71.71 ±0.16	89.07 ±0.77	93.81 ±0.33
F6	0	10.96 ±0.16	14.16 ±0.49	28.63 ±0.66	48.40 ±0.75	74.03 ±0.61	86.74 ±0.45	94.03 ±0.14
F7	0	6.87 ±0.17	8.23 ±0.88	15.14 ±0.78	29.65 ±0.54	65.21 ±0.36	78.52 ±0.34	93.21 ±0.49
F8	0	7.85 ±0.37	10.6±0.44	18.44 ±0.73	30.34 ±0.52	69.56 ±0.12	83.31 ±0.45	94.01 ±0.62
F9	0	9.89 ±0.22	12.2±0.32	20.74 ±0.26	31.02 ±0.15	72.75 ±0.33	86.23 ±0.63	93.54 ±0.65

n=3

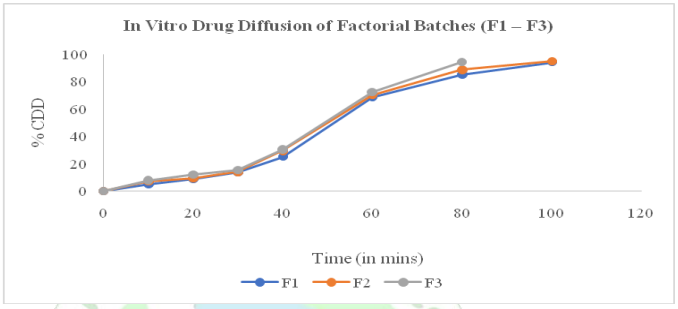

Figure 4: In Vitro Drug Diffusion of Factorial Batches (F1-F3)

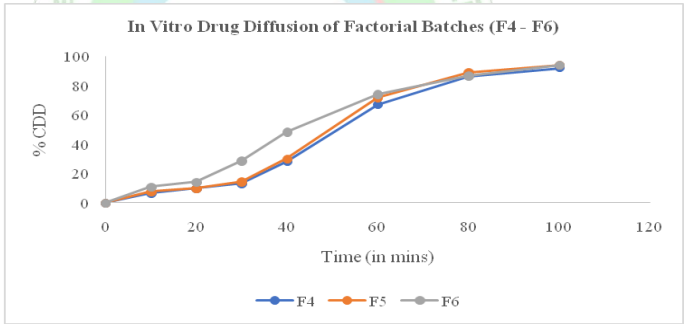

Figure 5: In Vitro Drug Diffusion of Factorial Batches (F4-F6)

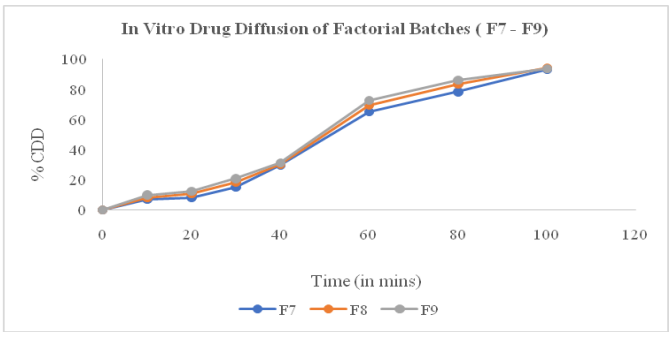

Figure 6: In Vitro Drug Diffusion of Factorial Batches (F7–F9)

VII. Accelerated Stability Study:

The Accelerated stability studies evaluation of batch F3 revealed that there is No significant change was observed over 4 weeks. No significant change was observed in % Drug Content, Disintegration Time, Mucoadhesion Strength, Surface pH and % Cumulative Drug Diffusion at storing condition 40°C ± 2°C / 75 ± 5% RH. Hence formulation F3 was found to be stable for 4 weeks.

Table 10: Accelerated Stability study at 40°C ± 2°C/75 ± 5% RH

Sr. No	Stability (40 ± 2^0C, 75 ± 5%RH)	Drug Content %	Disintegration Time(mins)	Mucoadhesive Strength(gm)	Surface PH Mean ±SD	% Cumulative Drug Diffusion
1	**0 Day**	99.62±0.662	3.50 ± 0.08	7.56 ± 0.65	6.38±0.31	94.4 ± 0.98
2	**1Week**	99.64±0.533	3.55 ± 0.75	8.02 ± 0.12	6.46±0.15	94.52±0.85
3	**2Weeks**	99.49±0.655	3.43 ± 0.36	7.86 ± 0.55	6.32±0.19	93.75±0.22
4	**3Weeks**	99.09±1.564	3.46 ± 0.55	7.90 ± 0.12	6.27±0.17	93.85±0.57
5	**4Weeks**	98.70±1.961	3.52 ± 0.41	7.58 ± 0.41	6.32±0.13	93.98±0.12

n=3

CONCLUSION

The Mucoadhesive Buccal Tablets of Midodrine Hydrochloride, formulated using crospovidone and Carbopol 934P, offer a promising immediate-release onset of action. Batch F3 (Crospovidone 16 mg and Carbopol 934P 8 mg) emerged as the optimized formulation, providing a high cumulative drug diffusion rate within a short duration, albeit with slightly lower mucoadhesive strength. The concentration of crospovidone affected disintegration and drug diffusion rates, while the mucoadhesive polymer concentration influenced mucoadhesive properties. The selected optimized batch balances these factors, ensuring immediate release while maintaining acceptable mucoadhesive strength. Accelerated Stability studies confirmed the tablets' integrity under storage conditions, highlighting their potential for practical use. The developed formulation addresses the challenge of acid degradation in the gastrointestinal tract, offering enhanced therapeutic action through buccal delivery.

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