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Formulation and Evaluation of Mouth Dissolving Tablet of Moexipril Hydrochloride

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Abstract: Mouth Dissolving Tablets (MDT) are the most accepted and exploited drug delivery for patients who are having difficulty swallowing, i.e., Geriatric patients. Moexipril Hydrochloride is used as an antihypertensive drug but goes under first-pass metabolism due to low bioavailability (13%). Fast onset of action is a major concern in the management of hypertension. Therefore the aim of this study was to formulate mouth-dissolving tablets of Moexipril Hydrochloride to improve its bioavailability and decreases dosing frequency, to achieve fast onset of action and increase patient compliance. Mouth dissolving tablets were prepared by direct compression method using super Disintegrating agents (croscarmellose and sodium starch glycolate) and evaluated for pre-compression parameters and post-compression parameters such as appearance, hardness, weight variation, friability, wetting time, water absorption ratio, disintegration and dissolution study. Prepared tablets were subjected to FT-IR study for characterization and compatibility study. No chemical interaction between the drug and excipients was indicated in the FT-IR. Optimized formulation showed a good release profile with Formulation (F-7) containing crosscarmellose showed 96.2% drug release in 15 min and a disintegration time of 28.24 sec.

Keywords: Mouth dissolving, Super-Disintegrants, Dysphasia, Bioavailability, Crosscarmellose sodium, Sodium starch glycolate

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Introduction

Mouth-dissolving tablets disintegrate or dissolve in saliva and are swallowed without the need for water. They offer an advantage over swallowing tablets and capsules. Difficulty to swallow is particularly experienced by paediatric and geriatric patients. Technique that is frequently employed in the preparation of mouth-dissolving tablets include, freeze drying, sublimation, spray drying, moulding, mass extrusion, and direct compression (Kuccherkar *et al*., 2003).

United States Food and Drug Administration (FDA) defined MDT as -- A solid dosage form

containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue. The disintegration time for mouth dissolving tablets generally range from several seconds to about 3 min (Bi *et al*., 1999; Adelli *et al*., 2017).

Due to the presence of super-disintegrants, it gets dissolved quickly, resulting in rapid absorption of drug which results rapid onset of action. In mouth dissolving tablets the absorption is taking place directly from mouth and do not suffers from the first pass metabolism, so bioavailability of drug increases (Dey and Maiti, 2010).

Moexipril Hydrochloride is an angiotensive II receptor antagonist and used as antihypertensive drug. The molecular weight of Moexipril Hydrochloride is 535 g/mol^{-1}, half life 2 to 9 h, and its Bioavailability 13%. It gets metabolized mainly in the liver. Mouth dissolving tablets are soluble in saliva and are absorbed from the mouth, pharynx and esophagus as the saliva passes down into stomach, thus enhance the bioavailability by avoiding first pass metabolism. Mouth dissolving tablets also leads to an increased patient compliance, and fast onset of action. Keeping all these factors in mind, it was considered appropriate to formulate mouth dissolving of Moexipril Hydrochloride (Jain and Naruka, 2009).

Materials and Methods

Moexipril Hydrochloride was received as a gift sample from Glenmark Life Sciences, Goa, India. Microcrystalline cellulose, Sodium starch glycolate, Croscarmellose sodium were purchased from Loba Chemicals Limited.

Pre-formulation studies:

Determination of wavelength using UV- visible spectroscopy:

50 mg drug was weighted and dissolved into 50 ml of phosphate buffer solution (pH 6.8) and water to prepare a 1000 µg/ml stock solution from which a 5 µg/ml dilution was prepared. Baseline correction was performed using Phosphate buffer solution (pH 6.8) and water sample was scanned between 200-400 nm and wavelength of maximum absorbance (λ) was noted.

Calibration curve of Moexipril Hydrochloride in distilled water:

Accurately weighted 50 mg of Moexipril Hydrochloride was transferred into a 50ml volumetric flask and dissolved. The volume was made up with distilled water to obtain a 1000 µg/ml stock solution of Moexipril Hydrochloride. 1 ml was taken into a 10 ml volumetric flask and volume was made up with distilled water to obtain a 100 µg/ml of solution. Further dilution was made. The absorbance of each dilution was noted.

Calibration curve of Moexipril Hydrochloride in Phosphate buffer pH 6.8:

Accurately weighted 50 mg of Moexipril Hydrochloride was transferred into a 50 ml volumetric flask and dissolved. The volume was made up with Phosphate buffer pH 6.8 to obtain a stock solution of Moexipril Hydrochloride. 1 ml was taken into a 10 ml volumetric flask and volume was made up with Phosphate buffer pH 6.8 to obtain a 100 µg/ml of solution. Further dilution was made. The absorbance of each dilution was noted.

Evaluation parameter:

Pre-compression Parameters (*Cooper et al., 1986*; *Subrahmanyam, 2007*):

Precompression parameter were evaluated on the basis of angle of repose, bulk density, tapped density, carr's index etc. and results were calculated on the basis of different formulas.

Post-Compression Parameters (*Indian Pharmaco-poeia, 2007*; *Jagadale and Patil, 2013*):

Weight Variation: Twenty tablets were selected randomly from every formulation and their average weight was determined. All tablets weighted individually and compared with average weight. If more than two tablets deviate from the range, retest 20 tablets and not more than 2 tablets should deviate from 40 tablets.

Hardness: The hardness of the tablet was determined using Monsanto hardness tester apparatus. Placed the tablet on the lower plunger and zero reading was taken from Monsanto tester scale. The range of Monsanto hardness tester is 0 to 20 kg.

Thickness: Thickness of the tablet was calculated by the use of Vernier caliper. The scale was set to zero and placed the tablet laterally between the jaws of Vernier caliper. Subsequently make sure certain jaws shall just touch object to be measured. The reading displayed was recorded.

Friability: Friability of the tablet was determined by Roche friabilator. Tablets were weighed before placing in friability apparatus. Placed 10 tablets in the friabilator and subjected to 100 revaluations for 4 min at 25 rpm and dropping the tablet at the height of 6 inch in each revolution. Taken out the tablet after 100 revaluations completed. The tablet was Reweight and degusted. A maximum loss of weight not greater than 1.0 % is acceptable for most tablets.

Drug content: The drug content was determined by calibration curve method as follow: The tablets were taken and amount of drug present in each formulation of tablet was determined. The tablet was crushed in a mortar-pestle and equivalent to 10 mg of drug was dissolved in phosphate buffer pH 6.8 in a 100 ml volumetric flask. Volume was made up to 100 ml. The sample was filtered through filter paper. From this solution 1 ml was taken in a 10 ml volumetric flask and diluted with phosphate buffer pH 6.8. Further, 1 ml was taken and diluted up to 10 ml and analyzed for drug content by UV spectrophotometer at 281.90 nm using phosphate buffer (pH 6.8).

Wetting time: Five tissue papers of 10 cm diameter were placed in a Petridis with a 10 cm in a diameter. Ten milliliters of water containing eosin, a water-soluble dye, was added to Petri dish. A tablet was placed carefully on the surface of the tissue paper. The time required to reach the water to upper surface of the tablet was noted as a wetting time.

Water absorption ratio: A piece of tissue paper folded twice was placed in a small Petridis containing 10 ml of distilled water. A tablet was put on the tissue paper and the time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch.

Disintegration time: First suspend the assembly in the beaker containing phosphate buffer pH 6.8 at 37±0.5 ˚C. The tablet was placed into each of the six tubes of the disintegrating apparatus and one disc was added to each tube. Operated the apparatus until the tablet completely disintegrated. Note down the time taken for the complete disintegration of the tablet without any residuals. The tablets were passed the test if all of them have disintegrated completely. The test was repeated on 12 additional tablets. Not less than the 16 tablets of the total of 18 tablets pass the test. If the tablets adhered to the disc and preparation under examination failed to comply, repeated the test and the disc was omitted. Disintegration time: mouth dissolving tablet: within 3 min.

In vitro drug release study: *In vitro* drug release study was determined by dissolution test apparatus. The water level was maintained in water bath up to specific mark and temperature was adjusted with the help of heater knob. The phosphate buffer (pH 6.8) was poured upto the mark in dissolving vessel and temperature was maintained at 37±0.5 °C. The shaft was positional in such a way that its axis is within 2 mm of axis of the vessel and lower edge of blade was 23-27 mm from the inside of bottom of vessel were lowered down. The tablet was put in each vessel and paddle was rotated at speed of 50 rpm for 30 min. Withdrawn 5 ml sample at every 5 min interval and replaced it by equal volume of fresh dissolution medium. Filtered the sample using Whatman filter paper and analyzed for drug release of the sample by UV- visible spectrophotometer at λ max 282 nm using phosphate buffer pH 6.8 as blank.

Table 1: Organoleptic Properties

S. No.	Organoleptic Properties	Specified	Observed
1	Color	White	White
2	Odor	Unpleasant	Unpleasant
3	Taste	Metallic	Metallic

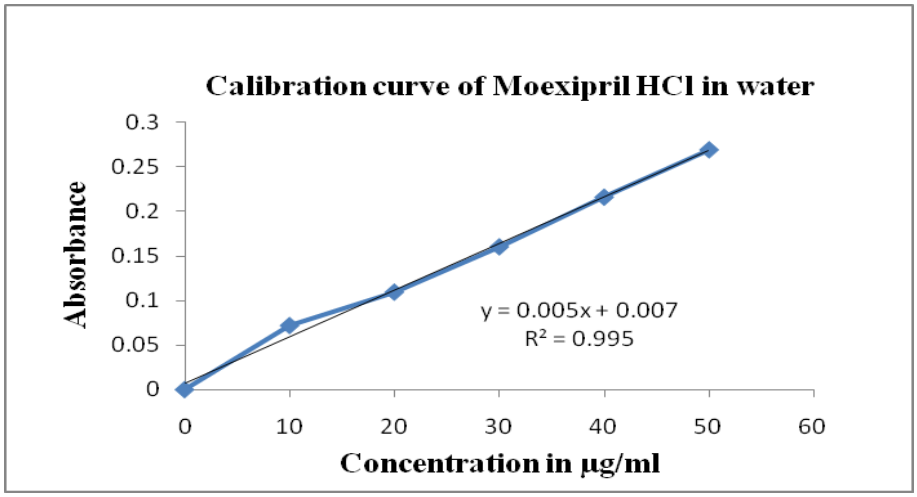

Fig. 1: Calibration curve of Moexipril Hydrochloride in water.

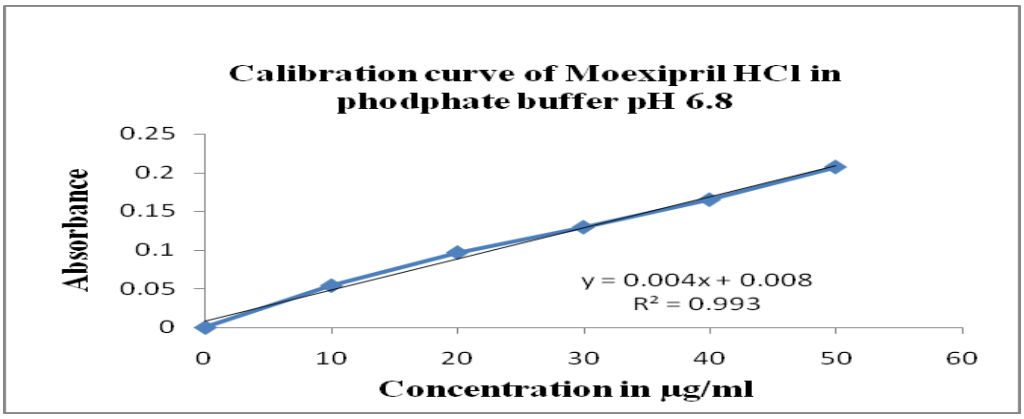

Fig. 2: Calibration curve of Moexipril Hydrochloride in phosphate buffer pH 6.8.

Stability study: The stability study of Mouth dissolving tablet was studied at different storage condition. The prepared batches was re-evaluated, on the basis of its appearance, drug content, *in vitro* drug release and disintegration behavior after being stored at 25 ˚C and 40% RH for one and two months, respectively.

Results and Discussion

Pre-formulation studies: Physical properties of drug were investigated (Table 1).

Determination of wavelength using UV-visible spectroscopy: The maximum Wavelength of Moexipril Hydrochloride was found to be 281.90 nm distilled water (Fig. 1).

Determination of wavelength using UV-visible spectroscopy: The maximum Wavelength Hydrochloride was found to be 282 nm at a phosphate buffer pH 6.8 (Fig. 2).

Melting point determination: Melting point of Moexipril Hydrochloride was determined by

Table 2: Solubility Studies

S. No.	Solvent	Solubility (mg/ml) Mean ±SD
1	Phosphate buffer 6.8	56.23±0.08
2	Distilled water	47.42±0.09

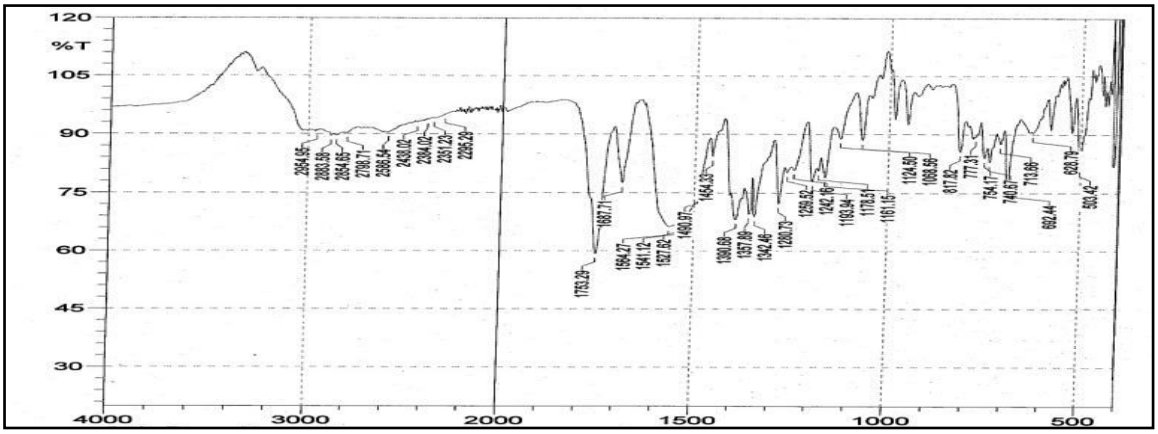

Fig. 3: FTIR of Moexipril Hydrochloride.

Table 3: Formulation batches of tablet

S. No.	Name of ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
1	Drug	15	15	15	15	15	15	15	15	15
2	Croscarmellose sodium	13	-	8	10	10	-	15	-	-
3	Sodium starch glycolate	-	12	8	5	-	15	-	14	10
4	Microcrystalline cellulose	37	38	34	35	40	35	35	36	40
5	D-mannitol	15	15	15	15	15	15	15	15	15
6	Talc	10	10	10	10	10	10	10	10	10
7	Mg. stearate	10	10	10	10	10	10	10	10	10
8	Total weight	100	100	100	100	100	100	100	100	100

capillary method. The melting point of Moexipril Hydrochloride was found to be 145-153˚C.

Solubility studies of Moexipril Hydrochloride: The solubility of Moexipril Hydrochloride in various medium was studied and the results are shown in Table 2.

Drug excipients interaction study: The drug (Moexipril hydrochloride) was found to be compatible with various excipients which were selected for formulation of mouth dissolving tablet. The compatibility was assessed by FTIR (Fig. 3) and the retention factors of all ratios found similar.

Preparation of Mouth Dissolving Tablet: Mouth dissolving tablets containing 15 mg of Moexipril Hydrochloride were prepared by direct compression method using formula give in Table 3 (Aitha *et al.*, 2010).

Evaluation of pre compression parameters: The various pre compression parameters were studied and the results are shown in Table 4.

Evaluation of post-compression parameters: After

Table 4: Evaluation of pre-compression parameters

Formulation	Bulk density (g/ml)	Tapped density (g/ml)	Angle of repose (0)	Carr's index (%)	Hausner's ratio
F1	0.5761±0.05	0.6263±0.07	30.59±0.89	14.62±0.74	1.08±0.5
F2	0.6741±0.07	0.5496±0.09	29.23±0.74	13.4±0.87	1.19±0.07
F3	0.5378±0.06	0.5134±0.08	30.79±0.95	14.57±0.65	1.05±0.04
F4	0.4856±0.04	0.5345±0.07	28.97±0.84	15.4±0.97	1.17±0.02
F5	0.5678±0.07	0.6145±0.04	29.34±0.79	13.45±0.94	1.23±0.07
F6	0.4978±0.03	0.5892±0.05	27.57±0.97	12.3±0.68	1.12±0.07
F7	0.4648±0.04	0.5262±0.09	26.09±0.97	9.52±0.67	1.10±0.09
F8	0.4561±0.09	0.5643±0.06	28.54±0.45	11.45±0.76	1.06±0.06
F9	0.4756±0.08	0.5123±0.08	27.89±0.86	21.42±0.46	1.25±0.05

Each value represents Mean±SD

Table 5a: Evaluation of post-compression parameters

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)
F1	100.87±0.055	2.8±0.057	3.5±0.057	0.442±0.04
F2	99.23±0.75	2.9±0.115	3.7±0.052	0.389±0.02
F3	98.75±1.0	3.0±0.057	3.9±0.1	0.360±0.01
F4	102.57±0.86	2.9±0.15	3.8±0.054	0.68±0.012
F5	101.49±1.57	3.0±0.14	4.0±0.057	0.76±0.02
F6	101.32±0.98	3.0±0.57	4.1±0.1	0.74±0.03
F7	98.44±0.77	2.4±0.28	3.7±0.15	0.77±0.01
F8	98.82±0.99	2.8±0.57	3.9±0.057	0.421±0.04
F9	97.56±0.56	3.2±0.059	3.8±0.1	0.67±0.01

Each value represents Mean±SD

Table 5 (b): Evaluation of post-compression parameters

Formulations	Disintegration Time (sec.)	Drug Content (%)	Wetting Time (sec.)	Water Absorption Ratio (%)
F1	32.34±0.30	96.4±1.78	38.91±0.530	21.69±4.30
F2	36.18±0.688	97.87±0.69	41.77±0.176	25.60±2.51
F3	34.69±0.587	98.44±0.72	35.48±0.301	28.51±3.56
F4	30.69±0.578	97.61±0.66	34.49±0.514	33.3±4.5
F5	32.52±0.567	97.37±0.73	39.35±0.687	34.4±2.24
F6	30.57±0.559	98.05±1.43	32.05±0.065	45.2±2.04
F7	28.24±0.592	98.51±0.96	29.11±0.130	40.9±3.05
F8	29.603±0.511	98.35±0.90	47.43±0.691	41.3±2.30
F9	39.77±0.380	97.98±0.78	35.21±0.251	47.76±3.89

Each value represents Mean±SD

Table 6: Evaluation of post-compression parameters

Time (in min)	% drug release (Mean±SD)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	22.2± 0.584	26.7± 0.665	54.3± 0.928	24.0± 0.928	42.2± 0.991	15.19± 0.15	72.2± 0.541	22.45± 0.06	18.54± 0.09
10	32.3± 0.645	41.3± 1.363	63.1± 0.408	51.9± 0.520	51.9± 1.411	29.82± 0.06	85.2± 0.896	33.12± 0.03	34.78± 0.33
15	45.1± 0.994	52.5± 2.377	72.0± 0.676	61.1± 0.504	61.1± 0.497	46.02± 0.21	96.2± 0.648	53.34± 0.15	52.92± 0.18
20	52.8± 0.895	63.5± 3.062	83.5± 0.624	72.8± 0.561	72.8± 0.688	75.24± 0.10	96.2± 0.648	69.24± 0.31	74.7± 0.41
25	64.7± 0.664	75.1± 1.982	92.1± 0.908	81.9± 0.681	81.9± 0.589	89.64± 0.10	-	89.22± 0.21	82.08± 0.88
30	75.0± 0.825	85.1± 1.956	-	91.8± 0.516	91.9± 0.361	95.58± 0.18	-	94.19± 0.22	83.71± 0.26

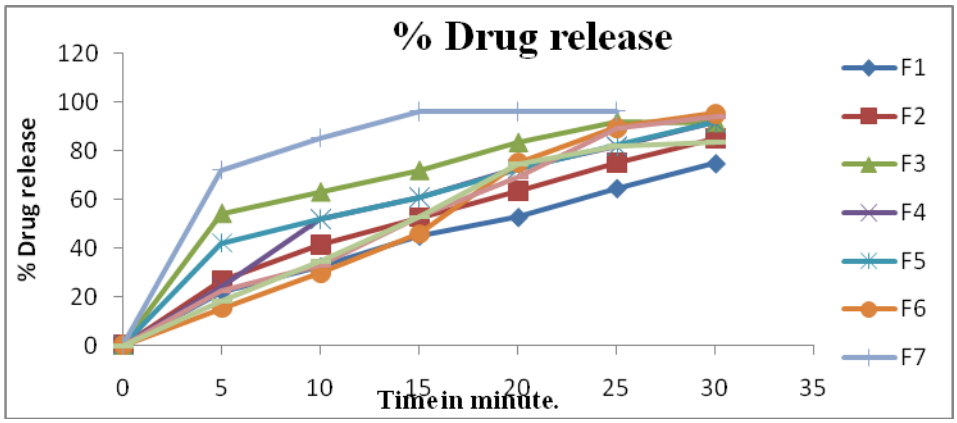

Fig. 4: Percentage *in vitro* drug release.

Table 7: Evaluation parameter of F7 batch (After storage 2 month)

S. No.	Parameters	Results
1	Weight variation (mg)	98.30±1.90
2	Thickness (mm)	3.8±0.05
3	Hardness (kg/cm^2)	2.17±0.28
4	Friability (%)	0.72±0.05
5	Wetting time (sec)	67.66±3.51
6	Disintegration time (sec)	61.66±2.51
7	Drug content (%)	98.46±1
8	Water absorption ratio (%)	58.28±6.26

compression of granules into tablets, various evaluation parameters were studied and the results are shown in Tables 5a, b.

In vitro drug release study of mouth dissolving tablet: The *In vitro* drug release study of mouth dissolving tablets were performed and release result along with release graph are shown in Table 6 and Figure 4.

Stability Study:

The stability study was carried out of selected batch F7. The tablets were wrapped in aluminum foil and stored at 40 ± 2˚C and 75 ± 5% RH for two months. After two month samples were withdrawn and tested. Table 7 shows that there was no considerable change in thickness, hardness, percent friability, drug content, disintegration time, wetting time, water absorption ratio and dissolution data of formulation F7 before and after stability study.

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