

Formulation and Evaluation of Sublingual Tablets of Meclizine Hydrochloride

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Received 11 Dec 2023,

Accepted for publication 22 Dec 2023,

Published 30 Dec 2023

ABSTRACT

The aim of the present research is to formulate sublingual tablet of Meclizine Hydrochloride using direct compression method. Moreover the purpose of developing this dosage form is to provide rapid onset of action beneficial in managing conditions of nausea, vomiting and vertigo, and also overcome the problems of solubility of drug by inclusion complexes. The disease like nausea and vomiting required fast onset of action which is necessary for the fast pharmacological action. So, the sublingual route of administration were better way of medication and overcome the problems like dysphagia. The Meclizine hydrochloride is histamine H1 receptor antagonist with antiemetic and antivertigo properties. The oral bioavailability is low (25%), with low solubility (BCS class 2 drug), and metabolized by Hepatic CYP2D6 enzyme by the process of hepatic hydroxylation. Sublingual tablet of antiemetic drug meclizine hydrochloride will be prepared by direct compression method. The Solubility of sublingual tablets will be enhanced by Inclusion complexes. These are prepared by weighed amount of drug mixed with β -cyclodextrin in different dose ratios [1:1,1:2] was wetted with small drops of water to form kneaded like paste and triturated in mortar pestle for several hours resulting in evaporation of solvent. The inclusion complexes was collected and dried for 48 hours and pulverized using mortar and pestle and then sieved through mesh #60. Then properly mixed with other excipients in polybag for 1 hour. The powder like complex was used for further evaluation studies and to form sublingual tablets by direct compression method.

Keywords: Meclizine Hydrochloride, Dysphagia, Solubility, Sublingual tablets.

INTRODUCTION

A solution is a homogenous mixture of one or more solutes in a solvent. A quality of a substance (solute) to dissolve in a given solvent at a given temperature and pressure, where a solute is any substance which can be either solid, liquid or gas dissolved in a solvent. Water is a universal solvent as it dissolves almost every solute except some types of drugs which have high Lipophilicity. Drugs administered via oral route in a solid formulation are first disintegrated into smaller parts or even in primary particles from which the drug molecules are free to dissolve and absorb through the absorption site. Depending on the

solubility and permeability in the GIT, drug substances are categorized in four BCS classes (biopharmaceutical classification system) Because of low solubility and high permeability, BCS class II drugs are associated with a slower dissolution rate in the GI tract, leading to low bioavailability. From the last few years pharmaceutical industries research scientists are majorly focusing on development of oral dosage forms of poorly aqueous soluble drugs by enhancing their solubility using different techniques. In these, Inclusion complexes is one of the widely used method to improve solubility and dissolution rate of poorly water soluble drugs. ^[1]

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Meclizine Hydrochloride is poorly water soluble drug having very slow onset of action and useful to treat nausea, vomiting and vertigo. Meclizine has CNS depressant, anticholinergic, antiemetic, antispasmodic, and local anaesthetic effects in addition to antihistaminic activity. The drug depresses labyrinth excitability and conduction in vestibular-cerebellar pathways. The antiemetic and antimotion-sickness actions of the Meclizine result, at least in part, from its central anticholinergic and CNS depressant properties. Meclizine's antiemetic duration of action may last up to 24 h and has a half-life of 6 h. It produces less drowsiness as compared to other antihistamines of its class and also has longer duration of action. Meclizine has a lag of 1 h in the onset of action hence should be taken 1 h prior to travel for protection against motion sickness. This lag in onset of action may be due to its poor solubility and mode of administration.^[2-3] It was very slightly soluble in water (0.0251 mg/ml). In particular, the drug exhibits very low solubility at pH values greater than 2.0. The poor solubility and wettability give rise to difficulty in pharmaceutical dosage forms meant for oral or parental use. To overcome these difficulties, an increase in the aqueous solubility of Meclizine hydrochloride is an important goal. Hence, the aim of the present study is to formulate and evaluate sublingual tablets of Meclizine Hydrochloride by using inclusion complexes technique with β -cyclodextrin as a solubility enhancer. Cyclodextrin are cyclic (α -1,4)-linked oligosaccharides of α -D-glucopyranose, containing a relatively hydrophobic central cavity and hydrophilic outer surface. Owing to the lack of free rotation about the bonds connecting the glucopyranose units, the cyclodextrin are not perfectly cylindrical molecules but toroidal shaped. Based on this structure, the primary hydroxyl groups are located on the narrow side of the cone shape, while the secondary hydroxyl groups are located on the wider edge.^[4] During the past two decades, cyclodextrin and their derivatives have been of considerable interest in the pharmaceutical

field because of their potential to form complexes with a variety of drug molecules. Cyclodextrin

are used to increase the solubility of water-insoluble drug through inclusion complexes formulation.

In the present research work study an effort was done to prepare inclusion complexes of Meclizine hydrochloride using β -cyclodextrin by kneading method at a 1:1 dose ratio. The drug-carrier compatibility study of drug with β -CD using FTIR, in vitro aqueous solubility and dissolution rate profile of complexes were performed. Sublingual tablet was prepared by using 1:1 ratio kneading complex of β -cyclodextrin with drug equivalent to 25mg and other excipients are sodium starch glycolate as a superdisintegrant, microcrystalline cellulose (binder), croscarmellose sodium (disintegrating agent), mannitol (sweetening agent), talc and magnesium stearate as a lubricant by using direct compression method. Evaluation studies of Precompression and Postcompression parameters were performed.^[4]

MATERIAL & METHODS MATERIALS:

Meclizine Hydrochloride was provided by JB Chemicals & Pharmaceutical Limited, Mumbai as a gift sample, β -cyclodextrin was obtained from gift sample of Alkem Laboratories, Mumbai and all other ingredients and chemicals was used of analytical grade and obtained from Loba chemie pvt. ltd, India.

Preformulation Studies:

Preparation of standard stock solution of drug in methanolic distilled water and methanolic phosphate buffer pH 6.8 (1:9 ratio):

Standard stock solution was prepared by dissolving 50mg of Meclizine Hydrochloride in a mixture of methanolic distilled water and methanolic buffer in 50ml volumetric flask in 1:9 ratio respectively. To get stock solution having concentration of 1000 μ g/ml in volumetric flask.^[5-6]

Determination of λ max in methanolic distilled water and methanolic buffer pH 6.8:

The substock solution were prepared by taking 1ml from standard solution (100 μ g/ml) in 10 ml volumetric flask and diluted up to the mark with distilled water and buffer pH 6.8. Then dilution of 10 μ g/ml was prepared and solution was scanned at range of 400-200nm using UV visible spectrophotometer (shimadzu 1800, Japan) for determination of maximum absorbance for Meclizine Hydrochloride in methanolic distilled water and methanolic pH 6.8 buffer.^[7-9]

Preparation of calibration curve of Meclizine Hydrochloride in methanolic distilled water:

The substock solution were prepared by taking 2ml from standard solution and dissolved in distilled water upto 20ml of concentration 100 μ g/ml and stirred properly for 2hrs at room temperature. Further dilutions was developed with distilled water in concentration range of 10-50 μ g/ml and were analysed on UV spectrophotometer at 229.60nm against reference solution. The absorbance data of different concentrations was noted.^[10]

Preparation of calibration curve of Meclizine Hydrochloride in methanolic phosphate buffer pH 6.8:

The substock solution were prepared by taking 2ml from standard solution and dissolved in phosphate buffer pH 6.8 upto 20ml of concentration 100 μ g/ml and stirred properly for 2hrs at room temperature. Further dilutions was developed with phosphate buffer pH 6.8 in concentration range of 10-50 μ g/ml and were analysed on UV spectrophotometer at 228.80nm against reference solution. The absorbance data of different concentrations was noted.^[11]

Solubility determination:

Take 5ml glass vials containing distilled water and phosphate buffer pH 6.8 in excess amount of drug was added and sonicated for 2hrs at room temperature after that the samples were placed on magnetic stirrer for 48hrs and keep aside for 24hrs. Then solution was filtered and evaluated for solubility using UV visible spectroscopy at

229.60nm and 228.80nm respectively and study carried out 3 times for accurate observations.

Melting point determination:

1mg of Meclizine Hydrochloride drug sample were filled in a capillary tube sealed at one side end and placed in melting point apparatus. Then temperature was noted when drug started melting.

Drug-excipients interaction study:

The FTIR spectrum of drug was recorded on FTIR spectrophotometer (Shimadzu). Fourier Transform infrared spectroscopy (FTIR) also called as FTIR spectroscopy is analytical technique used to identify organic, polymer, and inorganic materials. The samples were composed to form a pellets using hydraulic press and are transformed into disk. The final signal at detector represents a spectrum from 4000 to 400 cm^{-1} .^[12-13]

Preparation of Inclusion complexes of Meclizine hydrochloride in β -cyclodextrin containing three different ratios of dose (1:1, 1:2, 1:3) by Kneading method:

Firstly take drug (Meclizine hydrochloride) and β -cyclodextrin and separately weighed according to required ratios and precisely triturated in mortar and pestle for 1h and mixed in polybag for 15 minutes then passed through sieve number 60. This powdered mass further evaluated for drug content, % yield.^[14]

Determination of Solubility:

The prepared ratio of Meclizine Hydrochloride and β -cyclodextrin inclusion complexes was taken in excess amount at different concentrations (1:1, 1:2, 1:3) and separately dissolved in 5ml phosphate buffer pH 6.8 in vials and stirred continuously at room temperature for 48hrs. Then the solution was kept aside for 24hrs at room temperature and filtered properly by using whatman's filter paper. Then suitably diluted with phosphate buffer pH 6.8 and analysed by using UV visible spectrophotometer at 228.80nm.^[15-16]

Percentage Drug Content:

Inclusion complexes equivalent to 25mg of meclizine hydrochloride was precisely weighed and dissolved in 10ml of phosphate buffer pH 6.8

solution. The solutions were filtered through filter paper and diluted suitably.^[17] The drug content is calculated by UV Visible spectrophotometer at 228.80 nm and calculated by given formula:

% Drug content = Actual weight of drug in solid dispersion $\times$ 100 / Calculated theoretical weight of drug in solid dispersion

Preparation of Sublingual Tablet by direct compression method:

Since it was found that inclusion complexes containing Meclizine hydrochloride with β -cyclodextrin in ratio 1:1 ratio was more efficient as compared to other ratios. So this ratio was used in preparation of sublingual tablets. The sublingual tablet were prepared by direct compression method by mixing of other excipients directly with this ratio of drug and β -cyclodextrin and passed through sieve number 60. Then triturated for suitable time and mixed for 15 minutes in polybag. The mixed powder was evaluated for Precompression studies such as Bulk density, Tapped density, etc. Further that the tablet was prepared through tablet punching machine and prepared tablets were evaluated for various post granulation parameters.^[18-20]

Table 1: Formula Table for Sublingual tablet of Meclizine Hydrochloride

Ingredient (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug and β -cyclodextrin complex (1:1 ratio)	50	50	50	50	50	50	50	50	50
Microcrystalline cellulose	15	10	5	20	10	3	5	-	-
Crosscarmellose sodium	5	10	10	10	5	-	10	20	-
Sodium starch Glycolate	10	15	30	4	5	4	-	-	20
Mannitol	10	5	2	13	20	40	30	20	25
Talc	5	5	2	2	5	2	2	5	3
Magnesium stearate	5	5	1	1	5	1	3	5	2
Total (mg)	100	100	100	100	100	100	100	100	100

Evaluation Studies

Precompression Studies

Bulk Density: Precisely weighed all amount of powder was passed through sieve #60 and transferred in measuring cylinder. Value measured by volume occupied by powder without any tapping on cylinder so the formula given below:

Bulk density = Weight of blend or powder / Bulk volume of blend or powder (in ml).

Tapped Density: Accurately weighed amount of powder was transferred into measuring cylinder of 10 ml and fixed it on tapping apparatus. Reading was taken after tapped it upto 100 cycles. And calculated by using formula shown below:

Tapped density = Weight of blend or powder / Tapped volume of blend or powder (in ml).

Hausner's ratio: It is a number which is related to flowability of a powder and calculated using formula:

Hausner's ratio = Tapped / Bulk density.

Carr's index: The compressibility index is also called Carr's index.

Carr's Index (%) = $100 \times (\text{Tapped Density of powder} - \text{Bulk density of powder}) / \text{Tapped Density}$.

Angle of repose: The funnel was placed on burner stand and weighed quantity of powder was allowed to flow through funnel then height (h) and radius (r) of pile were measured by given formula:

$\tan \theta = \text{Height} / \text{radius}$.

Postcompression Studies

Weight variation: As per I.P. twenty tablets were selected from each formulation, and weighed individually with average weight was calculated. The average weight of one tablet was determined from collective weight.^[21-24]

Thickness: Vernier Caliper was used to measure diameter of each tablet. It was measured by simply placing the tablet in between the jaws of vernier caliper and slide the scale arm to press the tablet against the stationary arm then the reading displayed was noted.^[21-24]

Hardness: Monsanto hardness tester was used for tablets to measure hardness. The tablet was placed

between 2 jaws and the scale jaw moves towards by pushing it against fixed jaw until the tablet breaks. The pressure at which the tablet breaks is recorded and carried out 3 times for particular batch.

Friability: The 10 tablets from each formulation were taken and rotated at 25 rpm for 4 minutes at 25rpm using roche friabilator and dropped at height of 6 inch in each revolution. Then tablets were taken out, after 100 revolutions, dusted and weighed again. The percentage friability were calculated from equation given. The maximum loss in weight is not greater than 1%.^[21-24]

$$\text{Friability} = \frac{(\text{initial weight of tablets} - \text{final weight of tablets})}{(\text{initial weight of tablets})} \times 100$$

Drug Content: The tablets was taken and crushed in mortar – pestle equivalent to 10mg of drug and dissolved in phosphate buffer pH 6.8 in 100ml volumetric flask. Then the sample was filtered and further dilution of this solution was prepared by taking 1ml solution in 10ml volumetric flask & diluted using phosphate buffer pH 6.8 and drug content were calculated by UV visible spectrophotometer at 228.80nm.^[25]

In vitro Disintegration Study: 4 tablets were taken from each formulation and dissolve in 4 different test tubes in 600 ml of phosphate buffer 6.8 pH in disintegration apparatus and the whole assembly was placed in phosphate buffer pH 6.8 at $37 \pm 0.5^\circ\text{C}$ with beats added into the test tubes. The apparatus was started moving up and down in buffer to disintegrate tablets then time was noted of tablet disintegration in solution.^[26-27]

Water Absorption Ratio and Wetting time: A piece of tissue paper was taken and kept in petri dish containing 6 ml of water after giving two folds. After wetting tablet was taken out and further weighed.^[28]

$$\text{Water absorption ratio} = \frac{(W_a - W_b)}{W_b} \times 100,$$

Where, W_a = weight after water absorption & W_b = weight before water absorption

In vitro Dissolution Studies: In vitro drug release rate of Meclizine Hydrochloride sublingual tablets was carried out using United State Pharmacopoeia

(USP) dissolution testing apparatus type II (paddle method). The dissolution test was carried out in 900 ml jar of 6.8 pH phosphate buffer. A sample of 5ml solution was withdrawn from dissolution apparatus at 5, 10, 15, 20, 25, and 30 min. The samples were replaced with fresh dissolution. The samples were filtered through filter paper and analysed by UV spectrophotometer and percentage drug release was calculated.^[29-30]

Stability Study: The prepared tablets of batch F7 are selected for stability studies and the procedure were performed. The prepared tablets were stored in stability chamber maintained at $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ RH for two months after that the samples were collected and analysed for evaluation parameters.^[31]

RESULTS AND DISCUSSION

Preformulation Studies

Determination of λ_{max} by UV Visible Spectrophotometer: The λ_{max} of Meclizine Hydrochloride in methanolic distilled water was found to be 229.60nm and 228.80nm in methanolic phosphate buffer pH 6.8 on UV Spectroscopy.

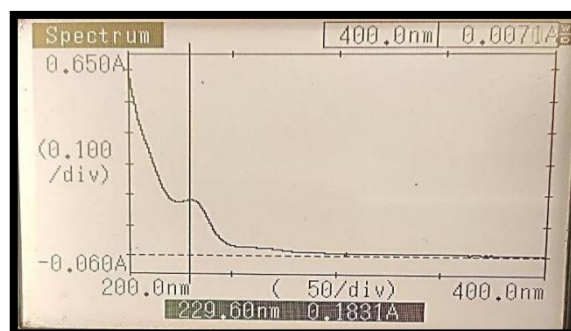


Figure 1: λ_{max} of Meclizine HCl in water

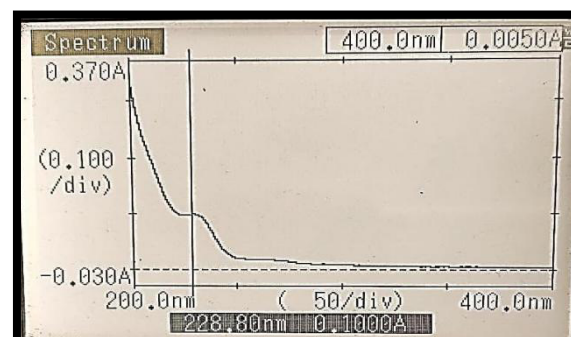


Figure 2: λ_{max} of Meclizine HCl in PBS pH 6.8.

Preparation of calibration curve of drug (Meclizine Hydrochloride): Calibration curve of Meclizine Hydrochloride in methanolic Distilled water: The prepared calibration curves are shown below:

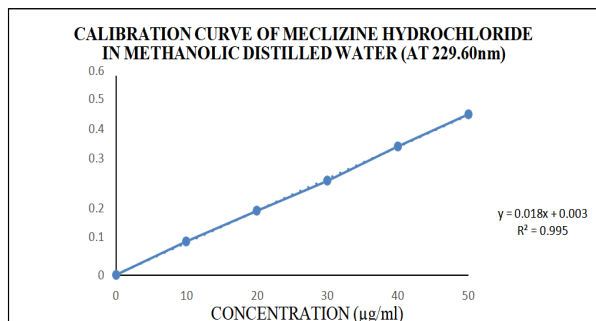


Figure 3: Calibration Curve of Meclizine HCl in methanolic distilled water

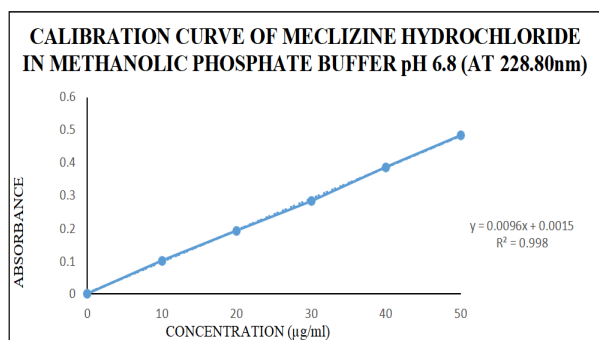


Figure 4: Calibration curve of Drug in methanolic phosphate buffer pH 6.8

Solubility determination of Meclizine Hydrochloride:

Table 6: Solubility of Meclizine Hydrochloride and inclusion complexes in different solvent

Name of Solvents	Solubility	Ratio of Drug and β -cyclodextrin Inclusion Complexes	
		1:1	1:2
Distilled water	0.0251 mg/ml	3.8042 mg/ml	5.2301 mg/ml
Phosphate Buffer pH 6.8	0.016902 mg/ml	7.79615 mg/ml	3.0602 mg/ml

Melting Point of Drug: The melting point of drug was determined by capillary method and melting point of Meclizine Hydrochloride was found in range of 210°C - 220°C.

Table 7: Melting point of Meclizine HCl

Observed values (range)	Average value	Reported value
210-214°C	212-220°C	210°C
212-216°C		
216-220°C		

Drug and Excipients Interaction Study: This was done to check drug and drug-excipient compatibility.^[32-33] FTIR graphs are given below. It was found to be compatible with various excipients which are selected for dosage form.

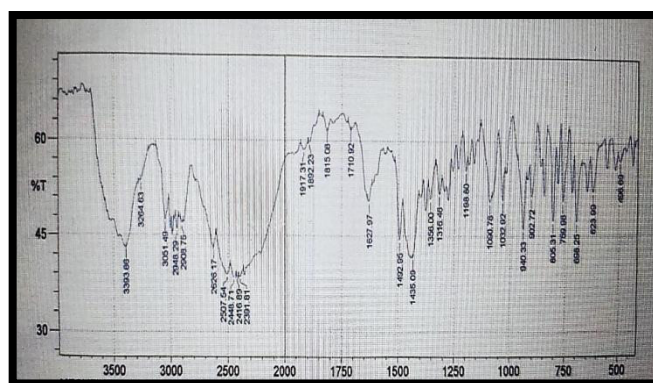


Figure 3: FTIR spectrum of Meclizine HCl

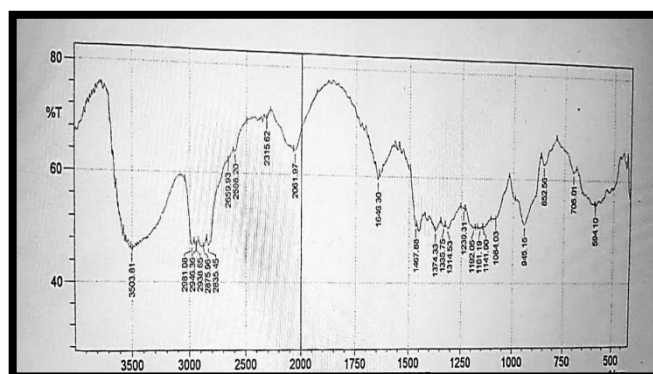


Figure 4: FTIR spectrum of Meclizine Hydrochloride with β -cyclodextrin

Formulation and Evaluation of Sublingual Tablet containing Meclizine Hydrochloride: Powder blend for the preparation of sublingual tablet containing various concentration of superdisintegrant and other excipients was prepared with 1:1 dose ratio has shown best results for drug content uniformity and in vitro dissolution test.^[34] Sublingual tablets was prepared by direct

compression method using tablet punching machine and evaluated for pre and post compressional evaluation parameters.

Precompressional Evaluation Parameters:

Table 8: Evaluation of Precompressional studies

Formula Code	Bulk density (gm/ml) Mean±SD	Tapped density (gm/ml) Mean±SD	Angle of repose (°) Mean±SD	Carr's Index (%) Mean±SD	Hausner's ratio Mean±SD
F1	0.48 ± 0.01	0.57 ± 0.01	29.80 ± 0.3	15.77 ± 0.52	1.18 ± 0.09
F2	0.456 ± 0.5	0.72 ± 0.12	35.49 ± 0.9	35.49 ± 25.2	1.60 ± 0.29
F3	0.50 ± 0.05	0.59 ± 0.03	33.74 ± 0.51	14.54 ± 22.79	1.17 ± 0.10
F4	0.44 ± 0.01	0.46 ± 0.01	29.28 ± 0.19	4.27 ± 8.18	1.04 ± 0.01
F5	0.44 ± 0.05	0.61 ± 0.03	34.11 ± 0.20	27.80 ± 9.54	1.38 ± 0.08
F6	0.47 ± 0.03	0.68 ± 0.04	31.94 ± 0.20	30.40 ± 12.52	1.44 ± 0.12
F7	0.47 ± 0.01	0.45 ± 0.50	29.90 ± 0.40	26.81 ± 6.84	1.36 ± 0.05
F8	0.57 ± 0.01	0.75 ± 0.02	30.45 ± 0.20	27.17 ± 12.76	1.31 ± 0.02
F9	0.55 ± 0.02	0.75 ± 0.09	33.19 ± 0.04	26.35 ± 5.31	1.35 ± 0.04

F8	100.6 ± 0.12	1.26 ± 0.24	3.39 ± 0.26	98.71 ± 0.004	0.42 ± 0.03
F9	99.43 ± 0.07	1.97 ± 0.02	2.72 ± 0.10	96.84 ± 0.01	0.56 ± 0.036

Table 10: In vitro disintegration test, wetting time and water absorption ratio are given below:

Formula Code	In vitro Disintegration test (sec) Mean±SD	Wetting time (sec) Mean±SD	Water absorption ratio (%) Mean±SD
F1	90 ± 2.78	58 ± 0.69	60.60 ± 0.29
F2	132.66 ± 1.01	74 ± 1.34	92.33 ± 0.05
F3	90 ± 3.16	125 ± 0.44	64 ± 0.15
F4	72.33 ± 1.91	98 ± 2.71	54.63 ± 0.06
F5	90 ± 3.16	67.33 ± 2.44	91.27 ± 0.06
F6	142.33 ± 0.97	146.66 ± 2.52	62.58 ± 0.031
F7	59 ± 1.24	62.33 ± 1.47	99.23 ± 0.003
F8	67.66 ± 0.86	90 ± 3.16	98.62 ± 0.009
F9	89.66 ± 1.00	78.33 ± 1.17	97.53 ± 0.012

Post Compressional Evaluation Parameters:

Table 9: Post compressional studies

Formula Code	Weight variation (mg) Mean±SD	Thickness (mm) Mean±SD	Hardness (kg/cm2) Mean±SD	Drug content uniformity (%) Mean±SD	Friability (%) Mean±SD
F1	110.6 ± 0.09	2.5 ± 0.06	2.76 ± 0.10	80.63 ± 0.007	0.56 ± 0.008
F2	99.33 ± 0.057	2.63 ± 0.21	2.65 ± 0.17	95.36 ± 0.003	0.35 ± 0.04
F3	98.9 ± 0.02	3.83 ± 0.09	3.01 ± 0.02	81.86 ± 0.009	0.67 ± 0.04
F4	99.12 ± 0.04	3.71 ± 0.02	3.13 ± 0.01	91.17 ± 0.01	0.25 ± 0.04
F5	97.77 ± 0.20	2.22 ± 0.19	2.5 ± 0.031	85.01 ± 0.09	0.44 ± 0.03
F6	102 ± 0.26	2.20 ± 0.17	1.8 ± 0.19	91.54 ± 0.01	0.38 ± 0.05
F7	100.33 ± 0.15	1.86 ± 0.23	2.36 ± 0.206	99.61 ± 0.005	0.16 ± 0.01

Table 11: Percentage drug release data of sublingual tablets

Time	% Drug release (Mean±SD) in Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
5 min	18.64±5.64	16.85±2.04	33.92±16.14	29.08±8.32	27.04±3.21	21.65±3.69	40.80±8.42	21.39±2.33	32.74±3.02
10 min	41.25±7.34	63.82±4.09	40.14±1.87	63.04±6.30	36.28±10.5	40.48±5.81	60.78±4.72	38.64±1.04	46.51±1.82
15 min	57.60±1.82	78.13±3.44	67.38±2.44	78.18±4.94	51.00±3.25	63.42±8.99	74.35±1.85	68.63±1.16	60.22±1.53
20 min	76.36±6.34	85.20±1.42	76.28±4.91	81.55±2.86	66.37±3.22	74.91±5.05	77.40±1.14	80.82±1.88	76.92±1.44
25 min	85.74±4.34	81.23±8.69	90.78±2.00	87.64±1.99	79.52±7.45	83.63±2.91	89.95±1.38	87.42±2.14	82.19±1.91
30 min	87.27±3.04	93.51±3.31	98.30±0.97	96.32±2.21	93.97±5.02	92.31±3.27	97.88±3.34	94.12±2.06	87.82±1.91

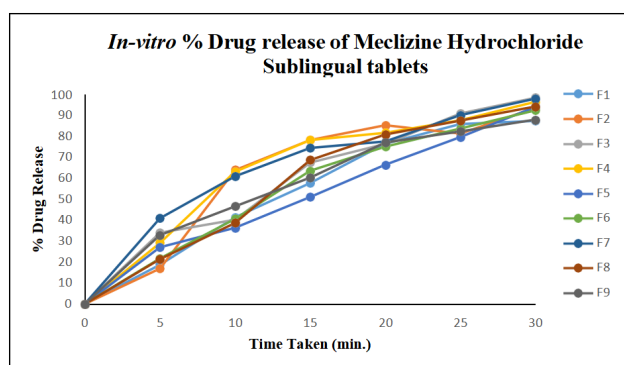


Figure 5: In vitro % drug release of sublingual formulation

Stability studies

The stability studies after storage of two months formulation F7 was examined by drug assay and in vitro dissolution studies given in table below and from statistical analysis there was significant difference between before and after storage [$P < 0.05$]. The tablets were analysed timely after two months and recorded studies are mentioned below.

Table 12: Stability studies of F7 formulation:

Parameter	Before storage	After 2 months	Inference
Weight variation	100.33 $\pm$ 0.15	99.89 $\pm$ 0.15	Within limit
Hardness	2.36 $\pm$ 0.20	2.36 $\pm$ 0.20	Within limit
Drug content	97.88% $\pm$ 0.05	96.21% $\pm$ 0.05	Within limit
Wetting time	62.33 $\pm$ 1.47	69 $\pm$ 1.45	Within limit
Water absorption ratio	99.23% $\pm$ 0.03	99.23% $\pm$ 0.03	Within limit
Disintegration time	59 $\pm$ 1.24	65 $\pm$ 1.20	Within limit
In vitro Drug release	99.14% $\pm$ 3.34	98.58% $\pm$ 1.01	Within limit

CONCLUSION

Meclizine Hydrochloride is an oral antiemetic drug also known as anti-nausea indicated for the prevention of nausea, vomiting, vertigo, and motion sickness. This medication is available in

generic form with initial dose of 25 to 50 mg per day before 30 min to travel for protection against motion sickness. The Meclizine Hydrochloride is histamine H1 receptor antagonist with antiemetic and antivertigo properties. The oral bioavailability is low (25%), with low solubility (BCS class 2 drug), because it is metabolized by Hepatic CYP2D6 enzyme by the process of hepatic hydroxylation. The half-life of Meclizine Hydrochloride is low due to its low solubility and extensive first pass metabolism. Hence it should have to improve the solubility of drug and to formulate in such dosage form or formulation which avoid first pass metabolism.

The present research work was aimed to formulate sublingual tablet containing inclusion complexes of Meclizine hydrochloride with β -cyclodextrin in 1:1 dose ratio prepared by mixing both substances with help of kneading method. The calibration curve was obtained in range of 10-50 μ g/ml with regression value of 0.998 in methanolic phosphate buffer pH 6.8. The FTIR results of drug, excipient and drug-excipient concluded that there is no interaction between them. From the prepared formulation results it was found that dissolution and solubility rate of Meclizine Hydrochloride sublingual tablets increases with minimum concentration of β -cyclodextrin.

Inclusion complexes prepared with β -cyclodextrin in 1:1 ratio of drug and solubility enhancer has shown best results for aqueous solubility, drug content, and dissolution of drug. Hence, the aim of the present research is to formulate sublingual tablet of meclizine hydrochloride using direct compression method. Moreover the purpose of developing this dosage form is to provide rapid onset of action beneficial in managing conditions of nausea, vomiting and vertigo, and also overcome the problems of solubility of drug by inclusion complexes technique.

This formulation was prepared by direct compression method and evaluated for Precompressional and post compressional evaluation parameters. Powdered blend of all batches before compression was evaluated for bulk & tapped density, Carr's & Hausner's ratio also angle of repose. It was determined that for all

sublingual tablets prepared was free flowing and compressed properly. Prepared sublingual tablets was evaluated Thickness, Hardness, Weight variation, friability, Disintegration time study, wetting time study, Water absorption ratio and Drug content uniformity. Thickness and Hardness was found to be in range and the friability of all batches was below 1%. Minimum wetting time and Water absorption ratio was found in F7 formulation so, it can be concluded that Meclizine Hydrochloride sublingual tablets can be a good choice for the treatment of nausea, vomiting and vertigo conditions with better patient compliance. Further, clinical investigation to be done before its exploitation in market.

Conflicts of Interest: The authors declare that there are no conflicts of interest.

Acknowledgement: The authors are thankful to JB chemicals and pharmaceuticals limited Mumbai for providing Meclizine Hydrochloride as a gift sample. The authors are also thankful to Management & Director of acropolis institute of pharmaceutical education and research Indore for continuous support, guidance and for providing necessary facilities throughout the research work.

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