ORIGINAL ARTICLE

Formulation and evaluation of meclizine hydro chloride mouth dissolving tablets: An attempt to enhance patent compliance

Nimisha, Pushplata Pal, Dipti Srivastava

Department of Pharmaceutics, Amity Institute of Pharmacy, Amity University, Lucknow, Uttar Pradesh, India

The purpose of this research work was to develop mouth dissolving tablets of Meclizine HCL by superdisintegrant addition and sublimation method. Meclizine HCl is an anti-emetic drug used for management of dyspepsia, heartburn, epigastric pain, nausea, and vomiting. Sodium starch glycolate was used as super disintregrant and camphor used for enhancement of porosity of the tablets Disintegration time of tablets prepared by superdisintegrant addition were significantly less ($P < 0.05$) than prepared by sublimation technique hence it was selected for further study. Tablets were evaluated for weight variation, thickness, hardness, friability, drug content, disintegration time. All tablet batches passesss evaluation parameters. The physical properties of the prepared tablets did not show any significant variations ($P > 0.05$) and were found to have good physical integrity. Stability studies showed that the physical and chemical properties of the tested tablets were not altered significantly and all the test formulations were found to be stable. The dissolution profile of fresh and aged Meclizine HCl. MDT showed no significant effect on drug release ($P > 0.05$).

Key words: *Camphor, mouth dissolving tablets, sublimation method, superdisintegrant addition method*

INTRODUCTION

Mouth dissolving drug delivery systems (MDDDS) are a new generation of formulations which combine the advantages of both liquid and conventional tablet formulations, and at the same time, offer added advantages over both the traditional dosage forms. They provide the convenience of a tablet formulation and also allow the ease of swallowing provided by a liquid formulation.[1]

Fast dissolving drug delivery systems, such as, MDTs rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration, an attribute that makes them highly attractive for paediatric and geriatric patients.[2] The fast-dissolving property of the MDTs is attributed to quick ingress of water into tablet matrix resulting in rapid disintegration. The basic approaches to develop MDTs include:

1. Maximizing the porous structure of the tablet matrix.
2. Incorporating the appropriate disintegrating agent/ agents.[3]
3. Using highly water-soluble excipients in the formulation.

The bioavailability of some drugs may be increased due to absorption of part of drug in the oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to conventional tablet.[4]

Meclizine HCl (MZ HCl) is a first generation antihistamine of the piperazine class. It has a shorter half-life of 6 hrs Meclizine is an antagonist at H_1 receptors. It possessesanticholinergic, central nervous system depressant, and local anesthetic effects. It is used as an antivertigo/antiemetic agent, specifically in the prevention and treatment of nausea, vomiting, and dizziness associated with motion sickness. Its antiemetic and antivertigo effects are not fully understood, but its central anticholinergic properties are partially

Address for correspondence:
Ms. Nimisha,
Amity Institute of Pharmacy, Amity University,
Lucknow Campus, India.
E-mail: nsrivastava3@lko.amity.edu

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responsible. The drug depresses labyrinth excitability and vestibular stimulation, and it may affect the medullary chemoreceptor trigger zone.[5] The objective of the present research work was to develop mouth dissolving tablets of Meclizine HCl (MZ HCl) and to compare the superdisintegrant addition method and sublimation technique using statistical analysis based on disintegration time.

Mouth dissolving tablets of Meclizine HCl would be highly convenientfor patients with persistent nausea, who are travelling and do not have immediate access to water asthere is no need of water to swallow the dosage from.

MATERIALS AND METHODS

Meclizine HCl and aspartame were the gift samples from Yes Pharma, Roorkee, India. All other chemicals were of analytical reagent grade.

Evaluation of mixed blend of drug and excipient

All the ingredients were passed through mesh no 60. The powder blend was evaluated for flow properties as follows:[6,7]

Angle of repose

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

$$\text{Angle of repose} = \tan \text{Ø } h/r \quad (1)$$

Bulk density

Bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight. The bulk density was calculated using the formula:

$$BD = \frac{\text{Weight of the powder}}{\text{Initial volume}} \quad (2)$$

Tapped density

Weighed quantity of pure drug was taken in measuring cylinder and it was tapped untill the constant height obtained. The tapped density was calculated using the formula.

$$\text{Tapped density} = \frac{\text{Mass of powder}}{\text{Volume of powder after tapping}} \quad (3)$$

Carr index: The Carr's index was calculated using the formula [Table 1].

$$\text{Carr index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \quad (4)$$

Preparation of tablets

Mouth Dissolving Tablets of Meclizine HCl prepared by Sublimation technique, specified quantity of drug, camphor, mannitol, talc, magnesium stearate were weighed accurately and passed through 60# screen prior to mixing. All the materials were transferred to mortar and triturated till it mixed uniformly. The resulting powder mixture was compressed into tablets using single punch tablet machine. The tablets were dried at 60° in oven till constant weight obtained.[8]

Tablets of Meclizine HCl also prepared by Superdisintegrant addition method, specified quantity of drug, Sodiumstarch glycolate, aspartame, micro crystalline cellulose, mannitol, talc, magnesium stearate were weighed accurately and passed through 45# screen prior to mixing. All the materials were transferred to mortar and triturated till it mixed uniformly. The resulting powder mixture was evaluated for angle of repose, bulk density, tapped density, and Compressibility index and compressed into single punch tablet machine [Tables 2 and 3].[9]

Evaluation of prepared tablets

Weight variation

Twenty tablets were selected randomly from each formulation and weighed individually using a digital balance. The individual weights were compared with the average weight for the weight variation.[10,11]

Thickness variation

Ten tablets from each formulation were taken randomly and their thickness was measured with a micrometer screw gauge (25 × 1 mm, lest count = 0.01 mm).[12]

Hardness

Hardness of the tablets was measured using the Monsanto Hardness Tester (Pharmalab, Ahmedabad, India).[13]

Friability

The friability of a sample of twenty tablets was measured using a USP type Roche friabilator (Pharmalab, Ahmedabad, India). Pre-weighed tablets were placed in a plastic chambered

Table 1: Formulation of mouth dissolving tablets of meclizine HCl by superdisintegrant addition method

Formulation ingredients	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	T11	T12
Meclizine HCL	30	30	30	30	30	30	30	30	30	30	30	30
AVICEL 102	70	70	70	70	70	70	70	70	70	70	70	70
Sodium starch glycolate	20	20	20	20	20	20	20	20	20	25	30	35
Manitol upto	200	200	200	200	200	200	200	200	200	200	200	200

All the quantities are in mg/tablet. All the tablets contain 1% aspartame, 1% magnesium stearate and 2% talc

friabilator attached to a motor revolving at a speed of 25 rpm for 4 min. The tablets were then dusted, reweighed and percentage weight loss (friability) was calculated using the formula [Figure 1 and Table 4].[14]

$$\% \text{ Friability} = \frac{\text{Loss in weight}}{\text{Initial weight}} \times 100 \quad (5)$$

Disintegration time

Disintegration test was performed in the USP disintegration apparatus. Buffer solution (pH 6.4) was used as the medium. The tablets were placed in the tubes of the container and the disks were placed over it. The average disintegration time of tablets from each formulation batch was noted [Figure 2].

Table 2: Evaluation of precompressed powder blend

Batch no.	Bulk density (g/cm³)	Tap density (g/cm³)	Angle of repose (°)	Carr's index (%)
T1	0.320	0.512	33.06	37.5
T2	0.319	0.486	33.47	34.32
T3	0.346	0.606	36.86	42.9
T4	0.371	0.484	25	23.22
T5	0.298	0.624	35.7	42.24
T6	0.283	0.485	32.88	41.5
T7	0.316	0.527	41.4	40.03
T8	0.233	0.466	35	30
T9	0.293	0.569	30.07	38.5
T10	0.224	0.411	43.6	45.5
T11	0.279	0.474	26.65	41
T12	0.297	0.505	39.53	41.18

Table 3: Formulation of mouth dissolving tablets of meclizine HCl by sublimation technique

Formulation ingredients	Quantity (mg)
Drug	30
Camphor	40
Mannitol upto	200

All the quantities are in mg/tablet. All the tablets contain 1% aspartame, 1% magnesium stearate and 2% talc

Dissolution study

In vitro release of Meclizine HCl from tablets was monitored by using 900 ml of SIF (USP phosphate buffer solution,

(pH 7.4)) at 37 ± 0.5° and rpm using programmable dissolution tester (Paddle type, model UDA-6DR, Veego). Aliquots were withdrawn at one minute time intervals and were replenished immediately with the same volume of fresh buffer medium. Aliquots, following suitable dilutions, were assayed spectrophotometrically (UV-ELICO INDIA LTD) at 232 nm [Figure 3].[15]

Statistical analysis

Each tablet formulations were prepared in duplicate and each analysis was duplicated. Effect of method of formulation on disintegration time was tested for significance by using independent *t*-test with the aid of SPSS-12.0. Difference was considered significant when $P < 0.05$.

Stability studies

The stability of selected formulations was tested according to International Conference on Harmonization guidelines for zones III and IV. The formulations were stored at accelerated (40 ± 2°/75 ± 5% RH) and long term (30 ± 2°/65 ± 5% RH) test conditions in stability chambers (Thermotech TH-7007, India) for six months following open dish method. Stability studies indicate that there is no major difference in hardness and disintegration time after storing formulations for six months. The dissolution profile [Figure 4] of fresh and aged Meclizine HCl MDT showed no significant effect on drug release ($P > 0.05$). Stability studies show that the physical and chemical properties of the tested tablets were not altered significantly ($P > 0.05$) and all the test formulations were found to be stable.[16,17]

RESULTS AND DISCUSSION

Two methods were tried for formulation of mouth dissolving tablets. The disintegration time of tablets prepared by both the methods are shown in Table 5.

Table 4: Evaluation of meclizine HCl mouth dissolving tablets prepared by superdisintegrant addition method

Batch	Weight (gm)	Hardness (Kg/Cm²)	Friability (%)	Thickness (mm)	Disintegration time (sec)	Drug content (%)
T1	330±16.5	3.5±0.224	0.49	6.4±0.2	20±0.58	99.11±0.81
T2	330±16.5	3.3±0.258	0.42	6.4±0.2	20±0.18	98.27±0.55
T3	330±16.5	2.3±0.22	0.36	6.4±0.2	20±0.68	99.22±0.65
T4	330±16.5	4.3±0.15	0.75	6.4±0.2	32±0.78	96.12±0.21
T5	330±16.5	3.3±0.90	0.60	6.4±0.2	25±0.58	101.0±0.20
T6	330±16.5	4.3±0.11	0.45	6.4±0.2	20±0.58	99.02±0.01
T7	330±16.5	2.9±0.024	0.51	6.4±0.2	20±0.44	97.02±0.02
T8	330±16.5	3.7±0.10	0.40	6.4±0.2	25±0.10	99.01±0.08
T9	330±16.5	2.5±0.40	0.62	6.4±0.2	25±0.10	100.1±0.13
T10	330±16.5	3.9±0.20	0.63	6.4±0.2	18±0.23	98.02±0.69
T11	330±16.5	3.4±0.324	0.59	6.4±0.2	28±0.58	99.02±0.84
T12	330±16.5	3.3±0.124	0.50	6.4±0.2	20±0.58	96.02±0.58

*(*N*=3)

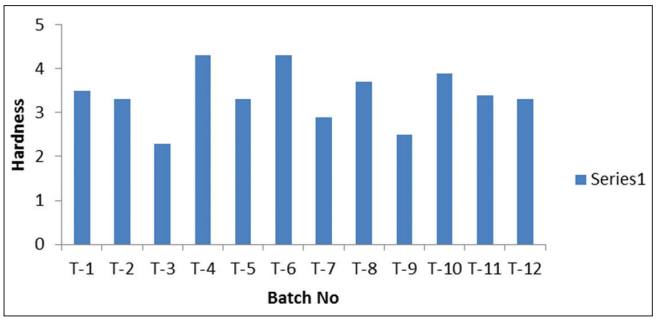

Figure 1: Hardness of meclizine HCL MDTs prepared by superdisintegrant addition method

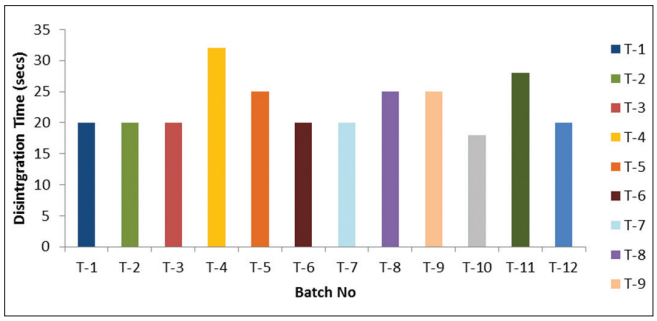

Figure 2: Disintegration time of meclizine HCL MDTs prepared by superdisintegrant addition method

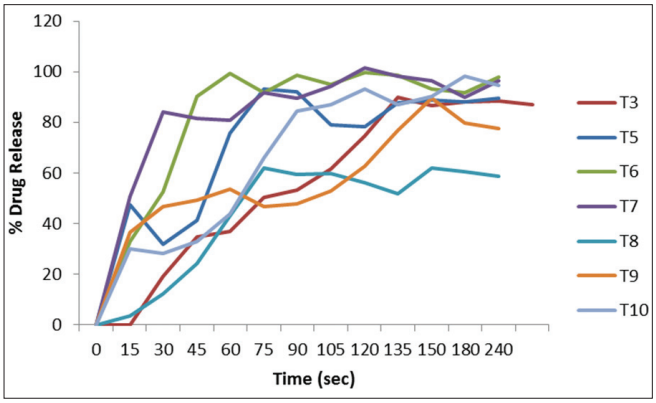

Figure 3: Drug release profile of mouth dissolving tablets of meclizine HCl

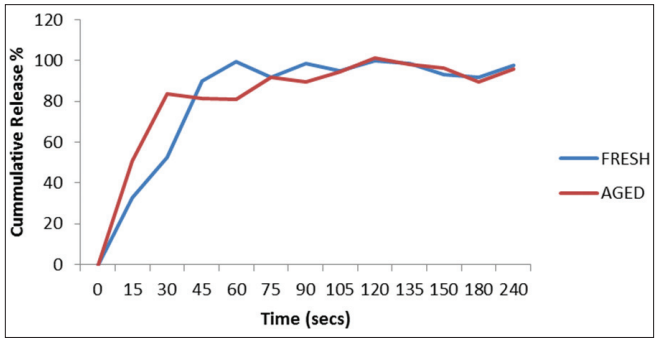

Figure 4: Dissolution profile of meclizine HCl MDT (Fresh and aged)

Table 5: Effect of method of formulation of meclizine HCl mouth dissolving tablets on disintegration time

Batch no.	Superdisintegrant addition method (DT secs)	Sublimation technique (DT secs)
T1	20±0.58	100±0.50
T2	20±0.18	105±0.12
T3	20±0.68	110±0.60
T4	32±0.78	115±0.17
T5	25±0.58	120±0.50
T6	20±0.58	105±0.18
T7	20±0.44	130±0.24
T8	25±0.10	105±0.14
T9	25±0.10	95±0.15
T10	18±0.23	115±0.13
T11	28±0.58	120±0.50
T12	20±0.58	115±0.04

*(*N*=3)

It shows that super integration addition method exhibits the lowest disintegration time(s) hence it was selected for further study. The quicker disintegration time may be attributed to faster water uptake by the tablets. Friability of all batches was in the range of standard limit (less than 1%) and no more significant differences. The minimum friability of the formulation was found to be 0.36%. The maximum friability of the formulation was found to be 0.75%. The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

The angle of repose for the entire formulations blend was found in the range 25° to 43.6°. Compressibility index was found to be in the range of 23.22 to 45.5%. All the formulations (T1-T12) tablets passed weight variation test as the % weight variation was within the IP limits ofof the weight. The average thickness of the all formulation was found to be 6.4 mm and within the limit of standard Pharmacopeia.

The hardness of the tablet was found to be 2.3-4.3 kg/cm^2. The results of drug content were within the limits specified by the IP.

In vitro disintegration time was found to be in the range 18 to 32 seconds. From all the formulations T 10 has the minimum time of disintegration.

In the present work, mouth dissolving tablets were prepared by superdisintegrant addition and sublimation technique, from these two, disintegration time of tablets prepared by superdisintegrant addition were significantly less ($P < 0.05$) than prepared by sublimation technique.

CONCLUSION

The present study demonstrated the potential for faster absorption, effective therapy and increased patient compliance. Mouth dissolving tabletsof MZ HCl were developed with sufficient mechanical integrity to assist

patients of any age group for easy administration. The MDTs were prepared byDirect compression method.

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