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Research Article

FORMULATION AND EVALUTION OF ORALLY DISINTEGRATING TABLETS OF MECLIZINE HYDROCHLORIDE

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ABSTRACT
The objective of necessary work to develop meclizine HCl fast disintegrating tablet using different disintegrant which would disintegrate tablet rapidly in oral cavity. Nine batches of meclizine HCl orally disintegrating tablets were prepared by direct compression method using sodium starch glycolate, crosscarmellose sodium, Crospovidone as disintegrant in different concentration in order to achieve faster disintegration of tablet. The influence of the disintegrant concentration on the release of meclizine HCl was studied. The formulated batches were characterized by different physical parameters. Physical parameters of all formulated tablets were within acceptable limits. The study reveals that the formulation containing Crospovidone as disintegrant shows faster disintegration compare to others.

Key words: Orally disintegrating tablet, Crospovidone, Direct compression, Meclizine HCl.

INTRODUCTION

Recent advances in novel drug delivery system aims to enhance the safety and efficacy of the drug molecule by formulating a dosage form being convenient for the administration. Difficulty in swallowing is major problem seen in pediatric, geriatric, bedridden and mentally ill patients in diseases conditions like Motion sickness, sudden episode of allergic attacks, pain, fever, migraine etc. in such condition fast action of drug is require hence resulting in higher incidence of noncompliance and ineffective therapy[1]. To improve quality of life and treatment compliance of such patients, orally disintegrating tablets (ODT) dosage form is a better alternative for oral medication. These dosage forms dissolve or disintegrate within matter of second. Usually, Superdisintegrant are added to a drug formulation to facilitate the break up of or disintegration of tablet content into smaller particles that can dissolve more rapidly than in the absence of disintegrants[2, 3]. Many substances like microcrystalline cellulose[4], Crospovidone[5], crosscarmellose sodium[6], sodium starch glycolate[7] have been used in the formulation of fast disintegrating tablets.

Meclizine HCl is an antiemetic drug use in the treatment of nausea and dizziness associated with motion sickness. The drug is currently available as conventional tablets taken in 25- or 50-mg doses at 1 to 2 h prior to a potential episode of motion sickness thereafter, the dose may be repeated every 24 h for the duration of the journey. So it is good candidate to formulate oral disintegrating tablet which disintegrates within a matter of second and provide quick onset of action hence it is very useful to pediatric and geriatric patients who generally shows problem in swallowing[8, 9]. It is also useful to the patients who are on travelling or in situation where drinking water is not easily available to take medicine b's ODT not require water to swallow dosage form.

MATERIALS AND METHODS

Meclizine HCl was received as a gift sample from UCB Pharma Pvt. Ltd.Vapi, Pearlitol SD200 obtained as gift from roqutte Mumbai, Avicel pH102 and Crospovidone XL 10 was obtained as gift from Vapi care Ltd. SSG and CCS was purchase from S.D Fine Chemicals Ltd. Other reagents were of analytical grade.

Preparation of Mixed blend of Drug and Excipients

All the ingredients were passed through mesh no 60. Required quantity of each ingredient was taken for each specified formulation (depicted in the Table-I) and all the ingredients were subjected to grinding to a required degree of fineness. The powder blend was evaluated for flow properties as follows.

Angle of Repose

Angle of repose was determined using funnel method[10]. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (q) was calculated using following the formula,

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

Bulk density

Apparent bulk density (Pb) was determined by pouring the blend into a graduated cylinder[11]. The bulk volume (V) and weight of the powder (M) was determined. The bulk density was calculated using the following formula,

$$Pb = M/V$$

Tapped density

The measuring cylinder containing a know mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (Pt) was calculated using the following formula,

$$Pt = M/Vt$$

Compressibility Index

The simplest way for measurement of free flow of powder is compressibility, a indication of the ease with which a material can be induced to flow is given by compressibility index (I) which is calculated as follows,

$$I = V0\text{-}Vt/Vbx$$

Where, V0 is bulk volume and Vt is tapped volume. The value below 15% indicates a powder with usually give rise to good flow characteristics, whereas above 25% indicate poor flowability.

Hauser's ratio

Hauser's ratio is an indirect index of ease of powder flow calculated by following formula[12],

$$\text{Hauser's ration} = Pt/Pd$$

Where Pt is tapped density and Pd is bulk density, Lower Hauser ratio (<1.25) indicates better flow properties than higher one (>1.25).

EVALUATION OF TABLET

Weight Variation

Twenty tablets were selected at a random and average weight was determined. The individual tablets were weighted and compared with average weight[13].

Friability

Friability of tablets was determined using Roche friability (Electrolab, Mumbai). This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. The tablets were de dusted using a soft muslin cloth and reweighed. The friability (f) is calculated by following formula[14],

$$f = (1\text{-}W0 / W) \times 100$$

Where, W0 is weight of the tablets before the test and W is the weight of the tablets after test.

Hardness

Hardness of tablet crushing strength (F0) (the force required to break a tablet in a diametric dimension) was measured using Monsanto the tablet hardness tester[15].

Drug Content

Five tablets were powdered and the blend equivalent to 12.5 mg of meclizine HCl was weighed and dissolved in suitable quantity of 0.01N HCl. The solution was filtered, suitably diluted and the drug content was analyzed spectrophotometrically at 232nm. Each sample was analyzed in triplicate[16].

***In Vitro* Disintegration time**

The disintegration time of the tablets was determined as per Indian Pharmacopoeia monograph. The time required for disintegration of six tablets from each batch placed in each tube of disintegration test apparatus were measured at 37±0.5 ^{o}C using 900 ml of distilled water. The time required to obtain complete disintegration of all the six tablets was measured[17].

Wetting time

Five circular tissue paper were placed in a petridish with a 10-cm diameter. Ten milliliters of water containing eosin, a water soluble dye was added to the petridish. The dye solution is used to identify the complete wetting of the tablet surface. A tablet was carefully placed on the surface of tissue paper in the petridish at room temperature. The time required for water to reach the upper surface and wet the tablets completely wet was noted as the wetting time[18]. The measurements were carried out in replicates (n=6)

***In-vitro* dissolution test**

The release rate meclizine HCl from orally disintegrating tablets was determined using United State Pharmacopoeia (USP) dissolution testing apparatus I (Basket method, Electrolab, TDT-06T, Mumbai, India). The dissolution test was performed using 900ml of 0.01N HCl at 37±0.5 ^{o}C and 100 rpm. A sample (10ml) of the solution was withdrawn from the dissolution apparatus at 5, 10,15,20,25 and 30min. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 232nm using a Shimadzu UV-1800 UV-visible double beam spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve[19, 20].

RESULTS AND DISCUSSION

Nine formulations of meclizine HCl were prepared with varying concentration of super disintegrants: crosscarmellose sodium, sodium starch glycolate and Crospovidone XL 10. Pearlitol SD 200 was used as diluent and sweetener. For each formulation, blend of drug and excipients were prepared and evaluated for various parameters as explained earlier. The powder blend was compressed using direct compression technique. Bulk density was found in the range of 043-0.46 g/cm^3 and tapped density between 0.51-0.57 g/cm^3 as mentioned in tablet II. Using these two-density data Hausner's and compressibility index was calculated. The powder blends of all the formulations had Hausner's ration of 1.2 of less indicating good flowability. The compressibility index was found between 15.9 and 21.8. The compressibility-flowability correlation data indicated a fairly good flowability of the powder blend. The good flowability of the powder blend was also evidenced with angle of repose (range of 27-30^0), which is below 40^0 indicating good flowability (Table-II). The tablets were prepared using direct compression technique. Since the powder material was free flowing, tablets were obtained of uniform weight variations as per Pharmacopoeial specifications. The drug content was found in the acceptable limit and the hardness of the tablet between 3.7-3.9 kg/cm^2 as mentioned in Table II. Friability of the tablets was found below 1% indicating a good mechanical resistance of tablets. The wetting time and disintegration time was found practically good for all formulations where F5 shows good correlation (Figure 1).

The in vitro disintegration time (DT) of the tablets was found to be less than 60 sec. The in vitro dissolution (Figure 2) indicated a faster and maximum of 99.5% drug release from formulation F6 proving the best disintegrant property of Crospovidone XL 10.

CONCLUSION

From all the above observations it was concluded that the formulation F6 containing 5% of Crospovidone XL 10 found to be better formulation in terms of rapid disintegration and maximum percentage drug release when compared with all other formulations. Prepared tablets disintegrate within few seconds without need of water; thereby enhance absorption leading to increase bioavailability. Thus the present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and increased patient compliance.

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Table I Formulation of meclizine HCl orally disintegrating tablet

S. No	Composition	F1 (mg)	F2	F3	F4	F5	F6	F7	F8	F9
1	Meclizine HCL	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
2	CCS	4.5	6	7.5	-	-	-	-	-	-
3	Crospovidone XL 10	-	-	-	4.5	6	7.5	-	-	-
4	SSG	-	-	-	-	-	-	4.5	6	7.5
5	Avicel PH102	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5
6	Na-saccharin	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
7	Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
8	Mg-stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
9	Pearlitol SD200	91	89.5	88	91	89.5	88	91	89.5	88
	TOTAL	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Table II Evaluation of Mixed Powder blend

S. No	Batch code	Angle of repose (degree)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)s	Compressibity Index (%)	Hauser's ration
1	F1	31.22±0.02	0.45±0.02	0.56±0.03	19.64±0.04	1.24±0.02
2	F2	30.34±0.03	0.46±0.01	0.56±0.04	17.85±0.06	1.21±0.30
3	F3	30.65±0.05	0.43±0.02	0.55±0.04	21.81±0.04	1.27±0.01
4	F4	28.89±0.01	0.45±0.03	0.53±0.07	15.90±0.06	1.17±0.07
5	F5	29.47±0.98	0.43±0.04	0.50±0.02	16.27±0.04	1.16±0.17
6	F6	30.04±0.29	0.44±0.01	0.51±0.10	17.70±0.03	1.15±0.02
7	F7	30.05±0.02	0.44±0.02	0.55±0.02	20.10±0.02	1.25±0.01
8	F8	29.19±0.01	0.46±0.01	0.57±0.01	19.29±0.01	1.23±0.02
9	F9	27.21±0.02	0.45±0.01	0.55±0.02	18.18±0.01	1.22±0.01

Table III Evaluation of Meclizine HCl orally disintegrating tablet

S.No	Batch code	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content	Disintegration time(sec)	Wetting time(sec)
1	F1	150±0.45	2.15±0.1	3.7±0.01	0.73±0.06	98.56±0.43	38±0.03	25±0.17
2	F2	150±0.13	2.19±0.2	3.8±0.02	0.74±0.18	99.13±0.68	33±0.16	23±0.11
3	F3	150±0.20	2.11±0.1	3.9±0.01	0.68±0.16	99.57±0.84	27±0.19	23±0.17
4	F4	150±0.11	2.17±0.4	3.7±0.01	0.63±1.13	98.96±0.32	28±0.07	19±0.09
5	F5	150±1.10	2.10±0.1	3.8±0.01	0.55±0.56	99.37±0.26	25±0.01	15±0.08
6	F6	150±0.78	2.13±0.1	3.9±0.01	0.44±0.48	99.26±0.47	19±0.01	11±0.01
7	F7	150±1.50	2.22±0.3	3.7±0.01	0.39±0.66	97.45±0.78	57±0.05	63±0.21
8	F8	150±1.17	2.14±0.2	3.8±0.01	0.40±0.14	98.14±0.12	36±0.04	43±0.31
9	F9	150±0.89	2.25±0.4	3.7±0.01	0.58±0.89	99.41±0.46	28±0.04	28±0.06

Table IV Dissolution profile of meclizine HCl ODT tablet

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	54.8±2.1	54.9±2.1	55.6±1.52	54.1±2.2	60.1±2.6	61.2±1.1	49.8±2.2	49.2±2.1	40.6±1.5
10	67.4±3.6	68.7±3.2	70.6±1.67	65.4±2.3	75.4±3.0	77.9±2.2	57.4±3.5	54.7±3.1	51.6±2.6
15	84.9±1.6	85.8±1.2	86.2±2.87	79.3±1.7	89.1±1.9	89.1±1.7	69.9±3.6	67.8±1.9	63.1±2.4
20	87.1±3.0	89.1±1.7	89.7±3.2	84.2±1.0	94.2±1.2	99.4±2.5	78.2±2.0	77.1±1.3	71.9±3.1
30	91.9±1.1	93.2±2.5	95.9±1.9	92.1±2.1	99.1±2.3	99.5±1.5	88.9±3.1	85.2±2.5	85.9±1.8

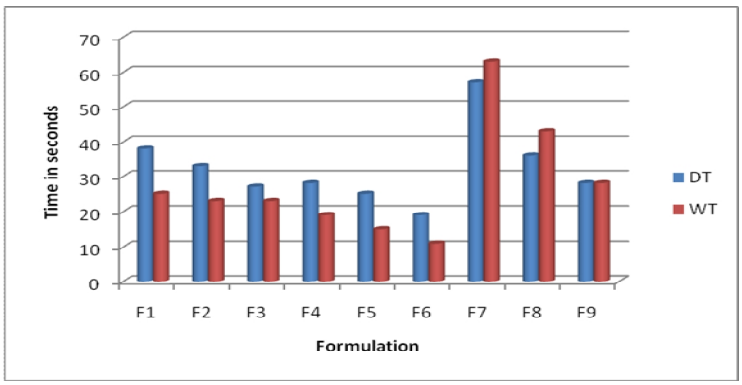

Figure I Comparison between Disintegration time and Wetting time

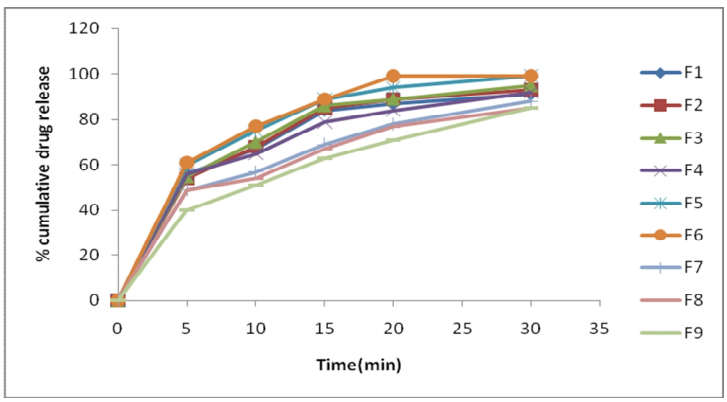

Figure II Dissolution profile of meclizine HCl oral disintegrating tablet

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