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Research Article

Formulation and evalution of mouth dissolving tablets of metoclopramide hydrochloride by direct compression technique

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Abstract

Fast dissolving drug delivery system offers a solution for those patients having difficulty in swallowing tablet. In the present study, an attempt has been made to prepare fast dissolving tablets of the drug Metoclopramide hydrochloride using superdisintegrants Crospovidone, Croscarmellose sodium and Sodium starch glycolate by direct compression technique. The prepared tablets were evaluated for hardness, friability, wetting time, weight variation, *in vitro* disintegration time and *in vitro* dissolution study. The hardness of the tablets was in the range of 2.0 - 4.0 Kg/cm². The percentage friability of the tablets was less than one. Weight variation test results showed that the tablets were deviating from the average weight within the permissible limits of ±7.5 %. Drug content uniformity study results showed that uniform dispersion of the drug throughout the formulation i.e. 98.54% to 101.23%. Tablets containing Crospovidone showed better disintegrating character along with the rapid release (97.42% drug within 1 minute).

Keywords: Fast-dissolving tablets, Metoclopramide Hydrochloride, Superdisintegrants.

Introduction

Solid dosage forms and capsules are most popular and preferred drug delivery system because of they have a high patient compliance. Many patient find difficulty to swallow tablet and hard gelatin capsule, consequently they do not take medication as prescribed. It is estimated that 50% of the population is affected by this problem which result high incidence of non-compliance and ineffective therapy1. The difficulty is experienced in particular by pediatric and geriatric patients, but it is applicable to people who are ill in bed and those active working patients who are busy or traveling, mentally ill, developmentally disable and patients who are uncooperative. To overcome this problem fast dissolving tablet is prepared. Metoclopramide HCl stimulates motility of the upper GI without stimulating gastric, pancreatic or biliary secretions which shows the metoclopramide HCl acts as an anti-emetic. With the view to all the above information, an attempt had been made to develop a rapidly disintegrating Metoclopramide HCl mouth dissolving tablets of which disintegrate in the oral cavity without the need of water within a matter of seconds. This will lead to the formation of suspension / solution form which can be easily swallowed, thereby improving dissolution rate and bioavailability of drug and onset of pharmacological action.

Materials and Methods

Materials

Metoclopramide HCl, Crospovidone, aspartame, Mannitol and Magnesium stearate were procured/gifted from Stallions laboratories pvt. Ltd., kerala G.I.D.C., Bawla, Gujarat , India, were used and all other chemicals/solvents used were analytical grade.

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Methodology

Method Formulation of mouth dissolving tablets of Metoclopramide Hydrochloride:

Tablet each containing 5 mg Metoclopramide Hydrochloride were prepared as per composition given in Table1. The drug and excipients were passed through sieve (#60) to ensure the better mixing. Mannitol was used as a direct compressible vehicle. Superdisintigrant like Crospovidone was used in different ratios. The powder was compressed using **Rimek compression machine equipped with 8 mm round** punch by direct compression technique. A minimum of 100 tablets was prepared for each batch

Pre Compression Parameters:

Angle of Repose:

Angle of repose was determined using funnel method4. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose was calculated using the formula

$$\theta = tan^{-1}\frac{h}{r}$$

Where, θ is the angle of repose, h is height of pile; r is radius of the base of pile.

Bulk Density:

Apparent bulk density (ρb) was determined by pouring the blend into a graduated cylinder4. The bulk volume (Vb) and weight of powder (M) was determined. The bulk density was calculated using the formula

$$\rho b = \frac{M}{Vt}$$

Tapped Density:

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and weight (M) of the blend was measured. The tapped density (ρb) 4 was calculated using the following formula

$$\rho t = \frac{M}{Vt}$$

Carr's Compressibility Index:
The simplest way of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility. The compressibility index of the granules was determined by Carr's compressibility index4 (I),
which is calculated by using the following formula

$$I = \frac{V0 - Vt}{Vo} \times 100$$

Post compression parameter:
Hardness:
The hardness of the tablet from each formulation was determined using Pfizer hardness tester4.
Weight Variation:
Twenty tablets from each formulation were selected at a random and average weight was determined. Then individual tablets were weighed and was compared with average weight 4.
Friability
Friability of the tablets4 was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to100 revolutions. Tablets were de dusted using a soft muslin cloth and re weighed. The friability (f) is given by the
formula.

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

Where W0 is weight of the tablets before the test and W is the weight of the tablet after the test.
***In vitro* Disintegration time:**
The disintegration time for all formulations was carried out using tablet disintegration test apparatus. Six tablets were placed individually in each tube of disintegration test apparatus
and discs were placed. The water was maintained at a temperature of 37°±2°C and time taken for the entire tablet to disintegrate completely was noted7.
Drug content:
Five tablets were powdered and the blend equivalent to 100 mg of Metoclopramide hydrochloride was weighed and dissolved in suitable quantity of distilled water. The solution was filtered, suitably diluted and the drug content was analyzed **spectrophotometrically at 239nm**. Each sample was analyzed in triplicate8.
***In vitro* Dissolution studies**9
In vitro dissolution studies for all the fabricated tablets was carried out by using USP Type II apparatus (USP XXIII Dissolution Test Apparatus) at 50 rmp in 900 ml of phosphate buffer pH 6.8, maintained at 37±0.5ºC. 5 ml aliquot was withdrawn at the specified time intervals, filtered through whatmann filter paper and assayed spectrophotometrically at 239nm using Shimadzu 1700 spectrophotometer. An equal volume of fresh medium, which was pre warmed at 37 0C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Dissolution studies were performed in triplicate.

Results and discussion

Nine formulations of Metoclopramide Hydrochloride were prepared with concentration of three superdisintegrants: Sodium Starch glycolate, Croscarmellose sodium, Crospovidone and microcrystalline cellulose were used as a direct compressible vehicle. 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 0.56-0.62 g/cm3 and the tapped density between 0.67-0.73 g/cm3 . Using these two density data compressibility index was calculated. The compressibility index was found between 13.432 and 17.808 % and the compressibility - flowability correlation data indicated a fairly good flowability of the blend. The good flowability of blend was also evidenced with angle of repose (range of 25 – 29º), which is below 40º indicating good flowability. Tablets were prepared using direct compression technique. Thickness of the tablets was measured by screw gauge by picking tablets randomly from all the batches. The mean thickness was (n=3) almost uniform in all the formulations and values ranged from 2.98 ± 0.013 mm to 3.18 ± 0.040 mm. The standard deviation values indicated that all the formulations were within the range. Since the powder material was free flowing, tablets were obtained of uniform weight due to uniform die fill, with acceptable weight variations as per pharmaceutical specifications. The drug content was found in the range of 96.20 % (acceptable limit) and the hardness of the tablets between 3.0 – 4.0 kg/cm^2 (Table II). Friability of the tablets was found below 1 % indicating a good mechanical resistance of tablets. Wetting time is closely related to the inner structure of the tablet. This showed that wetting process was very rapid in almost all formulations. This may be due to ability of swelling and also capacity of water absorption and causes swelling. The *invitro* dispersion time is measured by the time taken to undergo uniform dispersion. Rapid dispersion within few minutes was observed in all the formulations. The results showed that tablet containing Crospovidone having low dispersion time as compare to other superdisintegrants. The dispersion time increases as the concentration of superdisintegrants increases. The in vitro disintegration time of the tablets was found to be less than 60 sec. All the formulations showed enhanced dissolution rate as compared to superdisintegrants. The maximum increase in the dissolution rate was observed with Crospovidone amongst the three superdisintegrants. The order of enhancement of the dissolution rate with various superdisintegrants found to be Crospovidone > Croscarmellose sodium >Sodium starch glycolate. Stability study shows no significant changes in values during one-month study.

Conclusion

It was concluded that mouth-dissolving tablets of Metoclopramide hydrochloride can be successfully prepared by direct compression technique using selected superdisintegrants for the better patient compliance and effective therapy.

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Table 1: Composition of different batches of mouth dissolving tablets of Metoclopramide Hydrochloride

Ingredients (mgs)	Formulation Code(in mg)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Metoclopramide HCl	5	5	5	5	5	5	5	5	5
Mannitol	123.4	119.4	114.4	123.4	119.4	114.4	123.4	119.4	114.4
Sodium starch glycolate	14	18	23	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	14	18	23	-	-	-
Crospovidone	-	-	-	-	-	-	14	18	23
Aspartame	6	6	6	6	6	6	6	6	6
Menthol	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total	150	150	150	150	150	150	150	150	150

Table 2: Evaluation of tablets

Formulation code	Weight variation	Hardness	Thickness	Friability	Drug content	*In vitro* disintegration time	Wetting time	% Drug content
F1	151.0	3.87	3.13	0.3633	4.790	29	54	85.11
F2	150.5	3.76	3.17	0.2103	4.825	27	51	82.26
F3	150.5	3.70	3.18	0.1356	4.925	25	47	85.31
F4	149.6	3.76	2.97	0.3496	4.889	24	46	85.11
F5	150.0	3.24	3.13	0.3035	4.900	23	42	88.71
F6	150.1	3.66	3.15	0.2103	4.918	20	39	90.44
F7	150.1	3.24	2.90	0.4739	4.700	20	40	89.83
F8	148.4	2.96	2.97	0.4200	4.835	17	37	91.10
F9	148.6	2.90	2.98	0.4187	4.876	15	34	96.20

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