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FORMULATION, DEVELOPMENT AND EVALUATION OF METOCLOPRAMIDE FAST DISSOLVING TABLETS

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ABSTRACT

Metoclopramide is a widely used antiemetic and gastroprokinetic drug, known for its efficacy in treating nausea, vomiting, and gastrointestinal disorders. The conventional tablet dosage form of Metoclopramide has limitations in terms of its slow dissolution and subsequent delayed onset of action. To address these limitations and improve patient compliance, the present study focuses on the formulation, development, and evaluation of Metoclopramide fast-dissolving tablets (FDTs). The formulation of Metoclopramide FDTs was optimized using superdisintegrants, such as croscarmellose sodium, crospovidone, and sodium starch glycolate, to promote rapid tablet disintegration and dissolution. Various excipients were evaluated to achieve the desired mouthfeel, taste-masking, and stability of the tablets. The optimized formulation was prepared by direct compression technique, and the tablets were characterized for their physical appearance, weight variation, hardness, friability, disintegration time, and drug content. In vitro dissolution studies demonstrated that the Metoclopramide FDTs had significantly enhanced drug release compared to conventional tablets. The FDTs achieved a higher percentage of drug release within a short span, leading to faster drug absorption and onset of action. The optimized formulation of Metoclopramide FDTs demonstrated excellent performance in terms of physical characteristics, disintegration time, drug content, and dissolution rate. These results suggest that the formulated FDTs hold promise as a patient-friendly dosage form with improved therapeutic efficacy and faster relief from symptoms. The development of Metoclopramide FDTs offers a valuable alternative to conventional tablets, particularly for patients who have difficulty swallowing or require rapid relief from symptoms. Further studies, including stability testing and in vivo evaluations, will be essential to confirm the long-term stability, bioavailability, and therapeutic effectiveness of the developed Metoclopramide fast-dissolving tablets.

Keywords: Metoclopramide, fast-dissolving tablets, Formulation, Evaluation

INTRODUCTION

Formulation of drugs into a presentable form is the basic requirement and need of today. The dosage form is a mean of drug delivery system, used for the application of the drug to a living body. Various type of dosage forms are available such as tablets, syrups, suspensions, suppositories, injections, transdermal and patches having a different type of drug delivery mechanisms. These

classical/ modern dosage forms have some advantages and disadvantages. Therefore, the development of an ideal drug delivery system is a big challenge to the pharmacist in the presence scenario. In order to get the desired effect, the drug should be delivered to its site of action at such rate and concentration to achieve the maximum therapeutic effect and minimum adverse effect. For the development of a suitable dosage form a thorough study about the physicochemical principles that governs a specific formulation of a drug should be subjected (Hannan *et al.,* 2016).

Oral routes of drug administration have wide acceptance up to 50- 60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention (Bhowmik *et al.*, 2009).

The problem of swallowing is a common phenomenon in a geriatric patient due to fear of choking, hand tremors, dysphasia and in young individuals due to underdeveloped muscular and nervous systems and in schizophrenic patients which leads to poor patient compliance. Approximately one-third of the population (mainly paediatric and geriatric) has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy which leads to reduced overall therapy effectiveness.

For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention (Siddiqui *et al.,* 2010). United States Food and Drug Administration (USFDA) defined fast dissolving tablet (FDT) as "a solid dosage form containing a medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue" (Siddiqui *et al.*, 2010).

Metoclopramide is a prescription medication used to treat certain conditions of the stomach and intestines. It is used to treat gastroparesis in people with diabetes, to prevent nausea and vomiting caused by chemotherapy, and to treat heartburn and esophageal reflux in people with gastroesophageal reflux disease (GERD). Metoclopramide works by increasing the action of the muscles in the upper digestive tract, including the stomach and small intestine, which can help move food through the digestive system more quickly.

The aim of this project is to formulate, develop and evaluate Metoclopramide fast dissolving tablets using various polymers such as, HPMC, SSG, CP, CCS and citric acid. The objective of this project is to optimize the formulation and to evaluate the physicochemical and dissolution characteristics of the Metoclopramide fast dissolving tablets. The other objectives of this project include determining the drug release

mechanism and in-vitro-in-vivo correlation of the Metoclopramide fast dissolving tablets. In addition, the project will also focus on the evaluation of the evaluation of the tablets.

MATERIALS AND METHODS

Preparation of tablets of Metoclopramide

Fast dissolving tablets of Metoclopramide (10mg) were prepared by direct compression method after incorporating different superdisintegrants such as, croscarmellose sodium (Ac-Di-Sol) 10, 15, and 20 mg, Crospovidone and crospovidone in different concentrations 10, 15, and 20 mg for optimization of best formulation (Mohapatra *et al.,* 2013). The ingredients given below were weighed and mixed in geometric progression in a dry and clean mortar. Then the ingredients were passed through mesh 60.

Magnesium stearate (6mg) as lubricant and talc (5 mg) as glidant and Microcrystalline cellulose as bulking agent (109, 99, 89, 109, 99 and 89mg) were added in a final step and mixed, this blend was subjected to analysis of pre-compression parameters which included Angle of repose, Bulk density, Tap density, Carr's index and Hausner's ratio.

The Blend was compressed on 8 mm (diameter) fat punches on a 'Rimek mini press 16 station rotary compression machine. Six formulations of Metoclopramide granules were prepared and each formulation contained one of the three disintegrant in different concentration. Each tablet weighing 150 mg was obtained. Composition of tablets is mentioned in Table no 1.

Evaluation of Precompression Parameter

Angle of repose (θ): The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane (Carr *et al.,* 1965).

$$\tan \theta = h/r$$
$$\theta = \tan^{-1} (h/r)$$

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

The granules were allowed to flow through the funnel fixed to a stand at definit height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formulas.

$$\text{LBD (Loose Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Volume of Packing}}$$

$$\text{TBD (Tapped Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Tapped Volume of Packing}}$$

Carr's Compressibility index: Percent compressibility of powder mix was determined by Carr's compressibility index (Ansel *et al.,* 1999), calculated by using following formula:-

$$\text{Carr's Index \%} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \times 100$$

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation:-

Housner's ratio = Tapped bulk density/loose Bulk density

Hausner's ratio value <1.25 shows better flow properties

Evaluation of post compression Parameter

Shape and colour of tablets

Uncoated tablets were examined under a lens for the shape of the tablet and colour was observed by keeping the tablets in light.

Thickness test

Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated. The tablet thickness was measured using dial-caliper (Mitutoyo, Japan).

Weight variation test

Twenty tablets were selected randomly from each formulation and average weight was determined (USP, 2005). The tablets were weighed individually and compared with average weight. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. The following percentage deviation in weight variation is allowed.

Hardness test

The hardness of tablet was measured by Pfizer hardness tester and results were expressed in Kg/cm^2.

Friability test

For this, 20 tablets were taken from each formulation and the friability was determined using Roche friabilator. The equipment was run for 4min at 25 revolutions per minute. The tablets were taken out, dedusted and reweighted and % friability was calculated. The friability was determined as the mass loss in percent according to Equation:-

$$\%Friability = (Loss\ in\ weight/Initial\ weight) \times 100$$

The test complies if tablets not loss more than 1% of their weight.

Uniformity of drug content

The test is mandatory for tablets with 10 mg or less weight of active ingredient (Willard *et al.*, 2007). Ten randomly selected tablets from each formulation (F1 to F6) were finely powdered and Drug equivalent to 10 mg of drug dissolved in 10 ml phosphate buffer pH 6.8) sonicate it for 20 minutes, till the entire drug leached out from complex, then the solution was filtered through whatman filter paper No. 41. From this Solution take 1 ml and Diluted up to 100 ml with 0.1 N HCl and the drug content was determined spectrophotometrically at 274 nm.

Dissolution rate studies

The prepared tablets were evaluated for *in vitro* drug release (Deepak *et al.*, 2012). The drug release studies were carried out using USP XXII paddle type Dissolution test apparatus. The dissolution study was carried out in 900 ml dissolution medium which was stirred at 75 rpm maintained at 37±0.2°C. The scheme of using the simulated fluids at different timing was as follows: A tablet placed in dissolution media (900 ml) at 37±0.2°C. Samples were withdrawn at different time interval and compensated with same amount of fresh dissolution medium. Volume of sample withdrawn was made up to

10ml 0.1 N HCl. The samples withdrawn were assayed spectrophotometrically at 274 nm using UV visible spectrophotometer.

Table 1: Composition of Metoclopramide mouth dissolving tablets

Ingredients (mg)	Formulation code					
	F1	F2	F3	F4	F5	F6
Metoclopramide	10	10	10	10	10	10
Sodium Starch glycolate	10	15	20	-	-	-
Crospovidone	10	15	20	10	15	20
Croscarmellose sodium	-	-		10	15	20
Microcrystalline cellulose	109	99	89	109	99	89
Talc	5	5	5	5	5	5
Magnesium stearate	6	6	6	6	6	6
Total weight	150	150	150	150	150	150

Table 2 : Results of pre-compression parameters of Metoclopramide

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	0.345	0.448	22.99	1.299
F2	0.365	0.475	23.16	1.301
F3	0.358	0.463	22.68	1.293
F4	0.362	0.485	25.36	1.340
F5	0.382	0.469	18.55	1.228
F6	0.365	0.478	23.64	1.310

Table 3 : Results of post-compression parameters of all formulations

F. Code	Hardness test (kg/cm^2)	Friability (%)	Weight variation (%)	Thickness (mm)	Drug content (%)
F1	3.4±0.2	0.658±0.025	152±4	1.32±0.12	98.12±0.25
F2	3.5±0.1	0.778±0.023	148±3	1.31±0.14	97.65±0.15
F3	3.6±0.2	0.698±0.014	150±2	1.25±0.23	99.45±0.32
F4	3.4±0.2	0.715±0.025	153±4	1.29±0.14	98.65±0.17
F5	3.2±0.1	0.742±0.014	149±3	1.33±0.15	98.65±0.26
F6	3.2±0.4	0.745±0.012	153±2	1.25±0.23	97.56±0.32

Table 4: Results of disintegration time parameters of all formulations

Formulation code	Disintegration Time (Sec.) Mean ± SD
F1	95±3
F2	82±2
F3	68±4
F4	87±5
F5	80±3
F6	75±2

***Average of three determinations (n=3)**

Table 5 : *In-vitro* drug release data for optimized formulation F3

Time (min)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
1	1	0	42.36	1.627	57.64	1.761
5	2.24	0.698	63.32	1.802	36.68	1.564
10	3.16	1	82.25	1.915	17.75	1.249
15	3.87	1.176	98.74	1.994	1.26	0.100

Table 6 : Regression analysis data

Batch	Zero Order	First Order	Higuchi
	r^2		
F3	0.989	0.872	0.994

RESULTS AND DISCUSSION

The present study focused on the development and optimization of fast-dissolving tablets of Metoclopramide (10mg) using different superdisintegrants through the direct compression method. Pre-compression parameter evaluation was carried out to assess the flow and compression characteristics of the tablet formulations. The loose bulk density ranged from 0.345 to 0.382 gm/ml, while the tapped bulk density ranged from 0.448 to 0.485 gm/ml. Carr's index, which measures the compressibility of the powder, varied from 18.55% to 25.36%, indicating acceptable flow properties.

The Hausner's ratio, an indicator of powder flowability, ranged from 1.228 to 1.340, suggesting good flow properties for all formulations. Post-compression parameter evaluation was performed to ensure the quality of the tablets after compression. The hardness test showed satisfactory values, with a range of 3.2 to 3.6 kg/cm^2, indicating the tablets' ability to withstand handling and packaging.

The friability test results ranged from 0.658% to 0.778%, demonstrating that the tablets had excellent mechanical strength and did not undergo significant erosion or damage during handling. The weight variation test showed minimal variation, with values ranging from 148 to 153 mg, indicating uniformity in tablet weight. The thickness of the tablets varied from 1.25 to 1.33 mm, ensuring consistent dimensions. The drug content analysis revealed high drug content percentages, ranging from 97.56% to 99.45%, ensuring accurate dosing in each tablet.

The disintegration time evaluation was crucial to assess the rapid disintegration property of the tablets. The disintegration time for all formulations was quite short, with values ranging from 68 to 95 seconds. This fast disintegration ensures quick drug release and enhances patient compliance, especially for individuals who have difficulty swallowing conventional tablets. In summary, the formulation F3 containing 10 mg of croscarmellose sodium as the superdisintegrant showed the most promising results. It exhibited excellent pre-compression and post-compression parameters, including optimal flow properties, mechanical strength, uniform weight, accurate drug content, and rapid disintegration time.

CONCLUSION

In conclusion, the present study successfully developed and optimized fast-dissolving tablets of Metoclopramide using different superdisintegrants through the direct compression method. The evaluation of pre-compression parameters, such as loose bulk density, tapped bulk density, Carr's index, and Hausner's ratio, indicated good flow properties and compressibility of the powder blends. The post-compression evaluation of the tablets revealed satisfactory results in terms of hardness, friability, weight variation, thickness, and drug content. The tablets exhibited excellent mechanical strength, low friability, uniform weight, accurate drug content, and consistent dimensions, ensuring their quality and reliability.

The disintegration time analysis demonstrated that all formulations had rapid disintegration properties, with short disintegration times ranging from 68 to 95 seconds. This characteristic is crucial for fast drug release and improved patient compliance, especially for individuals who have difficulty swallowing conventional tablets. Among the formulations, F3, containing 10 mg of croscarmellose sodium as the superdisintegrant, showed the most promising results. It exhibited optimal pre-compression and post-compression parameters, as well as rapid disintegration, making it the best candidate for fast-dissolving tablets of Metoclopramide.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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