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Formulation and Evaluation of Mouth Dissolving Tablet of Metoclopramide HCl

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ABSTRACT

The objective of present study was to prepare mouth dissolving tablet of Metoclopramide HCl. Metoclopramide HCl is acting through its prokinetic action increasing gastric emptying. The tablets were prepared by direct compression method using 3^2 factorial designs. Croscarmellose sodium & crospovidone were used as super disintegrants. The tablets were evaluated for weight variation, friability, disintegration time, hardness, wetting time and drug release study. The tablets showed good results for weight variation, friability, hardness, disintegration time and drug release study.

INTRODUCTION

Nausea and vomiting may be a symptom of serious organic disturbances involving any of viscera of chest or abdomen or produced by drugs, radiation, movements, infection, metabolite and emotional disturbances, neoplasm or painful stimuli. Emesis is a complex reflux that is co-ordinated by the vomiting center in the medulla. Nausea is accompanied by reduced gastric tone and peristalsis.[1] In the emetic response fundus and body of stomach, oesophageal sphincter and esophagus relax, while duodenum and pyloric stomach contract in a retrograde manner. Rhythmic contractions of diaphragm and abdominal muscles then compress the stomach and evacuate its contents via mouth[2]. Vomiting occurs due to stimulation of emetic center situated in medulla oblongata. Metoclopramide HCl is acting through its prokinetic action. It increases gastric peristalsis while relaxing first part of duodenum- speeds gastric emptying.

Mouth dissolving tablet:[1]

Mouth dissolving tablet or Oral disintegrating tablets are also called as orodispersible tablets, quick disintegrating tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapid melts. However, of all the above terms, United States Pharmacopeia (USP) approved these dosage forms as ODTs. Recently, European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing. US-FDA defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue."

The concept of Fast Dissolving Drug Delivery System emerged from the desire to provide patient with conventional means of taking their medication. Difficulty in swallowing (Dysphasia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients.

On placing orodispersible tablet in the mouth, saliva serves to rapidly dissolve the dosage form. The saliva containing the dissolved or dispersed medicament is then swallowed and the drug is absorbed in the normal way. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva slide down into the stomach & it may produce rapid onset of action.

The dispersible tablets allow dissolution or dispersion in water prior to administration but the orodispersible tablet instead of dissolving or disintegrating in water is expected to dissolve or disintegrate in oral cavity without drinking water. The disintegrated mass in saliva then slides down smoothly along the esophagus. The main criteria for an orodispersible tablet is to disintegrate or dissolve rapidly in oral cavity with the help of saliva, without need of water and should have pleasant mouth feel.

Advantages:[1,2]

1. As ODTs are solid unit dosage forms, they provide good stability, accurate dosing, easy manufacturing, small packaging size, and easy to handle by patients.
2. No risk of obstruction of dosage form, which is beneficial for traveling patients who do not have access to water.
3. Easy to administer for pediatric, geriatric, and institutionalized patients (especially for mentally retarded and psychiatric patients)
4. Rapid disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action.
5. Medication as "bitter pill" has changed by excellent mouth feel property produced by use of flavors and sweeteners in ODTs.
6. Bioavailability of drugs that are absorbed from mouth, pharynx, and esophagus is increased.
7. Pre-gastric absorption of drugs avoids hepatic metabolism, which reduces the dose and increases the bioavailability.

Hence present study was aimed to prepare mouth dissolving tablet of Metoclopramide HCl using Crosscarmellose sodium & Crosspovidone as super disintegrant by applying 3^2 factorial design.

MATERIAL AND METHODS

Materials:

Metoclopramide HCl was obtained from Ipca lab. Pvt. Ltd., Mumbai. Croscarmellose sodium and crospovidone were procured from Concept Pharm. Ltd, Aurangabad. Aspartame was obtained from Concept Pharm. Ltd, Aurangabad. Strawberry flavors, magnesium stearate and

aerosil 200 was gifted by Ipca lab. Pvt. Ltd., Mumbai. All other chemicals used were of analytical grade.

Methods:

Preparation of mouth dissolving tablets:

For preparation of mouth dissolving tablet 3^2 factorial design[1, 2] was used. The two independent variables selected were croscarmellose sodium (X_1) and crospovidone (X_2).

Table 1: Coded values of variables

Coded value	Actual value (%)	
	X_1	X_2
-1	**2**	**2**
0	**4**	**4**
+1	**6**	**6**

Mouth dissolving tablet of complex was prepared using croscarmellose sodium and crospovidone as super disintegrants. Tablets were prepared by direct compression method. Nine batches were prepared by using the 2, 4, and 6% of super disintegrant. The weight of the tablet was kept constant to 100 mg. Resinate (drug-resin complex) 40mg, equivalent to 10 mg of Metoclopramide HCl was taken for further tablet development.

Table 2: Composition of Mouth dissolving tablet of Metoclopramide

Ingredients	Quantity of ingredients (mg)								
	F 11	**F 12**	**F 13**	**F 14**	**F 15**	**F 16**	**F 17**	**F 18**	**F 19**
Drug resin complex	Eq$^{\omega}$. 10 mg	Eq$^{\omega}$. 10 mg	Eq$^{\omega}$. 10 mg	Eq$^{\omega}$. 10 mg	Eq$^{\omega}$. 10 mg	Eq$^{\omega}$. 10 mg	Eq$^{\omega}$. 10 mg	Eq$^{\omega}$. 10 mg	Eq$^{\omega}$. 10 mg
Croscarmellose sodium	2	2	2	4	4	4	6	6	6
Crospovidone	2	4	6	2	4	6	2	4	6
Mannitol	47	45	43	45	43	41	43	41	39
Aspartame	5	5	5	5	5	5	5	5	5
Aerosil	2	2	2	2	2	2	2	2	2
Mag. Stearate	2	2	2	2	2	2	2	2	2
Total wt.	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Weight variation, drug content, friability and hardness[i,ii]:

Weight variation, drug content uniformity and friability of prepared tablets were determined using the methods given in Indian Pharmacopoeia and criteria. Drug content was analyzed by using a UV spectrophotometer (Shimadzu, UV-1700) at λ_{max} 309 nm. Tablet friability was measured using friability tester (Roche friabilator). Hardness of tablet was measured by using Monsanto hardness tester. Weight variation, drug content and hardness of tablet were represented as mean ± SD. The data obtained was shown in Table 3.

Wetting time[iii]

A piece of tissue paper folded twice was placed in small Petri dish (ID 6.5cm) containing 6 ml of distilled water. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each were performed. The data obtained was shown in Table 3.

Disintegration Time

In-vitro disintegration time was determined as described under procedure for an uncoated tablet in IP without disc. One tablet was placed in each six tubes of assembly. Apparatus was operated using distilled water as the immersion fluid. Time required for complete disintegration was noted for each tablet.

Method of drug analysis:

A stock solution of Metoclopramide HCl 100 µg/ml was prepared in pH buffer 0.1 N HCl. Then 10, 20, 30, 40, 50 µg/ml solutions were prepared from stock by appropriate dilutions with 0.1N HCl. The solutions were analyzed by Shimadzu UV 1700 at wavelength maximum of 309 nm.

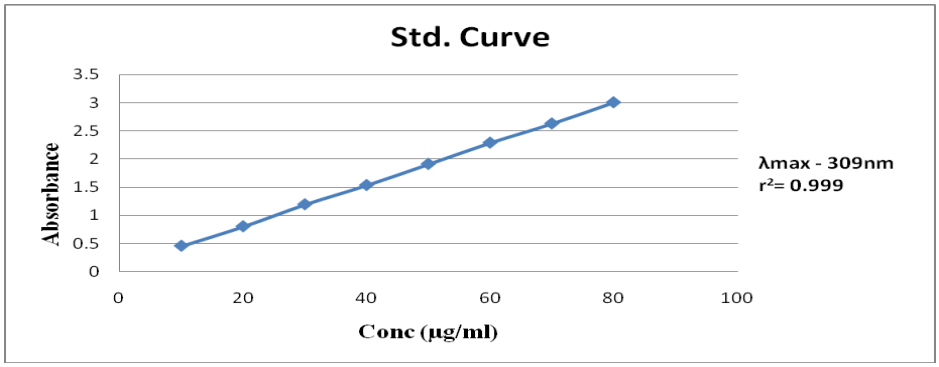

Figure 1 Standard curve of drug in 0.1 N HCL.

***In-vitro* release profile of formulated tablet:**

In-vitro drug release from tablet was determined using 0.1 N HCl with USP Type-II dissolution test apparatus at 50 rpm and 37.5^0C ± 0.5^0C temperature. Aliquots (5 ml) were withdrawn at specified time interval and replaced with fresh dissolution medium maintained at 37.5^0C ± 0.5^0C. The test sample was filtered through Whatman filter paper No 41 and analyzed using UV spectrophotometer at λ_{max} 309 nm.

RESULT AND DISCUSSION

Table 3: Evaluation of mouth dissolving tablet

Test	F11	F12	F13	F14	F15	F16	F17	F18	F19
Wt. variation	101.4 ±2.37	99.69 ±7.33	98.74 ±5.14	100.62 ± 6.01	100.97 ±3.27	**100.41 ±1.48**	100.62 ±6.01	103.99 ±4.05	101.08 ±4.73
Hardness (Kg/cm^2)	4.7 ±0.15	4.5 ±0.20	4.2 ±0.58	4.5 ±0.26	4.2 ±0.26	**3.5 ±0.2**	2.0 ±0.35	1.9 ±0.20	1.8 ±0.15
Friability (%)	0.80	0.79	0.76	0.75	0.74	**0.74**	0.72	0.71	0.72
Drug content (%)	99.3 ±0.81	99.6 ±0.45	99.8 ±0.43	90.66 ±5.68	99.93 ±1.52	**100.73 ±1.56**	99.93 ±1.52	96.66 ±6.80	99.3 ±0.81
Wetting time (Seconds)	10.71 ±1.32	11.4 ±1.53	12.63 ±1.52	18.46 ±1.15	10.06 ±0.35	**12.83 ±1.66**	9.48 ±0.20	17.76 ±1.20	14.33 ±3.45
DT (Seconds)	14.3 ±1.52	13.6 ±0.12	11.4 ±1.51	13.3 ±4.04	11.1 ±0.20	**8.06 ±0.86**	8.09±0.95	7.76 ±0.90	7.06 ±1.17

Table 4: Drug release at gastric pH

Batch No.	Drug release in 1 minute	Drug release in 3 minute
F11	59.34 ± 0.98	86.36 ± 1.87
F12	61.91 ± 1.24	94.81 ± 1.78
F13	60.31 ± 1.54	90.42 ± 1.29
F14	51.65 ± 1.78	98.07 ± 0.65
F15	63.92 ± 0.67	86.13 ± 0.54
F16	**80.61 ± 0.89**	**99.98 ± 0.76**
F17	66.98 ± .65	95.43 ± 0.67
F18	56.98 ± 0.45	92.55 ± 0.76
F19	71.01 ± 0.34	93.79 ± 0.78

Result of evaluation of factorial design batches showed that increase in super disintegrant concentration causes decrease in hardness. The disintegration time was also decreased by increasing the super disintegrant concentration. No significant difference was observed in friability, wetting time. The formulation F16 to F19 showed lowest disintegration time, the formulation F-17, F-18, F-19 did not produce good hardness. Also, drug release study showed that formulation F-16 released 80.61 % of drug within 1 minute and 99.98 % within 3 minutes. Formulation F16 which showed low disintegration time (8.06 seconds) and hardness in acceptable range (3.5kg/cm^2) was found to be good formulation as mouth dissolving tablet.

SUMMARY AND CONCLUSION

Combination of super disintegrants can be used for formulation of mouth dissolving tablet. Mouth dissolving tablet is a good drug delivery system for antiemetic drug candidate. The formulation containing 4% of croscarmellose sodium and 6% crospovidone showed minimum disintegration time & the hardness for tablet was also good. So, the tablets containing combination of both super disintegrants showed good effect on disintegration time.

REFERENCES

1. Zade P.S.; Kawtikwar P.S. “Formulation, Evaluation and Optimization of Fast dissolving tablet containing

Tizanidine Hydrochloride", *Int Jr. of Pharm.Tech*, **2009**,*1(1)*, 34-42.

2. Kuchekar B.; Badhan A.; Mahajan H. "Mouth dissolving tablets of Salbutamol sulphate: a novel drug delivery system". *Indian Drugs*. **2004,** *41*, 592-598.
3. Venkatesh D. P.; Geetha Rao, C. G. "Formulation of taste masked oro-dispersible tablets of ciprofloxacin", *Asian Journal of Pharmaceutics* 2008, 261-264.
4. Setty C.M.; Prasad D. V. K.; Gupt, V. R. "Development of fast Dispersible Aceclofenac tablets: Effect of Functionality of Superdisintegrants", Ijps [online], **2008**,*68 (4)*, 180-185.
5. Masareddy R. S., Kadia R. V. "Development of Mouth Dissolving Tablets of Clozapine using Two different Techniques", *Ijps* [online], **2008**, *70 (4)*, 526- 528.
6. Schwartz, J.B.; Connor, R.E. *Optimization techniques in pharmaceutical formulation and processing Modern Pharmaceutics*, 3rd; Marcel Dekker : New York , 2005, 727-752.
7. Lewis, G. A.; Mathieu, D. *Pharmaceutical Experimental Design*, Marcel Dekker :New York; 2005; 247-290.
8. Zade P.S.; Kawtikwar P.S. "Formulation, Evaluation and Optimization of Fast dissolving tablet containing Tizanidine Hydrochloride", *Int Jr. of Pharm.Tech*, **2009**,*1(1)*, 34-42.
9. Kuchekar B.; Badhan A.; Mahajan H. "Mouth dissolving tablets of Salbutamol sulphate: a novel drug delivery system". *Indian Drugs*. **2004,** *41*, 592-598.
10. Venkatesh D. P.; Geetha Rao, C. G. "Formulation of taste masked oro-dispersible tablets of ciprofloxacin", *Asian Journal of Pharmaceutics* 2008, 261-264