Academic Sciences

International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 7, Issue 2, 2015

Original Article

DESIGN AND EVALUATION OF FAST DISSOLVING TABLETS OF ERGOTAMINE TARTARATE

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Received: 16 Mar 2015, Revised and Accepted: 19 April 2015

ABSTRACT

Objective: The main objective of this study was to formulate and evaluate the fast dissolving tablets of ergotamine tartarate with synthetic superdisintegrants.

Methods: Various formulations were prepared by direct compression method using different concentrations of crospovidone (12.5%-62.5%) and croscarmallose sodium (12.5%-62.5%) as superdisintegrants. Formulations were evaluated for precompressional parameters and postcompressional parameters like uniformity of weight, thickness, hardness, friability, drug content, wetting time, the water absorption ratio, *in vitro* disintegration time and *in vitro* dissolution study.

Results: Results revealed that among the 10 formulations, the formulation F_5 containing 62.5% of crospovidone and formulation F_{10} containing 62.5% of croscarmallose sodium was found to be promising formulations. F_5 shown disintegration time of 12 seconds and the drug release was up to 96% in 30 minutes and F_{10} shown disintegration time of 18 seconds and the drug release was up to 89% in 30 minutes.

Keywords: Ergotamine tartarate, Crospovidone, Croscarmallose sodium, Fast dissolving drug delivery.

Conclusion: From the result obtained, it can be concluded that formulation of fast dissolving tablet using crospovidone as a superdisintegrant showed improved disintegration and solubility and hence better patient compliance

INTRODUCTION

Oral route is the most convenient way of administering drugs and among the oral dosage forms, tablets of different types are most common. Conventional tablets are popular because of their special properties such as suitability to self administration, improved stability, accurate dosing, ease of handling, versatility with respect to type and dose of the drug and suitability to scale up [1].

There is a variety of clinical expressions of swallowing dysfunction caused by ageing, acute or chronic disease conditions, decline in physiological functions and adverse drug reactions [2]. Swallowing problem is also common in young individuals because of their under developed muscular and nervous systems [3]. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and of drinking water, swallowing conventional tablets may be difficult [4].

To overcome these problems, formulators have considerably dedicated their effort to develop a novel type of tablet dosage form for oral administration i.e., one which disintegrates/dissolves rapidly in saliva without the need for drinking water. Due to the presence of superdisintegrants, it gets dissolved quickly, resulting in rapid absorption of drug which in turn provides the rapid onset of action. Since absorption is taking place directly from mouth, so bioavailability of drug increases. This type of drug delivery is becoming popular day by day due to its numerous advantages [5].

MATERIALS AND METHODS

Ergotamine Tartrate was purchased from *Inga LAB Ltd, Mumbai, Maharastra.* Crospovidone and Croscarmellose sodium were obtained from Wockhardt Research Centre, Aurangabad as a gift sample.

The important instruments used for the research are 10 station rotary tablet punching machine (Clit, Ahmedabad); UV-Spectrophotometer UV-1800 (Shimadzu, Japan); disintegration test apparatus ED, dissolution test apparatus TDT-08L, Friabilator USP EF-2 (Electrolab, Mumbai).

Formulation of fast dissolving tablets direct compression method [6]

Fast dissolving tablets of Ergotamine tartrate were prepared by direct compression method, using synthetic disintegrants crospovidone and croscarmellose sodium in different ratios and directly compressible MCC (PH-102) as diluent and mannitol to enhance the mouth feel. According to the formulae given in Table-1,

- All the ingredients were passed through #60 mesh separately.
- The drug and MCC (PH-102) were mixed by the small portion of both each time and blending it to get a uniform mixture and kept aside.

Then the ingredients were weighed and mixed in geometrical order. And the mixed blend of excipients was compressed using 8 mm flat bevel edged punches to get a tablet of 200 mg weight in a (Clit pilot press 10 station compression machine)

Evaluation of tablets [7, 8]

Tablets were subjected to various evaluation parameters which include weight variation, thickness, tablet hardness, friability, disintegration time, drug content uniformity and *in-vitro* drug release studies.

- **Weight variation**

In Indian Pharmacopoeia procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity. IP official limits of percentage deviation of tablet are presented in the table 2.

- **Tablet thickness**

Thickness of the tablet is important for uniformity of tablet size. Thickness was measured using Vernier Calipers. It was determined by checking the thickness of three tablets of each formulation.

- **Tablet hardness**

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was

determined using Monsato hardness tester. The average hardness of three determinations was recorded.

- **Friability**

Friabilator consist of a plastic-chamber that revolves at 25 rpm, dropping ten tablets at a distance of 6 inches with each revolution. The tablets were rotated in the Friabilator for 4 minutes for 100 revolutions. At the end of test tablets were dusted off and reweighed, the loss in the weight of the tablet was measured.

Percentage friability was calculated by using the formula

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

- **Content uniformity test [9]**

The tablets were tested for their drug content uniformity. At random 20 tablets were weighed and powdered. The powder equivalent to 10 mg of Ergotamine tartrate was transferred to 50 ml volumetric flask and 40 ml of ethanol is added. The solution was shaken thoroughly. Then the volume is adjusted to 50 ml with ethanol. The undissolved matter was removed by filtration through Whatmann No.41 filter papers. Then dilute the solution to obtain 10µg solution. The absorbance of the diluted solutions was measured at 314 nm. The concentration of the drug was calculated from the standard curve of the Ergotamine tartrate in ethanol. The mean percent drug content was calculated as an average of three determinations. The results were shown in Table-4.

- **Wetting time [10, 11]**

A piece of tissue paper (10.75 × 12 mm) folded twice was placed in a culture dish (d = 6.5 cm) containing 6 ml of simulated saliva (phosphate buffer pH 6.8). A tablet was carefully placed on the surface of tissue paper and the time required for simulated saliva to reach the upper surface of the tablet was noted as the wetting time.

- **Water absorption ratio[10, 11]**

A test was done with the same procedure as that of wetting time. In this test, initial weight of the tablet was noted before placing it on a Petridish. After complete wetting, the wetted tablet was then weighed. The results were shown in Table-4 and Figure-4.

The water absorption ratio 'R' was determined using the equation,

$$R = 100 \times \frac{Wa\text{-}Wb}{Wb}$$

Where, W_a = weight of tablet before water absorption,

W_b = weight of the tablet after water absorption.

- ***In-vitro* disintegration time [12]**

The test was carried out on 6 tablets using USP ED-2L disintegration test apparatus (Electrolab). Distilled water at 37°C±2°C was used as a disintegration media and the time taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

- **Dissolution study [13]**

In-vitro dissolution, of an Ergotamine tartrate fast dissolving tablets were studied in USP TDT-08L dissolution apparatus (Electrolab) employing a paddle stirrer. 900 ml of phosphate buffer pH 6.8 was used as the dissolution medium. The stirrer was adjusted to rotate at 50 rpm. The temperature of dissolution media was previously warmed to 37±0.5 °C and was maintained throughout the experiment.

One tablet was used in each test, 5 ml of sample of dissolution medium were withdrawn by means of the syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 316 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Percentage amount of Ergotamine tartrate released was calculated and plotted against time. The results are shown in (Fig. 5 to 6).

***In vitro* drug release studies details**

Apparatus used: USP TDT-08L dissolution test apparatus

Dissolution medium: 6.8 pH phosphate buffer solution.

Dissolution medium volume: 900 ml

Temperature: 37±0.5 °C

Speed of basket paddle: 50 rpm

Sampling intervals: 2 min & 5 min

Sample withdraw: 5 ml

Absorbance measured: 316 nm

RESULTS AND DISCUSSION

In the present study, an attempt has been made to design and evaluate fast dissolving tablets of Ergotamine Tartrate by direct compression method. Fast dissolving tablets of Ergotamine Tartrate were prepared by direct compression method using crospovidone and croscarmellose sodium as superdisintegrants in different ratios using directly compressible MCC (PH-102) as a diluent and mannnitol to enhance the mouth feel. The prepared formulations were evaluated for different biological, physical and mechanical parameters.

The evaluation results of all ten batches were found to be satisfactory within limit. The precompressional parameters of all the formulations were evaluated and found to be in the IP limit, from these values, it was evident that these blends had good flow properties.

The compressed tablets showed good hardness and friability. All the tablet formulations showed uniformity in drug content within the range of 98.76 to 101.8%. The disintegration time of eight formulations was less than one minute and the disintegration time of *crospovidone* found quite good than Croscarmellose sodium. This clearly indicates that crospovidone has good disintegrating property.

In vitro disintegration time, wetting time and water absorption ratio was found to be in the range of 12-78 sec, 8-31 sec and 31-49 respectively. The percent drug release of all the formulations was found to be in the range of 12–96%.

Table 1: Formulation table for ergotamine tartrate fast dissolving tablets

Ingredients (mg/tablet)	Formulation code									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Drug	4	4	4	4	4	4	4	4	4	4
Crospovidone	25	50	75	100	125	--	--	--	--	--
CCS	--	--	--	--	--	25	50	75	100	125
Magnesium stearate	2	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3	3
Mannitol	10	10	10	10	10	10	10	10	10	10
Orange flavor	2	2	2	2	2	2	2	2	2	2
MCC (PH-102)	154	129	104	79	54	154	129	104	79	54
Total weight	200	200	200	200	200	200	200	200	200	200

Drug-Ergatamine tartrate; CCS-Croscarmallose Sodium

Among all the formulations, the formulation F5 containing 62.5% of crospovidone emerged as the overall best formulation showing disintegration time of 12 secs and drug release of 96% in 30 mins. Whereas formulation F10 containing 62.5% of croscarmellose sodium shown disintegration time of 18 secs and released 89% drug release in 30 mins.

From the results, it was observed that with increments in superdisintegrants concentration in the formulations, there was a decrease in the values of wetting time and the disintegration time. This part of study confirmed that the crospovidone can be effectively used as super disintegrant. The comparative *in-vitro* drug release profile of all the ten formulations depicted in the Figure-6 showed a complete drug release within 20 min.

Table 2: Weight variation limits

S. No.	Average weight of tablet (mg)	Maximum % difference allowed
1	130 or less	10
2	130-324	7.5
3	324<	5

Table 3: Pre-compression parameters of formulations prepared by direct compression method

S. No.	Formulation code	Angle of repose (θ)	Bulk density (gm/cc)	Tapped density (gm/cc)	Carr's index (%)	Hausner's ratio
1.	F1	27.49	0.55	0.69	20.29	1.25
2.	F2	30.13	0.48	0.59	18.64	1.23
3.	F3	29.1	0.45	0.54	16.67	1.20
4.	F4	30.22	0.47	0.58	18.97	1.23
5.	F5	27.86	0.50	0.63	20.63	1.26
6.	F6	29.57	0.48	0.62	17.74	1.22
7.	F7	30.67	0.57	0.65	12.31	1.14
8.	F8	29.31	0.49	0.58	15.52	1.18
9.	F9	28.43	0.56	0.66	15.15	1.18
10.	F10	28.94	0.53	0.63	15.79	1.19

Table 4: Post-compression parameters of formulations prepared by direct compression method

Parameters	Formulation code									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Hardness*±SD (kg/cm^2)	3.07±0.15	3.40±0.26	3.23±0.28	3.53±0.35	3.17±0.40	3.27±0.15	3.40±0.10	3.37±0.21	3.10±0.44	3.57±0.15
Thickness*±SD (mm)	2.13±0.15	2.10±0.10	2.10±0.00	2.13±0.06	2.17±0.06	2.10±0.10	2.03±0.06	2.13±0.15	2.20±0.10	2.03±0.06
Friability (%)	0.85	0.61	0.76	0.55	0.96	0.50	0.70	0.45	0.80	0.85
In-vitro disintegration time*±SD (Sec)	47.67±1.53	34.00±3.61	20.33±1.53	14.33±1.53	9.33±1.15	73.67±1.53	61.33±2.08	42.67±3.51	32.33±2.08	17.33±1.53
Wetting Time*±SD (Sec)	23.33±1.53	18.33±2.59	16.00±1.00	12.33±0.58	9.67±0.58	32.67±0.58	27.00±1.73	26.33±2.08	20.00±2.00	12.33±2.08
Water Absorption ratio*±SD (%)	74.47±1.03	62.21±1.74	83.87±0.93	63.66±1.09	60.48±0.93	51.60±0.17	73.40±2.82	65.05±1.36	85.58±2.02	70.54±2.07
Percent Drug Content*±SD	99.78±0.05	98.76±0.10	99.97±0.11	101.40±0.04	99.55±0.27	99.68±0.07	100.76±0.05	99.59±0.12	101.68±0.15	98.86±0.43
Weight Variation (%)	(188.6-204.7 mg) Within the IP limits of±7.5%									

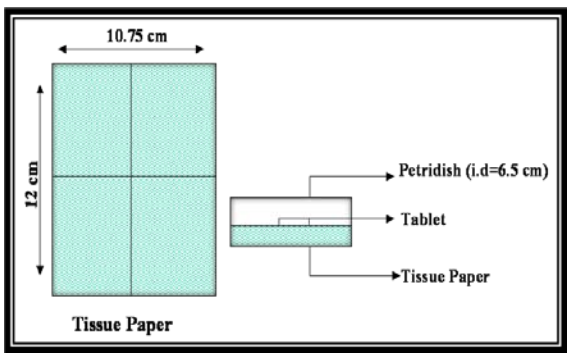

Fig. 1: Schematic representation of wetting time/water absorption ratio determination

Fig. 2: Dissolution apparatus (USP TDT-08L)

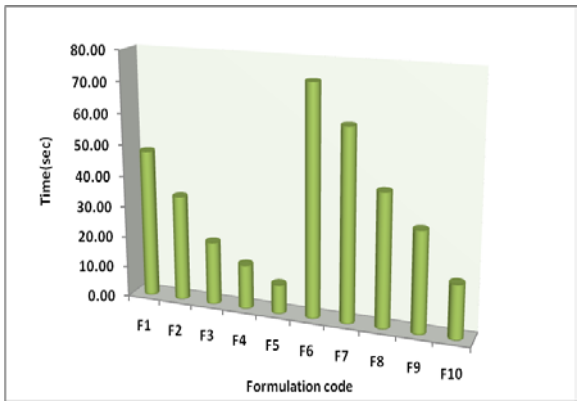

Fig. 3: *In vitro* disintegration time of Ergotamine Tartrate tablets prepared by direct compression method

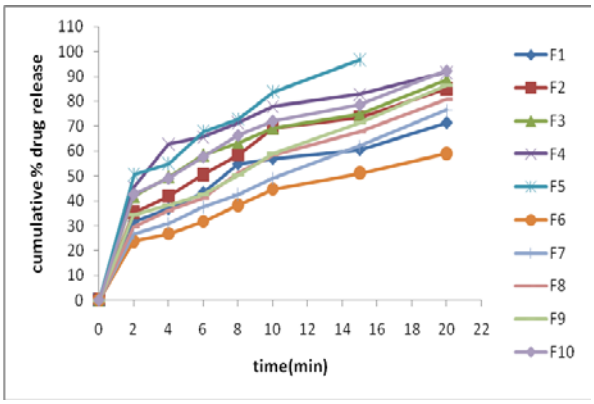

Fig. 5: Cumulative percent drug released Vs time plots (zero order) of formulations F1–F10 in pH 6.8 Phosphate Buffer

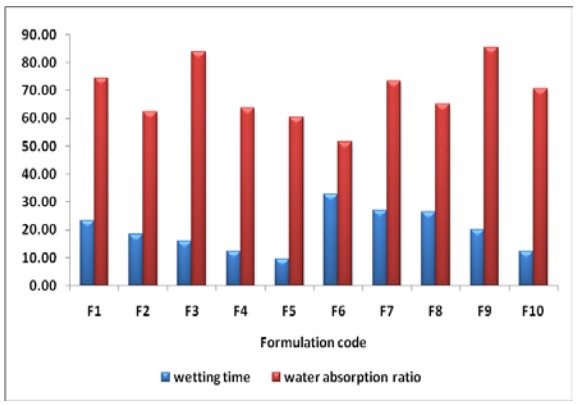

Fig. 4: Wetting time and water absorption ratio of Ergotamine Tartrate tablets prepared by direct compression method

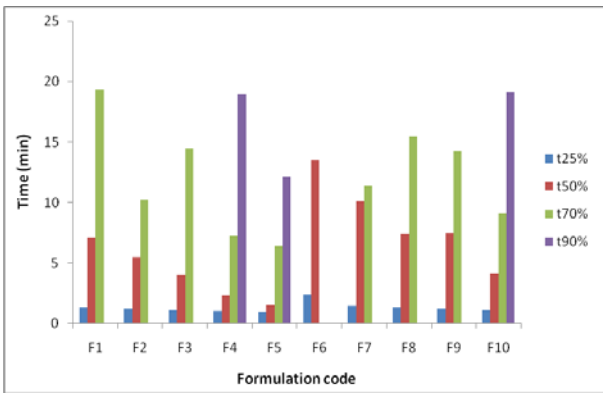

Fig. 6: Comparison of dissolution parameters ($t_{25\%}$, $t_{50\%}$, $t_{70\%}$ and $t_{90\%}$) of fast dissolving tablets of Ergotamine Tartrate

CONCLUSION

In the present study, direct compression technique was evaluated for the development of fast disintegrating tables. Two types of superdisintegrants were used namely crospovidone and cros caramellose sodium. From the result obtained, it can be concluded that formulation of fast dissolving tablet using crospovidone as a superdisintegrant showed improved disintegration and solubility and hence better patient compliance.

CONFLICT OF INTERESTS

Declared None

REFERENCES

1. Shahiwala A. Formulation approaches in enhancement of patient compliance to oral drug therapy. Drug Dev Ind Pharm 2011;8(11):1521-9.
2. Sastry S, Nyshdham J, Fix J. Recent technological advances in oral drug delivery: a review. AAPS Pharm Sci Tech 2000;13:138-4
3. Nagar P, Singh K, Chauhan I, Verma M, Mohd Yasir, Khan A, *et al.* Orally disintegrating tablets: formulation, preparation techniques and evaluation. J Appl Pharm Sci 2011;01(04):35-45.
4. Khan T, Nazim S, Shaikh S, Shaikh A, Khairnar A, Ahmed A. An approach for rapid disintegrating tablet: a review. Int J Pharm Res Dev 2011:3(3):170-83.
5. Dey P, Maiti S. Orodispersible tablets: A new trend in drug delivery. J Nat Sci Biol Med 2010;1:2-5.
6. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets of salbutamol sulphate: a novel drug delivery system. Indian Drugs 2004;41:592-8.
7. Liberman H, Lachman L. The theory and practice of industrial pharmacy. 3rd ed. Bombay: Verghese Publication House; 1991. p. 171-93.
8. Jeevanandham S, Dhachinamoorthi D, Chandrashekhar KB, Muthukumaran M, Sriram N. Formulation and evaluation of naproxen sodium orodispersible tablets-A sublimation technique. Asian J Pharm 2010;4(1):48-51.
9. Indian Pharmacopoeia. 4th ed. Vol. II: Controller of Publications, Govt. of India, Ministry of Health & Family Welfare, New Delhi; 1996. p. 735.
10. Chaudhari PD, Chaudhari SP, Kolhe SR, Dave KV, More DM. Formulation and evaluation of fast dissolving tablets of famotidine. Indian Drugs 2005;42(10):641-9.
11. Malik K, Arora G, Singh I. Ocimum sanctum seeds, a natural superdisintegrant: formulation and evaluation of fast melt tablets of nimesulide. Polim Med 2012;42(1):49–59.
12. Saroha K, Kumar G, Paul Y. Formulation and evaluation of fast dissolving tablets of amoxicillin trihydrate using synthetic superdisintegrants. Int J Pharm Bio Sci 2013;4(1):254-62.
13. Bhagwati ST, Hiremath SN, Sreenivas SA. Comparative evaluation of disintegrants by formulation cefixime dispersible tablets. Indian J Pharm Edu Res 2005;39(4):194-7.