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FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLET OF TINIDAZOLE

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ABSTRACT

Tinidazole mouth dissolving tablet were prepared to achieve quick onset of action and for maximum bioavalability. The purpose of the present research work was to compare the efeect of different superdisintegrants on the mouth dissolving property of tinidazole tablets. Mouth dissolving tablet of tinidazole were prepared using crospovidone, crosscarmellose, and sodium starch glycolate as superdisintegrants by direct compression technique. Prepared tablet were evaluated for weight variation, hardness, friability, content uniformity, wetting time, in vitro dispersion time, in vitro disintegration time and dissolution studies. Disintegration time of all prepared formulation was found to be in order: M9<M8<M6<M7<M3<M5<M4<M2<M1. Disintegration time was found to be rapid in M9 formulation. The in vitro dissolution time was found to be 96.50% in 10 minutes for the formulation M9. Crospovidone showed faster disintegration of tablets among all other superdisintegrants.

Key words: Tinidazole, mouth dissolving tablet, direct compression, superdisintegrants.

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. Mouth dissolving tablets are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed. Mouth dissolving tablets undergo disaggregating in the mouth when in contact with the saliva in less than 60 seconds, preferably in less than 40 seconds, forming a suspension which is easy to swallow. The target population for these new fast-dissolving / disintegrating dosage forms has generally been pediatric, geriatric, and bedridden or mentally disabled patients. A major claim of some mouth dissolving tablets is increased bioavailability compared to traditional tablets. Because of dispersion in saliva while still in the oral cavity, there can be pregastric absorption from some formulation, in cases where the drug dissolves quickly. Buccal, pharyngeal and gastric region are areas of absorption of the formulation. [1-4] Objective of present study was to develop such as novel drug delivery systems for tinidazole by simple & cost effective direct compression method. Crospovidone, crosscarmellose, sodium starch glycollate were used as superdisintegrant in the formulation for faster disintegration. Micro crystalline cellulose (MCC) is used as diluents and disintegrant. It is one of the fastest growing segments in the pharmaceutical market.[3,4,11] Tinidazole is a prodrug and antiprotozoal agent. The nitro group of tinidazole is reduced in *Trichomonas* by a ferredoxin-mediated electron transport system. The free nitro radical generated as a result of this reduction is believed to be responsible for the antiprotozoal activity. It is suggested that the toxic free radicals covalently bind to DNA, causing DNA damage and leading to cell death. It is a to light yellow crystalline compound insoluble in water. [5-15]

MATERIALS AND METHODS

Materials: Tinidazole was received as a gift sample from Schon Pharma, Indore. B-cyclodextrin, sodium starch glycolate, crosscarmellose, crospovidone,

microcrystalline cellulose, aspartame, aerosol, talc, mannitol are all of laboratory scale.

Methods

Tablets are prepared by direct compression technique. The composition of mouth dissolving tablet of tinidazole was shown in Table 1. Weighed quantities of drug with appropriate concentrations of superdisintegrants along with excipients were weighed and mixed in geometric progression in a dry and clean mortar. Then the blend was passed through sieve no 60 for direct compression. The powder blend for direct compression was then compressed in convex faced punches in 10 station rotary tablet machine. The fabricated tablets were evaluated.

EVALUATION

Weight variation test[6,9,11]: 20 tablets were selected at random, individually weighed and the average weight was calculated. None of the tablets deviated from the average weight by more than ±7.5%.

Hardness test[7,9]: Tablets require a certain amount of strength or hardness and resistance to friability to with stand mechanical shocks. The hardness of tablet was measured by Monsanto hardness tester.

Friability[6,8,11]: Twenty tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted, and reweighed. The percentage friability of the tablets was calculated by

$$\% \text{ friability} = \frac{\text{initial weight} - \text{finalweight}}{\text{initial weight}} \times 100$$

Content uniformity[9,15]: The content of tinidazole was determined according to the method described by IP for tinidazole tablets. In brief, 1 ml of water was added to one tinidazole tablet, stood for 15 min, then 80 ml of a 0.5% (w/v) solution of sulfuric acid in methanol. The obtained solution was stirred for 15 min and the volume was adjusted to 100 ml with 0.5% (w/v) solution of sulfuric acid in methanol. The filtrated solution was diluted appropriately and the drug content was measured spectrophotometrically at 310 nm.

Wetting time[10,14]; A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured.

In Vitro Dispersion Time[11,12,15]: In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of phosphate buffer pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. Six tablets from each batch were randomly selected and in vitro dispersion time was performed.

In Vitro Disintegration Time[11,13,15]: 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°C using 900 ml of distilled water. The time required to obtain complete disintegration of all the six tablets was noted.

Dissolution Studies[14,15]: In vitro dissolution studies were performed using type II (paddle) dissolution apparatus at 100 rpm, and 900 ml of phosphate buffer (pH 6.8) was used as a dissolution medium. Temperature of dissolution medium was maintained at 37±0.5°C. Five milliliters aliquot of the dissolution medium was withdrawn at specific time intervals. Absorption of filtered solution was measured by UV–visible spectrophotometer at 310 nm, and the percent of drug released was determined using standard curve. Dissolution rate was studied for the prepared formulations.

RESULTS

Formulations were prepared by direct compression techniques using different disintegrating agents are shown in Table 1. Parameters are mentioned in Table given below. Disintegration time was determined by using disintegration test apparatus. Out of all batches M9 showed minimum disintegration time 25.37 ± 1.77 seconds indicating that drug is rapidly available for dissolution. Drug content of all formulations was determined and results are shown in table 6.7. M9 showed drug content 98.33 ± 0.67% indicating the content uniformity and homogeneity in preparation. *In-vitro drug* releases of all formulations were determined. Out of all batches M9 showed maximum drug release 96.50% in 10 minutes indicating that drug was quickly released at salivary pH.

DISCUSSION

Different formulations were prepared using 3,5 and 7% superdisintegrants. The tablets prepared by direct compression technique were found to have adequate hardness, friability, content uniformity and in vitro dispersion time. Prepared tablets disintegrate within few seconds without need of water: thereby enhance

absorption resulting in increased bioavailability and increased patient compliance. Among all superdisintegrant crospovidone showed maximum effect of disintegration. Effect of superdisintegrant from all the prepared formulation was found to be in following order: Crospovidone>crosscarmellose> sodium starch glycolate. The formulated tablet M9 showed fast disintegration may be useful for pediatric and geriatric population.

Table 1. Formulation of MDT's

Ingredients	**Quantity (mg)**								
Formula	M1	M2	M3	M4	M5	M6	M7	M8	M9
Complex equivalent to 130 mg	220	220	220	220	220	220	220	220	220
SSG	3 (1%)	9 (3%)	15 (5%)						
CCS				3 (1%)	9 (3%)	15 (5%)			
CP							3 (1%)	9 (3%)	15 (5%)
MCC	30	30	30	30	30	30	30	30	30
Aspartame	1	1	1	1	1	1	1	1	1
Aerosil	1	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1	1
Mannitol	44	38	32	44	38	32	44	38	32
Total	300	300	300	300	300	300	300	300	300

Table 2. Disintegration time of MDT'S

Parameters	**Formulation batch no.**								
	M1	M2	M3	M4	M5	M6	M7	M8	M9
Disintegration time (second)	61.30 ± 3.02	52.21 ± 2.04	42.49 ± 0.79	47.31 ± 2.46	45.21 ± 1.11	35.12 ± 2.31	40.50 ± 1.54	34.98 ± 4.09	25.37 ± 1.77

Table 3. Drug content of MDT'S

Parameters	**Formulation batch no.**								
	M1	M2	M3	M4	M5	M6	M7	M8	M9
Drug content (%)	96.78 ± 0.97	95.33 ± 1.90	96.83 ± 1.57	95.66 ± 2.04	93.33 ± 0.83	98.35 ± 1.05	97.32 ± 0.48	97.51 ± 1.09	98.33 ± 0.67

Table 4. % Cumulative drug release of MDT'S

Time (min)	Cumulative % drug release of different formulations								
	M1	M2	M3	M4	M5	M6	M7	M8	M9
0	0	0	0	0	0	0	0	0	0
2	67.36 ± 1.00	68.87 ± 1.30	73.47 ± 2.48	68.30 ± 1.37	70.12 ± 1.88	79.42 ± 2.37	78.11 ± 1.41	82.47 ± 1.04	85.09 ± 2.20
4	68.92 ± 1.24	70.25 ± 1.00	77.95 ± 1.16	69.87 ± 1.72	73.25 ± 0.98	82.37 ± 2.15	82.29 ± 1.24	83.93 ± 0.71	88.41 ± 1.72
6	70.25 ± 1.47	71.89 ± 0.92	80.82 ± 2.52	71.67 ± 1.09	76.50 ± 2.18	85.49 ± 0.85	83.97 ± 1.36	85.41 ± 2.02	90.04 ± 0.92
8	71.86 ± 1.50	75.01 ± 1.34	83.68 ± 1.52	72.98 ± 0.85	78.87 ± 1.55	88.27 ± 1.73	86.78 ± 2.25	88.36 ± 1.20	92.95 ± 1.34
10	73.47 ± 2.02	76.39 ± 2.38	87.41 ± 2.29	75.99 ± 2.08	80.62 ± 1.09	92.38 ± 2.54	90.50 ± 0.68	93.12 ± 1.02	96.50 ± 1.87

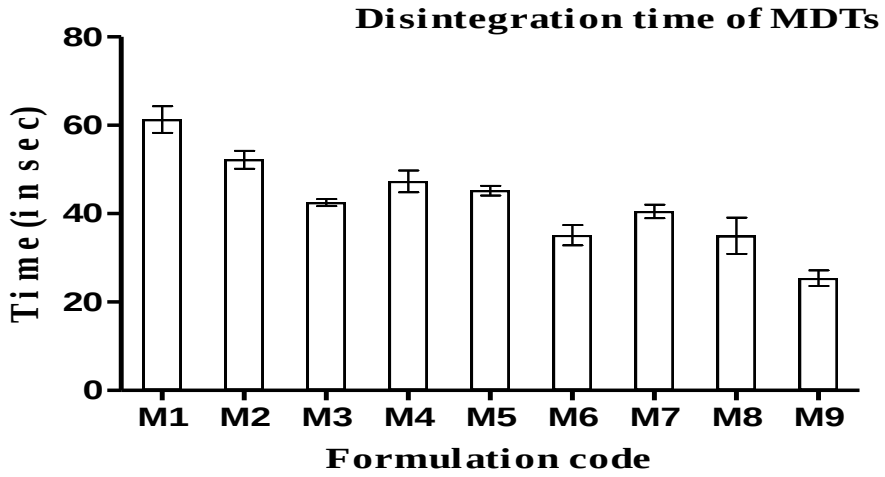

Figure 1. Disintegration time of MDTs

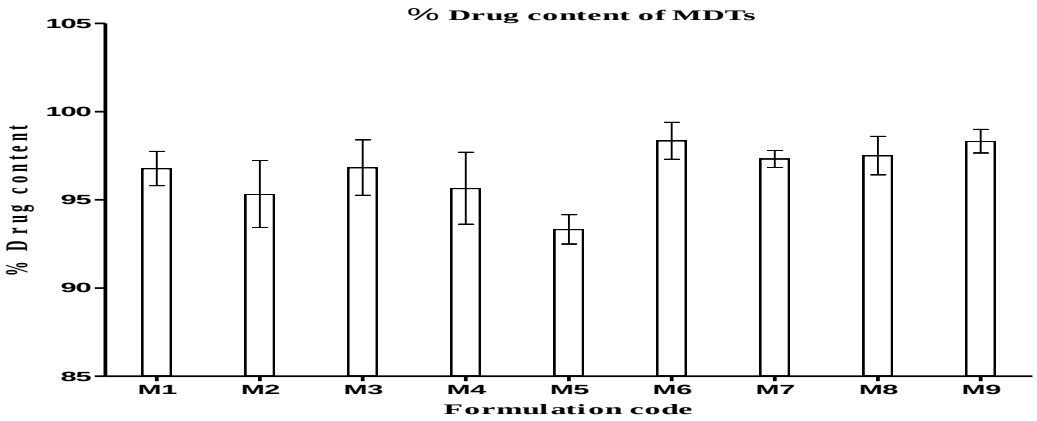

Figure 2. % Drug content of MDTs

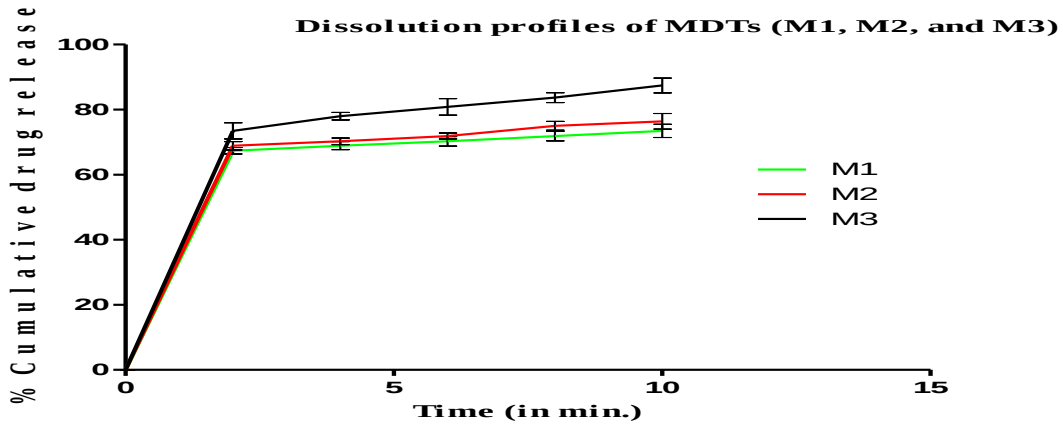

Figure 3.Dissolution Profiles Of MDTs (M1, M2, M3)

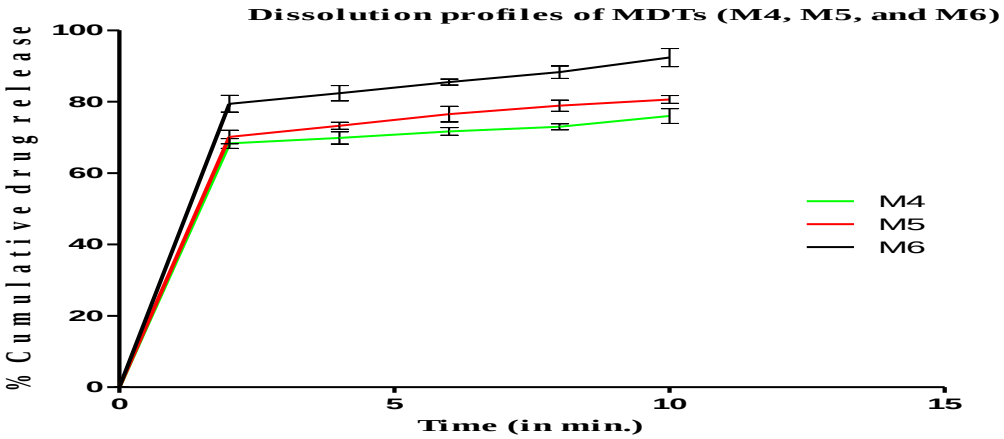

Figure 4. Dissolution Profiles Of MDTs (M4, M5, M6)

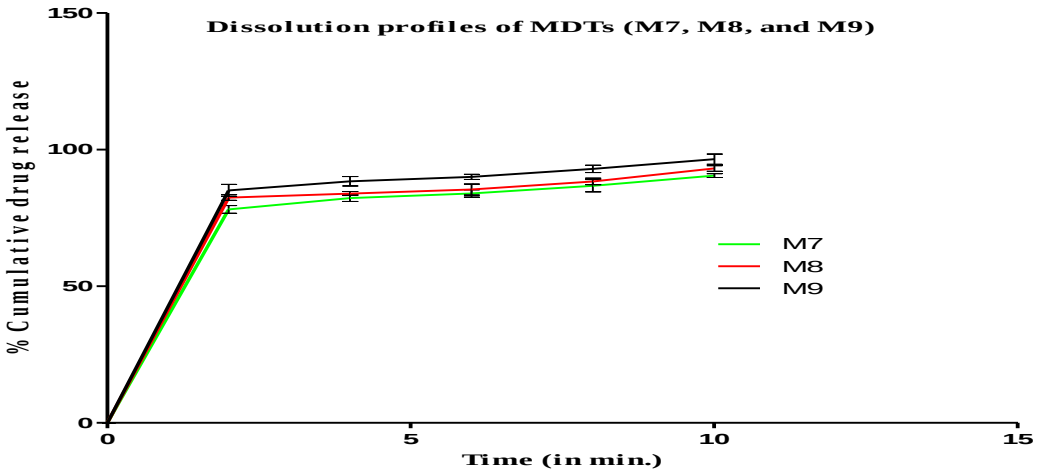

Figure 5. Dissolution Profiles Of MDTs (M7, M8, M9)

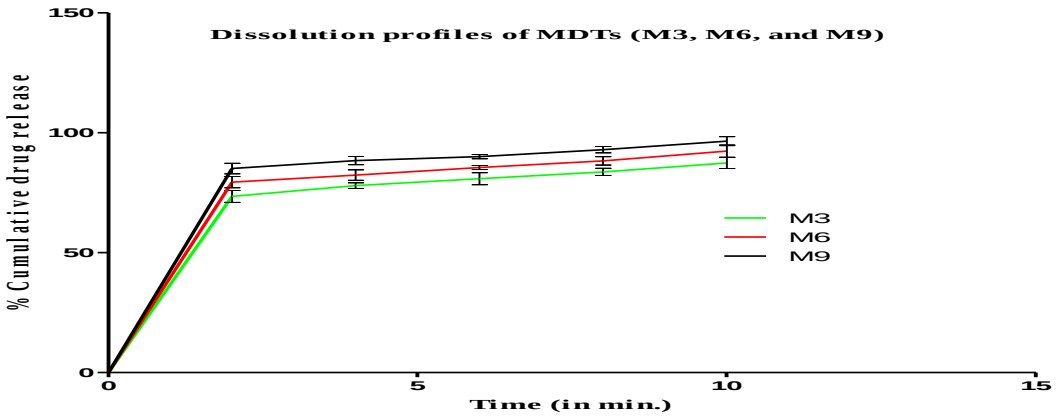

Figure 6. Dissolution Profiles Of MDTs (M3, M6, M9)

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