ejpmr, 2023, 10(11), 272-277

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FORMULATION AND EVALUATION OF ORAL FAST DISINTEGRATING TABLET CONTAINING METRONIDAZOLE

Sindhu A.C.*, Harshitha B.M., Mahalakshmi A.S., Meghana H.C. and Vismaya C.J.

Department of Pharmaceutics Bharathi College of Pharmacy, Bharathi Nagar, MaddurTaluk, Mandya District, Karnataka -571422.

***Corresponding Author: Sindhu A.C.**

Department of Pharmaceutics Bharathi College of Pharmacy, Bharathi Nagar, Maddur Taluk, Mandya District, Karnataka -571422.

Article Received on 03/09/2023 **Article Revised on 24/09/2023** **Article Accepted on 15/10/2023**

ABSTRACT

The drug delivery pharma industry is currently experiencing intense competition and quick evolution due to an ever-growing demand. One such novel and distinctive drug deliverymethod that is quickly gaining popularity in the realm of rapid dissolving technology is the fast-dissolving tablets (FDT). Due to oral route's simplicity, adaptability, patient compliance, and precise dose, it is favored. For those with dysphasia a disorder that makes swallowing difficult, oral administration is not recommended. Additionally, oral delivery may not be the preferable method for many elderly and pediatrics patients. Oral disintegrating tablets (ODT) offer a helpful substitute in this regard. ODT tablets instantly (within30 seconds) breakdown upon contact with saliva, releasing the medication. Additionally, as it escapes first pass metabolism due to pre gastric absorption, this can be advantageous for medications with significant hepatic metabolism.

KEYWORDS: oral disintegrating tablets, oral films, swallowing problems, orodispersable tablets, dysphasia.

INTRODUCTION

Many patients complain about having trouble swallowing pills and hard gelatine capsules, which leads to non-compliance and inefficient treatment. Recent development in new drug delivery system (NDDS) aim to improve patient compliance while improving the safety and efficacy of therapeutic molecules by creating a convenient dosage form for administration. Fast dissolving tablets were developed as a result of one such strategy 2-4. This drug delivery system has several benefits, including the ability to administer medication without the use of water, ease of administration and accurate dosing when compared to liquids, portability, the ability to provide the benefits of liquid medication in the form of a solid preparation, suitabilityfor pediatric and geriatric patients, and rapid drug absorption that may results in a quick onset of action. Some medications are absorbed from the mouth, pharynx, and esophagus as saliva travels down into stomach, which increases the drug's bioavailability. Pre-gastric absorption can also improve bioavailability, which can lead to a smaller dosage form and improve clinical performance by reducing side effects.[1]

Mouth-dissolving tablets are a helpful solution to these issues. Since they break down and dissolve quickly in saliva, drinking water is not necessary. A market line expansion may be positive as a result of the creation of a fast-dissolving tablet.[2]

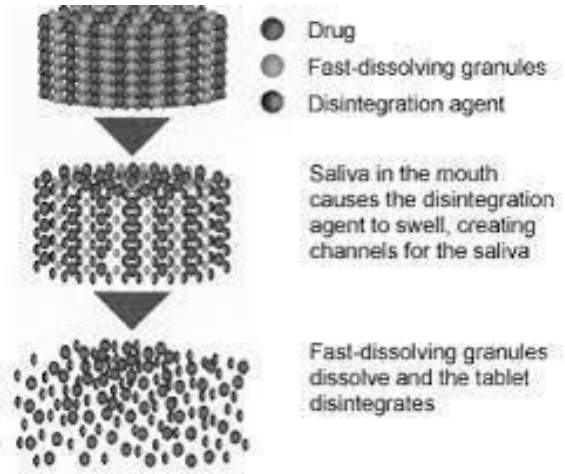


Figure No 1: Fast dissolving tabletCharacteristics of oral disintegrating tablets.

1. Bioavailability.
2. Constancy.
3. Quick start of healing process.
4. Well suited to development technologies.

Benefits of oral disintegrating tablets

1. It can be given to patients who cannot swallow dosage forms, such as those who are bedridden, old, or suffering from renal disease, which increases patient compliance.
2. A pleasant mouthfeel helps to hide the harshness of

medication.
3. Rapidly intervening pharmacological therapy.
4. It offers improved medication absorption and quick bioavailability.[3]

MATERIALS AND METHODS

Materials

Metronidazole was given by the Cipla pvt Ltd, Bengaluru as a gift sample. Direct compressible mannitol, magnesium stearate, crospovidone, guar gum, talc, saccharin sodium, direct compressible micro crystalline cellulose (MCC) and vanillin of Pharma grade (or) the best possible laboratory was used as supplied by the manufacturers.[4]

Method of formulation

Since ODT's are formulated to disintegrate in oral cavity. If excipients have good water solubility, they will facilitate dissolution and disintegration.[5]

Metronidazole oral fast disintegrating tablets were prepared by direct compression method- Formulations F1-F6, were prepared by blending each super disintegrant in three different proportions. In oral fast disintegrating tablets were formulated by using micro crystalline cellulose as directly compressible binder, crospovidone and guar gum is added as a super disintegrant and helps the tablet to break up into smaller pieces when contact with aqueous solution. Saccharin sodium used as a sweetening agent and vanillin is used as flavorings agent and it enhances palatable feel. Talc and magnesium stearate were added as a lubricatingagent and Mannitol is added as a diluent. Composition of all formulations is listed in table: 1 was mixed in a mortar and pestle for 10 minutes for uniform mixing. The powder mixtures with excipients were compressed into tablets with single punch tablet compression machine.[4,5]

Table No 1: Formulation of Metronidazole (FDT).

Ingredients (mg\tablets)	F1	F2	F3	F4	F5	F6
Metronidazole	125	125	125	125	125	125
Crospovidone	5	10	15	-	-	-
Guar gum	-	-	-	5	10	15
Mannitol	41.5	36.5	31.5	41.5	36.5	31.5
Magnesium stearate	2	2	2	2	2	2
Talc	1	1	1	1	1	1
MCC	20	20	20	20	20	20
Saccharin sodium	5	5	5	5	5	5
vanillin	0.5	0.5	0.5	0.5	0.5	0.5
Total	200	200	200	200	200	200

1. Preformulation studies

1. **Organoleptic evaluation of Pure drug:** Drug's organoleptic characteristics, such ascolor, smell, and taste, were noticed using descriptive terminology.[6]
2. **FT-TR Studies:** The IR absorption spectra of the Metronidazole drug and with different super disintegrants was taken. Spectral scanning was done in the range between 4000-450 cm- 1 using KBr disc method, 1-2 mg of drug examined was triturated with 300-400 mg, specified quantity of finely powdered and dried potassium bromide at 1 ton\cm2. These quantities are usually sufficient to give a disc of 10-15 min diameter and pellets of suitable concentration by a hydraulic press. The scan was examined for the presence of principal drug peak shifting and masking caused by super disintegrants and additives.[4,7]

i. **Angle of repose (q):** The angle of repose (q) can be used to calculate the friction forces present in loose powder. It is a sign of the powder's flow characteristics. It is characterized as the greatest angle that can be formed between the surface of the powder pile and the horizontal plane.

$$Tan(q)=h/rq = \tan^{-1}(h\backslash r)$$

Where, q is the angle of reposeh is the height in cm

r is the radius in cm

The powder combination was permitted to pass through a funnel that was mounted to a stand at a specific height (h). The height and radius of the newly created heap of powder were then measured, and the angle of repose was determined. It was carefully watched that the powder particles did not collide with one another as they passed through the funnel's sides. Relationship between the powder flow characteristics and the angle of repose.[8]

Table No 2: Angle of Repose As Indication of Flow Properties.

Sl No.	Angle of repose	Type of flow
1	<20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very poor

ii. **Bulk density (Db):** It is the ratio of the powder's total mass to its bulk volume. The weight powder, which had been put through a standard sieve #20, was poured into a measuring cylinder, and the starting weight was recorded. The bulk volume is the original volume. Using this information, the bulk

density is computed using the following formula. It is expressed in g/ml and is given by [8]

Db = M/ Vb

Where, M = mass of powder

Vb = bulk volume of the powder.

iii. **Tapped Density (Dt):** It is the ratio of total mass of the powder to the tapped volume of the powder. The powder was tapped 750 times to determine its volume, and if there was adifference of less than 2% between the two volumes, the tapped volume was documented. If it is higher than 2%, tapping is repeated 1250 times, and the volume of taps is recorded. The tapping process was continued (in a bulk density apparatus) until the difference between succeeding volumes was less than 2%. It is denoted by g/ml. and is given by [8]

$$Dt = M / Vt$$

Where, M = mass of powder

Vt = tapped volume of powder

iv. **Carr's index (or) % compressibility:** It indicates powder flow properties. It is expressedin percentage and is given as [8]

I = Dt-Db/Dt ×100

Dt = tapped density of powder.

Db = bulk density of powder.

Table No 3: Relationship between % Compressibility and Flow Ability.

% compressibility	Flow ability
5-12	Excellent
12-16	Good
18-21	Fair Passable
23-35	Poor
33-38	Very Poor
<40	Very Very Poor

v. **Hausner's ratio:** The degree of densification that could be caused by feed hopper vibration is shown by Hausner's ratio. Better flow is suggested by a lower value of andvice versa.[8]

Hausner's ratio = (tapped density-fluff density) \ tapped density

1. Post Formulation Studies

i. **Thickness of tablets:** Tablet thickness is a crucial element in both duplicating appearance and counting with filling machinery. The uniform thickness of the tablets is used as a counting mechanism by some filling equipment.[9]

ii. **Weight variation:** From each formulation, 20 tablets were chosen at random and weighed separately using a Shimadzu digital balance (BL-220H). The weight variance was calculated by comparing the individual weights to the average weight. [10,11,12]

PD = $(W_{avg})-(W_{initial})\backslash(W_{avg})\times100$ Where, PD=Percentage deviation

W_{avg} = Average weight of tablet $W_{initial}$ = Individual weight of tablet

Table No 4: Weight variation and accepted % deviation.

Avg. weight of tablet	% deviation
80 mg or less	±100
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5.0

iii. **Hardness:** The FDT's maximum allowable hardness is typically kept in the lower range to encourage early disintegration in the mouth. Typically, hardness testers (like the Monsanto tablet hardness tester) can be used to determine the tablet's hardness. It is expressed in kilograms or pounds.[12]

iv. **Friability:** For this, Roche friabilator was employed. By using a plastic chamber that rotates at 25 rpm while dropping the tablets at a distance of 6 inches with each revolution, this device causes a number of tablets to experience the combined effects of abrasion and shock. The friabilator was loaded with 20 pre-weighed tablets and run for100 rotations. Then, the tablets were reweighed and dusted. The loss in the weight of tablet is the measure of friability and is expressed in % as [9,11]

% friability = loss in weight \ initial weight × 100

v. **Wetting time test:** Tissue paper that had been twice folded was put in a Petri dish with an interior diameter of 5 cm and 6 ml of water. On top of the tissue paper in the Petri dish, a tablet was carefully positioned. The amount of time that it took for water to completely wet the tablet's upper surface was recorded as wetting time.[10]

$$R = Wa - Wb /Wb\times100$$

Wa= tablet weight after water absorption Wb=tablet weight before water absorption

vi. **Dissolution studies:** A 10 ml sample volume was taken at regular intervals from a region that was at least 1 cm from the vessel wall and situated halfway between the surface of the dissolving media and the top of the rotating paddle. To keep the medium's volume constant, the volume that was withdrawn was substituted with new dissolving media. With pH 7.4 buffer used as a blank, the filtered samples were spectrophotometrically examined at 320 nm. The calibration curve was used to determine the drug content of the dissolving sample.[13]

vii. **Disintegration test:** The traditional tablet test outlined in the pharmacopoeia was initially used to gauge the disintegration time for oral dispersible tablets. Tablets were inserted in the disintegration tubes, and the amount of time needed for full disintegration without any residues remaining on the screen was noted. The disintegration time was also verified using a modified approach. A sample of 7.4 pH buffer in the amount of 6 to 8 ml was taken. The disintegration time was measured whenthe tablet had completely dispersed throughout the cylinder.[14]

viii. **Content uniformity:** This is determined using any

standard assay method specified forthe specific API in any of the standard pharmacopoeia. The estimation of the API content in each strip is used to determine the homogeneity of the content 85-115 % is the maximum content homogeneity.[14]

ix. **Stability studies:** By keeping the tablets of the promising formulations F3 in amber- colored rubber stopper glass vials at 40^{o} at 75% RH for one month, the tablets were subjected to accelerated stability experiments. The tablets were visually inspected for any physical changes and assessed for changes in drug content and in vitro dispersiontime at intervals of 1 month.[10]

RESULT AND DISCUSSION

The specific objective of this study is to develop an oral fast disintegrating tablet of Metronidazole by using natural and synthetic super disintegrants like guar gum and to study antibacterial effects and urinary tract infection and vaginal infection. In this regard formulation studies were carried out and the results for the experiment conducted are as follows.

1. PRE-FORMULATION STUDIES

a. Melting point determination

Table No 5: Melting point of metronidazole.

Reported	Method	Observed
159-161℃	Thile's tube	161℃
	DSC	160℃

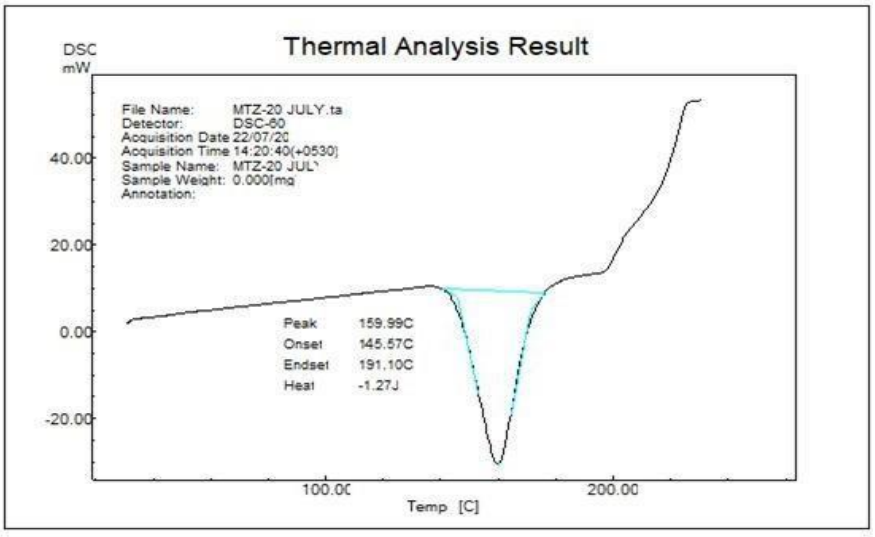


Figure No. 2: DSC Thermograph of metronidazole.

B.Solubility Analysis

Metronidazole was found to be slightly soluble in water, sparingly in methanol, practically soluble in phosphate buffer pH 7.4. the obtained results are in agreement with other researchersi.e., metronidazole is slightly soluble in water highly soluble in phosphate buffer pH 7.4.

C.Compatibility studies by FTIR

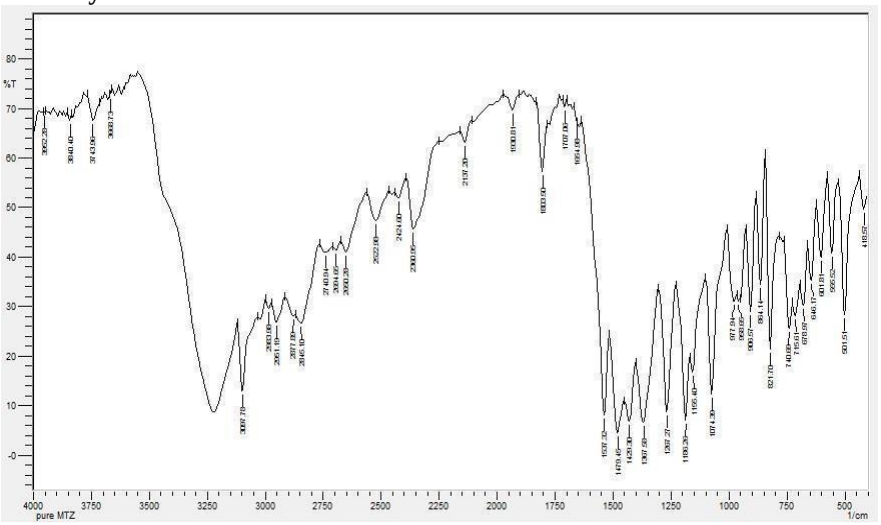


Figure No 3: FTIR spectra of Metronidazole Micromeritic characters of oral fast disintegrating tablets of Metronidazole.

Table No 6: Micromeritic Characters of Oral Fast Disintegrating Tablets.

Code	Bulk density(g/cm^3)	Tapped density(g/cm^3)	Hauser's ratio	Carr's index (%)	Angle of repose (□)
F1	0.373	0.412	1.079	7.28	28.27
F2	0.382	0.414	1.056	7.60	22.39
F3	0.386	0.414	1.094	9.65	31.15
F4	0.348	0.377	1.084	7.75	24.28
F5	0.352	0.388	1.013	9.04	27.29
F6	0.356	0.405	1.038	8.17	25.35

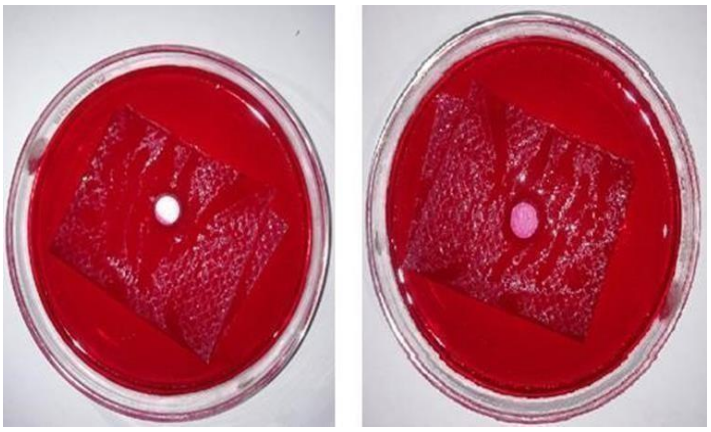
2. Post compression parameter of fast disintegrating tablets

Table No 7: Results of hardness, thickness, friability, and weight variationformulations F1-F6.

Formulation batches	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight Variation
F1	4.00	2.94	0.46	0.75
F2	3.99	2.33	0.40	0.74
F3	3.96	2.47	0.37	0.65
F4	4.2	3.25	0.67	0.90
F5	3.99	3	0.50	0.87
F6	3.98	3.21	0.57	0.83

Table No 8: Results of Wetting Time and Disintegration Time of F1-F6.

Formulation	Disintegration time (sec)	Wetting time (sec)
F1	24	33
F2	19	32
F3	12	29
F4	25	35
F5	23	32
F6	20	31



Time = 0 sec
time = 29 sec

Figure No 4: Wetting time for optimized formulation F3.

Table No 9: In-vitro drug release study of formulations F1-F6 in phosphate buffer pH7.4 Percentage of drug release.

Time(min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	7.49	7.25	8.86	6.49	6.736	8.57
3	25.16	30.14	33.14	20.65	28.08	33.65
6	37.59	45.9	51.13	31.17	39.50	54.13
9	59.9	67.21	72.64	48.28	58.75	69.70
12	78.78	81.10	88.11	65.65	72.9	83.65
15	91.79	93.37	99.4	81.27	84.23	92.65

CONCLUSION

Oro dispersible tablets have potential advantages over conventional solid dosage form. From the present research it was concluded that formulated Oro dispersible tablet of metronidazole containing crospovidone by direct compression method has exhibited a good physical parameter. The overall results indicated that formulation F3 had a higher rank compared to other formulation containing super disintegrants. From the accelerated stability study findings, F3 is having faster disintegration and drug release. Hence formulation F3 is considered as an optimized formulation.

REFERENCE

1. Patel B, Patel D, Parmar R, Patel C, et al, Development and invitro evaluation of fast dissolving tablets of glipizide. Int J Pharm Pharm Sci., 2009; 1(1): 145-50.
2. Bhardwaj S, Jain V, Jat R C, Mangal A, et al. Formulation and evaluation of fast dissolving tablet of aceclofenac. Int J drug delivery, 2010; 2(1): 93-97.
3. Bhavana AG, Deekshitha A, Ranjith Gowda TN, Sindhu AC. Oral fast disintegrating tablet: An overview. European J Pharm medical res., 2021; 8(11): 299-303.
4. Sindhu AC, Kumar M, Bhanushree S, Sinchana R, et al. Formulation and evaluation of oral dispersible tablets of stavudine with different super disintegrants. World J pharm Res., 2022; 11(5): 1-11.
5. Jeong SH, Takaishi Y, Fu Y, Park K. Material properties for making fast dissolving tablets by a compression method. J Materials Chemistry, 2008; 18(30): 3527-35.
6. Thakur R, Mahant S, Singla S, Goyal S. Formulation and evaluation of immediate release tablet of carvedilol with natural super disintegrant and synthetic disintegrants, 2018; 5(2): 187-94.
7. Jacob S, Shirwaikar A, Joseph A, Srinivasan K. Novel co-processed excipients of mannitol and microcrystalline cellulose for preparing fast dissolving tablets of glipizide. Indian J Pharm Sci., 2007; 69(5): 633-39.
8. Pawar PB, Mansuk AG, Ramteke KH, Sharma YP, et al. Mouth dissolving tablet: A review. Int J Herbal Drug Res., 2011; 1(2): 22-29.
9. Gupta AK, Mittal A, Jha KK. Fast dissolving tablet-A review. The Pharma innovation, 2012; 1(1): 1-8.
10. Nagendra Kumar D, Raju SA, Shirsand SB, Para MS. Design of fast dissolving granisetron HCL tablets using novel co-processed super disintegrants. Int J Pharm Sci Rev and Res., 2010; 1(1): 58-62.
11. Narmada GY, Mohini K, Prakash Rao B, Gowrinath DX, et al. Formulation, evaluation and optimization of fast dissolving tablets containing amlodipine besylate by sublimation method. ARS Pharm., 2009; 50(3): 129-44.
12. Siddiqui M N, Garg G, Sharma P K. Fast dissolving tablets: Preparation, characterization and evaluation: an overview. Int J Pharm sci review Res., 2010; 4(2): 87-96.
13. Aglawe SB, Gayke AU, Sancheti VP, Metkar PS. Formulation and evaluation of mouth dissolving tablets of oxcarbazepine. World J Pharm Res., 2017; 6(10): 1130-37.
14. Bhyan B, Jangra S, Kaur M, Singh H. Orally fast dissolving films: innovations in formulation and technology. Int J Pharm Sci Res., 2011; 9(2): 50-57.