Research Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

FORMULATION AND *IN VITRO* EVALUATION OF ORNIDAZOLE FILM COATED TABELTS FOR COLON TARGETED DRUG DELIVERY

V. Rajasekhar Reddy*[1] and M. Niranjan Babu[2]

[1]*Department of Pharmaceutics, Seven Hills College of Pharmacy, Tirupati, Andhra Pradesh, India.
[2]Department of Pharmacognosy, Seven Hills College of Pharmacy, Tirupati, Andhra Pradesh, India.

ABSTRACT

The aim of the study was to develop colon targeted film coated tablets of Ornidazole using HPMC K4M, HPMC K100 and Eudragit S100 as carriers. Ornidazole is used for the treatment of amoebiasis. The different approaches are designed based on prodrug formulation, pH-sensitivity, time-dependency (lag time), microbial degradation and osmotic pressure etc to formulate the different dosage forms like tablets, capsules, multiparticulates, microspheres, liposomes for colon targeting. The tablets are prepared by using compression method. The prepared tablets are evaluated in terms of their precompression studies, hardness test, thickness test, weight variation test, friability test, *in vitro* study and stability studies. The results of the study showed that formulation FOT-3 is most likely to provide targeting of Ornidazole for local action in the colon. The most satisfactory formulation was stable during stability studies conducted for 60 days as per ICH guidelines. It showed no significant changes in the physicochemical parameters and in vitro release of drug.

KEYWORDS

Ornidazole, Film coated tablets, Colon targeted drug delivery, Carriers, *In vitro* study and Stability studies.

Author for Correspondence:

Rajasekhar Reddy V,
Department of Pharmaceutics,
Seven Hills College of Pharmacy,
Tirupati, Andhra Pradesh, India.

Email: rajasekharreddy.vr@gmail.com

INTRODUCTION

Targeted drug delivery into the colon is highly desirable for local treatment of a variety of bowel diseases such as ulcerative colitis, crohn's disease, amoebiosis, colonic cancer, local treatment of colonic pathologies, and systemic delivery of protein and peptide drugs[1,2]. The colon specific drug delivery system (CDDS) should be capable of protecting the drug en route to the colon i.e. drug release and absorption should not occur in the stomach as well as the small intestine, and neither

the bioactive agent should be degraded in either of the dissolution sites but only released and absorbed once the system reaches the colon[3]. Ornidazole is the nitroimidazole or analogs compound and it is used for the treatment of amoebiasis. Ornidazole is readily absorbed after oral administration and bioavailability approaches 90%[4-6].

MATERIAL AND METHODS

Materials

Ornidazole was obtained from Arati Chemicals Ltd, Mumbai. HPMC K_4M, HPMC K100 and Eudragit S100 were gifted from Apex Pharmaceutical Pvt. Ltd, Chennai. Di basic calcium phosphate, Talc and Magnesium Stearate were purchased from Qualigens fine chemicals, Mumbai, India. All other chemicals and ingredients were used for study are of Analytical grade.

Method

Method of preparation of colon targeted ornidazole tablets

Ornidazole, HPMC K_4M, HPMC K100, Eudragit S100 and Dicalcium phosphate were taken in required quantities mixed and passed through #60 sieves, lubricated with magnesium stearate and talc then was compressed into tablets in 9 mm die cavity of rotary tablet punching machine. Then film coating is done by 6% w/v solution of Eudragit S100 in isopropyl alcohol using 2% PEG-400 as plasticizer in coating pan.

Evaluation Parameters[7-10]

Pre-formulation Studies

Fourier Transform Infrared Spectroscopy The Fourier transform infra-red analysis was conducted for the structure characterization. FTIR spectra of the pure drug, polymers and formulations were recorded by using BOMEN MB SERIES FTIR instrument. Approximately 5mg of samples were mixed with 50mg of spectroscopic grade KBr, samples were scanned in the IR spectroscopy.

Pre-compression studies of tablet powder

Bulk density

3gm of powder were weighed separately and transferred into 100ml measuring cylinder, initial volume was measured and calculated according to the formula

Formula

Bulk density = Mass / Volume

Tapped density

Tapped density is determined by placing a graduated cylinder containing a known mass of powder and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the powder in the cylinder and this minimum volume, the tapped density may be computed.

Formula

Tapped density = Weight of Powder/ Tapped volume of Powder

Angle of Repose

The manner in which stresses are transmitted through a bead and the beads response to applied stress are reflected in the various angles of friction and response. The most commonly used of this in angle of repose, which may be determined experimentally by number of methods. The method used to find the angle of repose is to pour the powder a conical on a level, flat surface and measure the included angle with the horizontal.

Formula

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

Where,

θ = Angle of repose, h = Height of the powder cone, r = Radius of the powder cone.

Compressibility Index or Carr's Index Carr's Index is measured using the values of bulk density and tapped density.

The following equation is used to find the Carr's Index,

$$CI = \frac{(TD-BD)}{TD} \times 100$$

Where, TD = Tapped density BD = Bulk density.

Hausner's Ratio

It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder.

Formula

Hausner's Ratio = Tapped density/Bulk density

Post compression studies of Ornidazole tablets

Hardness or Crushing strength Test

Hardness of the tablet was determined using the Monsanto hardness tester (The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

The force required to break the tablet is measured in kilograms and a crushing strength of 4Kg is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4 to 10 kg; however, hypodermic and chewable tablets have a hardness of 3 kg and some sustained release tablets have a hardness of 10 -20 kg.

Thickness Test

The thickness of the tablet is mostly related to the tablet hardness can be uses as initial control parameter. Ten tablets were randomly selected from each tablet thickness was determined using a Venire caliper and the reading was recorded in millimeters.

Friability Test

The pre-weighed tablets were placed in the friabilator (EF-2, Electro lab, Mumbai) which was then operated for 100rpm, then dusted and reweighed. The compressed tablets that lose less than 0.5-1.0% of their weight are generally considered acceptable.

$$\text{Friability index} = \frac{I - F}{I} \times 100$$

Where,

I - Initial weight

F - Final weight Weight variation test

Weights of 20 individual tablets were noted and their mean weight also calculated. The percentage deviation was calculated by using the following formula,

Percentage deviation = $[X-X^*/ X] \times 100$

X - Actual weight of the tablet X^*- Average weight of the tablet.

Estimation of Drug Content

An accurately weighed amount of powdered Ornidazole (100 mg) was extracted with water and the solution was filtered through 0.45 µ membrane filter paper. The absorbance was measured at 312 nm after suitable dilution.

Calculation

The amount of Ornidazole present in tablet can be calculated using the formula

$A_t/As \times S_w/100 \times 100$ Where,

A_t = Absorbance of sample preparation A_s = Absorbance of Standard preparation S_w = weight at Ornidazole working standard (mg).

***In vitro* drug release studies**

The dissolution was carried out using rotating basket method (USP dissolution testing apparatus I); freshly prepared 0.1N Hcl (pH 1.2) (900 ml) was placed in dissolution flask and allowed to obtain temperature at 37±0.5°C and 100 rpm for first 2 h. Then replaced with 6.8 pH phosphate buffer and continued for 24 h. Aliquot volume of 10 ml was withdrawn at regular intervals and replaced with fresh buffer diluted. The samples were replaced with fresh dissolution medium. After filtration, the sample is measured the absorbance at 312 nm by using UV Spectrometer. The dissolution data obtained were plotted as percentage drug release versus time.

Stability Studies

To assess the drug and formulation stability, the stability studies were carried out of the most satisfactory formulation (FOT-3) as per ICH guidelines. The formulation is sealed in aluminum packaging and kept in humidity chamber maintained at 30 ± 2 °C /65 ± 5% RH and 40 ± 2 °C / 75 ± 5 % RH for 60 days. At the end of studies, samples were analyzed for the drug content, *in vitro* dissolution, and other physicochemical parameters.

RESULTS AND DISSCUSION

Compatability studies (Fourier Transform Infrared Spectroscopic studies)

The fourier transform infra-red analysis was conducted for the surface structure characterization. FTIR spectrum of the formulated tablets, pure drug

and different polymers was recorded. The tablets were taken in a KBr pellet by using BOMEN MB SERIES FTIR instrument. The Fourier Transform Infrared Spectroscopy study reveals that there is no interaction between the different polymers and pure drug. Then all the functional groups are found in the IR spectrum of pure drug and different polymers.

Bulk density

The packing properties of the drugs and their formulations widely depend upon bulk density. It has been stated that bulk density values less than 1.2gm/cm^3 indicate good flow and values greater than 1.5 gm/cm^3 indicate poor flow. From the results it can be seen that the bulk density values are less than 1.2gm/cm^3. This indicates good flow characteristics of the powders. Values showed Table No.2.

Tapped density

From the results it can be seen that the Tapped density values indicate good flow characteristics of the powders. Values showed Table No.2.

Angle of Repose

Angle of repose is less than or equal to 40° indicates free flowing properties of the powders. However angle of repose is greater than 40° indicates poor flow of material. It can be observed that the angle of repose for various batches of the powders is found to be less than 40^0, it indicates good flow properties of the powders. Values showed Table No.2.

Compressibility Index or Carr's Index

Carr's Index is less than or equal to <10 indicates free flowing properties of the powders. However Carr's Index is greater than <10 indicates poor flow of material. It can be observed that the Carr's Index for various batches of the powders is found to be less than >10; it indicates good flow properties of the powders. Values showed Table No.2.

Hausner's Ratio

Hausner's Ratio is less than or equal to 1.069 indicates free flowing properties of the powders. However Hausner's Ratio is greater than 1.35 indicates poor flow of material. It can be observed that the Hausner's Ratio for various batches of the powders is found to be less than 1.35; it indicates good flow properties of the powders. Values showed Table No.2.

Post Compression studies

Hardness Test

The hardness of the tablet various batches were determined. The various batches of the tablets of hardness values are found within limits and it indicates good strength of the tablets. Values showed Table No.3.

Thickness Test

The thicknesses of tablets were almost uniform in the all formulations and were found to be in the range of 0.48mm. Values showed Table No.3.

Friability Test

The tablets friability values are found to be less than 1% in all cases and considered to be satisfactory. Values showed Table No.3.

Weight variation test

All this tablets passed weight variation test as the % weight variation was within the pharmacopoeia limits. The weight of the all tablets was found to be uniform with low standard deviation values. Values showed Table No.3.

Estimation of Drug Content

Drug content of all the batches are within the acceptable range which shows the proper mixing of the drug and excipients. Values showed Table No.3.

***In vitro* drug release studies**

Among all the batches FOT-3 formulations showed the better *in vitro* release of drug (Table No.4 and Figure No.1).

Stability studies

Stability studies were carried out of the most satisfactory formulation FOT-3 at 30 ± 2 °C / 65 ± 5 % RH and 40 ± 2 °C / 75 ± 5 % RH for two months as per ICH guidelines. At various time intervals of 30 days and 60 days end, samples were evaluated. There was no major change in the various physicochemical parameters evaluated.

Table No.1: Formulation of different batches of Ornidazole colon targeted tablets

S.No	Ingredients	FOT-1	FOT-2	FOT-3	FOT-4	FOT-5	FOT-6	FOT-7
1	Ornidazole	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg
2	HPMC K4M	120 mg	-	-	60 mg	-	60 mg	7.0 mg
3	HPMC K100M	-	120 mg	-	60 mg	60 mg	-	7.0 mg
4	Eudragit S100	-	-	120 mg	-	60 mg	60 mg	7.0 mg
5	Di basic calcium phosphate	150 mg	150 mg	150 mg	150 mg	150 mg	150 mg	150 mg
6	Talc	15mg	15mg	15mg	15mg	15mg	15mg	15mg
7	Magnesium stearate	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg

Total weight of the tablet – 500mg/Tab

Table No.2: Precompression studies of powders

S.No	Formulations	Bulk Density(gm/cm^3)	Tapped Density(gm/cm^3)	Angle of Repose (θ)	Carr's Index (%)	Hausner's Ratio
1	FOT-1	0.585	0.606	28.05	3.46	1.035
2	FOT-2	0.587	0.610	29.46	3.77	1.039
3	FOT-3	0.572	0.594	28.12	3.70	1.038
4	FOT-4	0.585	0.613	29.25	4.56	1.047
5	FOT-5	0.590	0.617	29.08	4.37	1.045
6	FOT-6	0.595	0.616	27.94	3.40	1.035
7	FOT-7	0.581	0.609	28.36	4.59	1.048

Table No.3: Post compression studies of Ornidazole colon targeted tablets

S.No	Formulations	Hardness Test (kg/cm)	Thickness Test (cm)	Friability Test (%)	% of Weight variation test	Estimation of Drug Content
1	FOT-1	8.45	0.48	0.6	99.6	99.5
2	FOT-2	8.62	0.48	0.6	99.6	99.5
3	FOT-3	8.94	0.48	0.5	99.8	99.8
4	FOT-4	8.58	0.48	0.6	99.5	99.2
5	FOT-5	8.75	0.48	0.6	99.5	99.2
6	FOT-6	8.62	0.48	0.6	99.6	99.4
7	FOT-7	8.72	0.48	0.5	99.6	99.4

Table No.4: Comparative dissolution study of different formulations with various ratios of polymers

S.No	Time (hrs)	% of drug release (FOT-1)	% of drug release (FOT-2)	% of drug release (FOT-3)	% of drug release (FOT-4)	% of drug release (FOT-5)	% of drug release (FOT-6)	% of drug release (FOT-7)
1	0	00.00	00.00	00.00	00.00	00.00	00.00	00.00
2	1	02.54	02.23	02.05	02.36	02.16	02.52	02.12
3	2	08.42	06.56	05.82	07.84	06.12	07.25	06.04
4	3	20.83	16.26	12.74	18.25	14.52	15.34	14.67
5	6	36.27	28.18	24.35	33.53	26.28	30.54	27.54
6	9	53.59	47.86	37.26	49.12	40.37	46.62	40.21
7	12	71.26	62.18	48.76	68.73	53.78	66.25	51.92
8	15	87.65	76.32	63.23	80.16	69.02	77.68	66.12
9	18	102.3	89.65	75.58	93.64	82.13	91.02	78.46
10	21	-	105.6	87.12	107.05	94.18	104.7	90.24
11	24	-	-	99.34	-	106.4	-	103.1

Table No.5: Stability studies of Ornidazole colon targeted tablets (FOT-3)

S.No	Time (hrs)	After 30 days		After 60 days	
		30±2°C /65±5% RH	40±2°C /75±5% RH	30±2°C /65±5% RH	40±2°C /75±5% RH
1	0	00.00	00.00	00.00	00.00
2	1	02.05	02.05	01.98	01.82
3	2	05.82	05.82	05.45	05.36
4	3	12.74	12.74	12.02	11.52
5	6	24.35	24.35	23.47	22.13
6	9	37.26	37.26	36.52	35.86
7	12	48.76	48.76	48.05	47.59
8	15	63.23	63.23	62.64	62.02
9	18	75.58	75.58	74.68	73.94
10	21	87.12	87.12	86.63	85.78
11	24	99.34	99.34	98.94	98.24

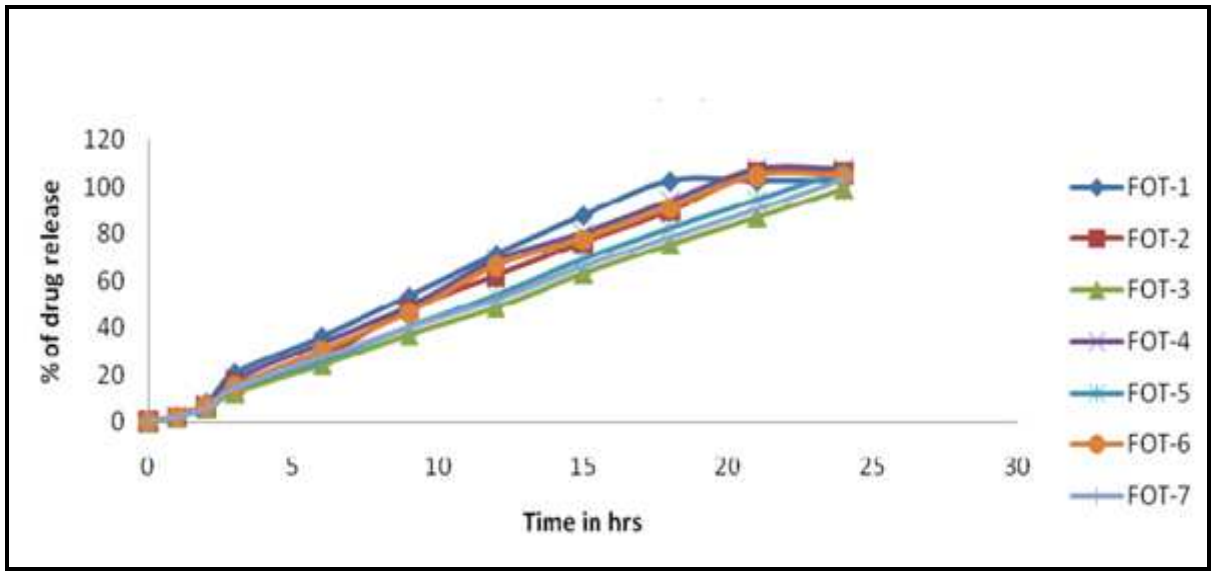

Figure No.1: Comparative dissolution study of different formulations with various ratios of polymers

CONCLUSION

The present investigation was concerned with the development of the colon targeted tablets, which after oral administration were designed to prevent the drug release in stomach and small intestine. It improves the bioavailability of the drug as well as its half life. The tablets possessed the required physicochemical parameters such as hardness, friability, weight variation, drug content. The *in vitro* drug release showed best formulation is FOT3 compared all. The most satisfactory formulation (FOT-3) had showed no significant change in physicochemical properties, drug content, in vitro dissolution pattern after storage at 30 ± 2 °C / 65 ± 5 % RH and at 40 ± 2 °C /75 ± 5 % RH during stability studies for two months. Therefore, it was concluded that the most satisfactory formulation (FOT-3).

ACKNOWLEDGEMENT

We are thankful to Seven Hills College of Pharmacy, India for providing facility to carry out the research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Philip A K, Dabas S, Pathak K. Optimized prodrug approach: A means for achieving enhanced anti-inflammatory potential in experimentally induced colitis, *J Drug Target*, 17(3), 2009, 235-241.
2. Oluwatoyin A O, John T F. *In vitro* evaluation of khaya and albizia gums as compression coating for drug targeting to the colon, *J Pharm Pharmacol*, 57(2), 2005, 163-168.
3. Akala E O, Elekwachi O, Chase V, Johnson H, Marjorie L, Scott K. Organic redox initiated polymerization process for the fabrication of hydrogel for colon specific drug delivery, *Drug Dev Ind Pharm*, 29(4), 2003, 375-386.
4. Goodman and Gilman's. The Pharmacological basis of therapeutics, Ornidazole: Chemotherapy of Parasitic Infections, *Mcgrawhill medical publisher*, 11th edition, 2006, 1050.
5. Sinem Y, Zeynep A Y, Mine O. Bioavailability File: Ornidazole, *Fabad J. Pharm. Sci*, 29, 2004, 133-44.
6. Singh P, Mittal R, Sharma G C, Singh S, Singh A. Ornidazole: comprehensive profile,

text book of profiles of drug substances and related methodology, 30, 2003, 123-73.
7. Tablet aimed for colonic drug delivery, *Eur J Pharm Sci,* 20(1), 2003, 125-31.
8. Jhansi rani M, Surendra A, Sudhakar babu A M S, Nagoor A. Formulation and evaluation of domperidone fast dissolving tablets using natural superdisintegrants, *International Journal of Research in Pharmaceutical and Nano Sciences,* 2(2), 2013, 152-157.
9. Anonymous. Hardness or Crushing strength, *Pharmainfo.net,* 1, 2008, 1-4.
10. Indian Pharmacopoeia, Government of India, Ministry of Health and Family Welfare, *Controller of Publications, New Delhi,* 2(P-Z), 1996.

Please cite this article in press as: Rajasekhar Reddy V and Niranjan Babu M. Formulation and *in vitro* evaluation of ornidazole film coated Tabelts for colon targeted drug delivery, *International Journal* of *Research in Pharmaceutical and Nano Sciences,* 2(6), 2013, 768-775.