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

International Journal of Research in Pharmaceutical and Nano Sciences

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

DESIGN, FORMULATION AND *IN VITRO* EVALUATION OF SATRANIDAZOLE TABLETS OF COLON TARGETED DRUG RELEASE

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ABSTRACT

The objective of the study was to develop colon targeted drug release of Satranidazole by using HPMC K_4M, HPMC K100 and Eudragit S100 as carriers. Satranidazole is used for the treatment of amoebiasis. The tablets are prepared by using direct 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. The results of the study showed that formulation FOS-1 is most likely to provide targeting of Satranidazole for local action in the colon.

KEYWORDS

Satranidazole, Colon targeted drug delivery, Carriers such as HPMC K_4M, HPMC K100, Eudragit S100 and *Invitro* study.

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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, amebiosis, 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].

Amebiasis affects about 10% of the world's population, causing invasive disease in about 50 million people and death in about 100,000 of these annually. In the United States, amebiasis is seen most commonly in the states that border Mexico and among individuals living in poverty, crowded conditions, and areas with poor sanitation. Two morphologically identical but genetically dis-tinct species of Entamoeba (E. histolytica and E. dispar) have been isolated from infected persons. While the proportions vary worldwide, E. dispar accounts for approximately 90% of human infections, with E. histolytic responsible for only 10%. However, only E. histolytica is capable of causing disease and thus requires treatment. The two organisms can be differentiated by antigen-detection enzyme-linked immunosorbent assays (ELISAs) or by polymerase chain reaction (PCR)-based diagnostics[4].

MATERIAL AND METHODS

MATERIAL

Satranidazole was a gift sample from Alkem, Mumbai, India. 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 of preparation of colon targeted Satranidazole tablets[5]

Satranidazole, 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.

EVALUATION PARAMETERS[5-7]

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 bulk density according to the formula

Formula

$$\text{Bulk density} = \text{Mass} / \text{Volume}$$

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

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

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 Satranidazole tablets

Hardness or Crushing strength Test[8]

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,

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

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

Estimation of Drug Content

An accurately weighed amount of powdered Satranidazole (100 mg) was extracted with water and the solution was filtered through 0.45 µ membrane filter paper. The absorbance was measured at 313.8 nm after suitable dilution.

Calculation

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

$$A_t/A_s \times S_w/100 \times 100$$

Where,

A_t = Absorbance of sample preparation
A_s = Absorbance of Standard preparation
S_w = weight at Satranidazole 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 313.8 nm by using UV Spectrometer. The dissolution data obtained were plotted as percentage drug release versus time.

RESULTS AND DISSCUSION

Pre formulation studies

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.

Precompression studies of powders

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.

Postcompression 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 FOS-1 formulation showed the better *invitro* release of drug (Table No.4 and Figure No.1 (a and b).

Table No.1: Preparation of different batches of Satranidazole colon targeted tablets

S.No	Ingredients	FOS-1	FOS-2	FOS-3	FOS-4	FOS-5	FOS-6	FOS-7
1	Satranidazole	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
2	HPMC K4M	90 mg	-	-	45 mg	-	45 mg	30 mg
3	HPMC K100M	-	90 mg	-	45 mg	45 mg	-	30 mg
4	Eudragit S100	-	-	90 mg	-	45 mg	45 mg	30 mg
5	Dibasic calcium phosphate	110 mg	110 mg	110 mg	110 mg	110 mg	110 mg	110 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 – 250mg/Tab

Table No.2: Precompression studies of powders

S.No	Formulations	Hardness Test (kg/cm)	Thickness Test (cm)	Friability Test (%)	% of Weight variation test	Estimation of Drug Content
1	FOS-1	2.26	0.30	0.8	99.5	99.2
2	FOS-2	2.12	0.30	0.8	99.6	99.5
3	FOS-3	2.15	0.30	0.8	99.4	99.8
4	FOS-4	2.18	0.30	0.6	99.2	99.3
5	FOS-5	2.14	0.30	0.6	99.7	99.6
6	FOS-6	2.13	0.30	0.6	99.4	99.5
7	FOS-7	2.15	0.30	0.6	99.6	99.4

Table No.3: Postcompression studies of Satranidazole colon targeted tablets

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

Table No.4: Comparative dissolution study of Satranidazole colon targeted tablets

S.No	Time (mints)	FOS-1	FOS-2	FOS-3	FOS-4	FOS-5	FOS-6	FOS-7
1	0	00.00	00.00	00.00	00.00	00.00	00.00	00.00
2	1	08.52	06.52	04.95	07.32	05.75	04.46	04.26
3	2	23.41	18.25	16.42	22.86	16.54	14.95	13.52
4	3	42.72	34.56	32.26	41.23	33.72	29.26	28.12
5	6	61.63	53.75	51.24	60.72	52.52	47.48	48.45
6	9	81.42	73.34	68.42	79.27	69.56	66.74	64.62
7	12	97.25	93.52	89.35	96.58	92.15	88.42	85.36

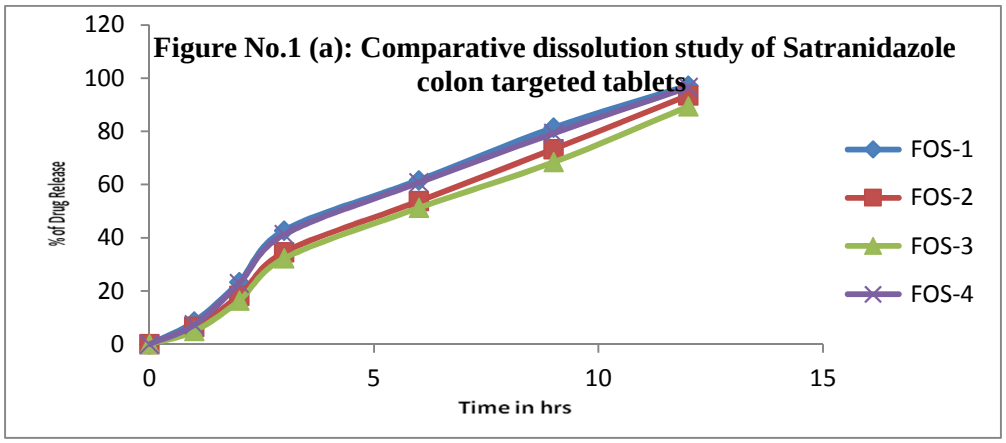

Figure No.1 (a): Comparative dissolution study of Satranidazole colon targeted tablets

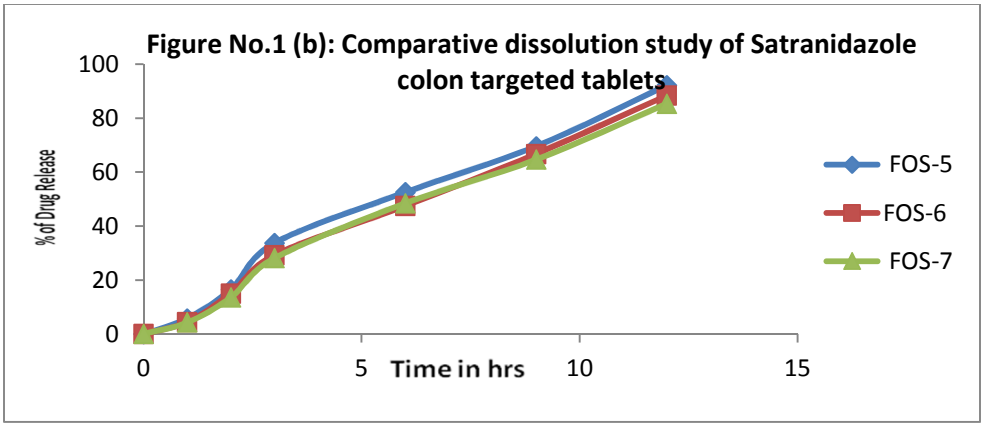

Figure No.1 (b): Comparative dissolution study of Satranidazole colon targeted tablets

CONCLUSION

The aim of the study was concluded that, all the batches showed good to satisfactory free flowing properties which made it suitable for direct compression. The results of the study showed that formulation FOS-1 is most likely to provide targeting of Satranidazole for local action in the colon.

ACKNOWLEDGEMENT

All authors would like to thanks SIMS College of Pharmacy, Guntur, Andhra Pradesh, India for continuous support and encouragement throughout this work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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Please cite this article in press as: Salimetti Gopi. *et al.* Design, formulation and *in vitro* evaluation of satranidazole tablets of colon targeted drug release, *International Journal of Research in Pharmaceutical and Nano Sciences*, 3(3), 2014, 235-241.