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Design and Evaluation of Delayed Release Enteric Coated Tablets of Tenetoprazole

C. Srinivas[1]*, L Srividya[2], K. Mounika Reddy[1]

1. Department of Pharmaceutics, Saraswathi College of Pharmaceutical Sciences, Hyderabad-Ranga Reddy (dist), India.

2. Department of pharmaceutical medicinal chemistry, Bojjam Narasimhulu Pharmacy College, Saidabad, Hyderabad - India.

ABSTRACT

The Present study was undertaken with an aim to formulate delayed release enteric coated tablets of Tenatoprazole to avoid the degradation in stomach, as it is an acid labile drug and to improve bioavailability. The method adopted for development was direct compression. Different core tablets were prepared by using approved excipients and evaluated for parameters like hardness, friability, thickness and disintegration time. Sub coating was done for the optimized formulation (F5) by using Hydroxy propyl methyl cellulose 5cps with buildup of 3%w/w and finally enteric coating was done by using polymers like Hydroxy propyl methyl cellulose phthalate (HPMCP), Eudragit L30 D55 and Hydroxy propyl methyl cellulose acetate succinate (HPMCAS) with an average weight build up of 5%, 8% & 10% w/w. All the formulations were evaluated for their physicochemical parameters and compared with marketed sample. Results indicated that all the tablets prepared possess good integrity, desirable for enteric coated tablets. At the end it was found that prepared formulation gave satisfactory results compared with market sample dissolution profile. Among the polymers studied, the methacrylic acid polymers exhibited better dissolution rate than the cellulose polymers. The selected formulation (F5h with 8% w/w) was subjected for stability studies as per ICH guidelines and were found to be stable, as no significant change was observed in the evaluated parameters. Hence prepared formulation by-pass the degradation of Tenatoprazole by enteric coating and thus a pharmaceutically equivalent, robust formulation of Tenatoprazole enteric coated tablet was developed.

Keywords: Tenatoprazole, sub-coating, enteric coating, HPMCP, Eudragit L30 D55, stability studies.

*Corresponding Author Email: srinucsagar@yahoo.co.in

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INTRODUCTION

Tenatoprazole is a novel proton pump inhibitor, which has been developed by Mitsubishi Pharma in Japan and is now under active development by SIDEM (France). In contrast to all the other PPIs (Ex: Omeprazole, Ilaprazole etc), this compound is not a benzimidazole derivative, it consists of one imidazopyridine ring connected to a pyridine ring by a sulfinyl methyl chain. It therefore represents a new chemical entity[1]. Tenatoprazole (TPZ) is chemically, 3-methoxy-8- [(4-methoxy-3,5-dimethyl-pyridin-2 yl) methyl sulfinyl] 2,7,9-triazabicyclo [4.3.0] nona-2,4,8,10-tetraene. (Figure 1).It is a prodrug of the proton pump inhibitor (PPI) class, which is converted to the active sulfenamide or sulfenic acid by acid in the secretory canaliculus of the stimulated parietal cell of the stomach. This active species binds to luminally accessible cysteine of the gastric H+ K+ -ATP ase resulting in disulfide formation and acid secretion inhibition[2.]

The stability of Proton pump inhibitors is a function of pH; these are rapidly degraded in acid media, and are stable under alkaline conditions. Therefore exposure of Tenatoprazole to the acidic content of the stomach would lead to significant degradation of the drug and hence, reduced bioavailability[3.] Delayed release dosage forms are the best formulations which are used for drugs that are destroyed in the gastric fluids, or cause gastric irritation, or are absorbed preferentially in the intestine. Such preparations contain an alkaline core material comprising the active substance, a separating layer and enteric coating layer[4-6].

Enteric coatings are usually formulated with synthetic polymers that contain ionizable functional groups that render the polymer water soluble at a higher pH value. Commonly used enteric coatings may be made from: methacrylic acid copolymers, cellulose acetate (and its succinate and phthalate version), polymethacrylic acid/acrylic acid copolymer, hydroxypropyl methyl cellulose phthalate, polyvinyl acetate phthalate, hydroxyethyl ethyl cellulose phthalate, cellulose acetate tetrahydropthalate, acrylic resin[7].

The present study was aimed to formulate a delayed release enteric coated tablets of Tenatoprazole to prevent degradation of drug by acid in the gastric lumen, by using Hydroxy propyl methyl cellulose 5cps with buildup of 3%w/w and finally enteric coating was done by using polymers like Hydroxy propyl methyl cellulose phthalate (HPMCP), Eudragit L30 D55 and Hydroxy propyl methyl cellulose acetate succinate (HPMCAS) with an average weight buildup of 5%, 8% & 10% w/w. All the formulations were evaluated for their physicochemical parameters like thickness, disintegration time, drug content and dissolution studies and compared with marketed sample.

MATERIALS AND METHODS

Materials:

Tenatoprazole was received as a gift sample from LARA DRUGS PVT LTD, Hyderabad. Lactose Anhydrous, Microcrystalline cellulose, (Avicel PH101), Sodium starch glycolate, Crosscarmellose sodium, Magnesium stearate, HPMCAS, Eudragit L30 D55, HPMCP, HPMC 5cps, Dibutyl phthalate Isopropyl alcohol, Dichloromethane were purchased from S.D fine chemicals, Mumbai. All the chemicals used in the study were of analytical grade.

Method of Preparation of Core Tablets[8-9]

The core tablets of Tenatoprazole were prepared by direct compression method. The weighed quantities of drug & all other ingredients were passed through sieve no # 30 and mixed thoroughly for 10 minutes in octagonal blender to get uniformly distributed and uniform sized particles. Then accurately weighed magnesium stearate was shifted through sieve no # 40 and mixed with the blend given in Table 1. Then the mixture is put for the compression on 16 station rotary tablet compression machine (Cadmach, Ahmadabad). Detailed composition of Tenatoprazole core tablets is given in Table 2.

Table 1: Selected formulation (Core tablets) for enteric coating

Ingredients	Qty. /tab (mg)	%w/w	Qty. for 100 Tablets (g)
Tenatoprazole	60	24	6
Microcrystalline cellulose	141.6	56.64	14.16
Lactose	28.4	11.36	2.84
Sodium starch glycolate	15	6	1.5
Magnesium stearate	5	2	0.5
Total weight	250	100	25

Table 2: Composition of Core tablet formulations of tenatoprazole.

Ingredients	QTY. /tab (mg)					
	F1	F2	F3	F4	F5	F6
Tenatoprazole	60	60	60	60	60	60
Microcrystalline cellulose	175	_	28.4	113.2	141.6	56.8
Lactose	_	175	141.6	56.8	28.4	113.2
Sodium starch glycolate	10	_	15	_	15	_
Cross carmellose sodium	_	10	_	15	_	15
Magnesium stearate	5	5	5	5	5	5
Total weight	250	250	250	250	250	250

Coating of compressed Tenatoprazole tablets

The enteric coating solution was prepared by simple solution method using 6 % w/w and 8% W /W and 10% W/W of HPMCP 5cps (H1 and H2) and Eudragit L30 D55 (E1 and E2) as an enteric polymer Table 3. The PEG (1.5% w/w) was used as plasticizer and Isopropyl alcohol &

Dichloromethane were used as solvent. This mixture was constantly stirred for 1h with paddle mechanical stirrer and the stirred coating solution was again filtered through muslin cloth to obtain coating solution[10-11].

Table 3: Sub-coating for all the formulations (3% weight buildup)

S.no	Ingredients	Qty./ tablet(%)
1	HPMCP 5cps, Eudragit L30 D55 &.HPMCAS	6.0/8.0/10.0
2	PEG	1.5
3	Isopropile alcohol & Dichloromethane(1:1)	58.5
% weight build up	3%	

Enteric coating of Tenatoprazole compressed tablets:

The mixture of isopropyl alcohol and dichloromethane (1:1) was taken in a beaker and required quantity of enteric coating material (polymer) was weighed and added to above beaker containing a mixture of solvents. Then the specified amount of Dibutyl phthalate was added and stirred for about 30 min to get uniform dispersion of the coating material. The compressed tablets were coated with above prepared dispersion in Conventional coating pan the coating conditions was specified in Table 4. The tablet coating was continued till the desired weight gain was achieved. The composition of coating material was given in Table 5. Then the Prepared coated tablets were studied for its weight variation, thickness, uniformity of drug content and in vitro dissolution study.[10-11]

Table 4: Coating conditions

S.no	Parameters	Limits
1.	Pan speed	18rpm
2.	Inlet air temperature	30 to 40^{o}c
3.	Exhaust air temperature	30 to 35 ^{o}c
4.	Bed temperature	30 to 35 ^{o}c
5.	Atomizing air pressure	0.5-1.0kg/cm^{2}
6.	Spray rate	12mL to 15mL/min
7.	Spray gun nozzle diameter	1.0mm

Table 5: Enteric coating (5%, 10% and 8% weight build up)

Ingredients	Qty./tab(mg)								
	5%			10%			8%		
	F5a	F5b	F5c	F5d	F5e	F5f	F5g	F5h	F5i
HPMCP	12.9	_	_	25.8	_	_	20.64	_	_
Eudragit L30 D55	_	12.9	_	_	25.8	_	_	20.64	_
HPMCAS	_	_	12.9	_	_	25.8	_	_	20.64
Dibutyl phthalate	1.28	1.28	1.28	1.28	1.28	1.28	1.28	1.28	1.28
Isopropyl alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Di chloro methane	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Evaluation Parameters

Pre Compression Parameters (Evaluation of powder blend)

Angle of repose [12]

The angle of repose of powder blend was determined by the funnel method. The accurately weighed powder blends were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\tan\theta = h/r$$

Where, h and r are the height and radius of the powder cone respectively.

Bulk density and tapped density[13]

A quantity of 2gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced into 10ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5cm at second intervals. Tapping was contin-ued until no further change in volume was noted. Bulk density (ρ**B**) and tapped density (ρ**T**) were calculated using the following equations.

ρ**B**= Weight of the powder blend/Untapped Volume of the packing

ρ**T**=Weight of the powder blend/Tapped Volume of the packing

Compressibility Index[14]

The Compressibility Index of the powder blend was determined by Carr's compressibility index using the formula (Martin, 2001)

$$\text{Carr's index (\%)} = \rho T - \rho B \rho T \times 100$$

Hausner's ratio[14]

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material. The ratio of tapped density to bulk density of the powders is called the Hausner's ratio. It is calculated by the following equation (Martin, 2001).

$$H = \rho T \rho B$$

Post Compression Parameters [15]

Average weight:

Average weight was determined by weighing (using Sartorius weighing balance) twenty tablets selected randomly. It can be measured by using the formula.

Average weight = weight of 20 tablets/20

Thickness:

The thickness of the tablets in mm was measured using Digital Vernier calipers, measured in terms of micrometer. Average of three readings were taken and results were tabulated (n=3)

Hardness (crushing strength):

The hardness of the tablets is one of the official tests for tablets as per IP. It was determined using Monsanto hardness tester. It was expressed in Kg / cm^2

Friability (F):

Tablet strength was tested by Roche friabilator. Pre weighed tablets were allowed for 100 revolutions (4min), taken out and were dedusted. The percentage weight loss was calculated by reweighing the tablets. The % friability was then calculated by,

% Friability = Initial weight-Final weight / Initial Weight x100

Weight variation:

The enteric coated tablets of Tenatoprazole were tested for their drug content. Ten tablets were finely powdered; quantities of the powder equivalent to 60mg of Tenatoprazole were accurately weighed and transferred to a 100ml of volumetric flask. The flask was filled with phosphate buffer pH 6.8 and mixed thoroughly. Volume was made up to mark with phosphate buffer pH 6.8 and filtered. The absorbance of the resulting solution was measured at the 270nm using a UV/Vis double beam spectrophotometer. The linearity equation obtained from calibration curve as described previously was used for the estimation of Tenatoprazole in the tablet formulations.

Disintegration time:

Disintegration test was carried out using the tablet disintegration test apparatus (Servewell Instruments pvt. Ltd., Electrolab ED-2L, India). Phosphate buffer (pH 6.8 was used as the disintegration media at 37 ± 0.5 ºC and the time in second were observed for their completion of disintegration of the tablets.

Physicochemical evaluations of coating films: [16]

The same polymer solution was used to prepare the polymeric films and was subjected for The thickness of the dried films was determined by digital micrometer. The film solubility was studied with pH 0.1N HCl and 6.8 phosphate buffer. The 1×1 cm2 coating film was selected, weighed and transferred in a beaker containing 20 mL of specified medium, which was mixed in a magnetic stirrer for 1 h at 37 °C and finally film solubility was examined.

In vitro dissolution studies[16]

Dissolution Conditions

- Dissolution Medium and time

a) Gastric Resistance: 0.1N HCl for 2 hour.

b) Dissolution: phosphate buffer pH 6.8 for 1 h.

- Volume: 900ml
- Apparatus: Type II (paddles)
- Rotation Speed: 75 rpm
- Temperature: 37 ^{0}C+ 0.5 ^{0}C

USP dissolution apparatus type II (Electrolab TDT-08L,Mumbai,India) was used to determine the in vitro release of Tenatoprazole from the prepared formulations. The dissolution medium was 900 mL of acidic buffer 0.1 N HCl for 2 h and phosphate buffer (pH 6.8) for 1 h. The tablet was kept in to the basket at 37 ± 0.5 °C and 75 rpm. Samples (5 mL) were withdrawn at regular time intervals and the dissolution medium was replaced with equal volume fresh dissolution medium. The samples were measured by UV spectrophotometer at 270 nm against a blank.

Stability Studies

Accelerated stability studies: [15]

Accelerated stability studies were performed as per the ICH guidelines. Selected formulations of Tenatoprazole tablet were sealed in aluminum foil cover and stored at 25^{0}C ± 2^{0}C / 60% ± 5% RH, 30^{0}C ± 2^{0}C /65% ± 5% RH & 40^{0}C ± 2^{0}C / 75% ± 5% RH for a period of 3 months and evaluated for physical appearance, drug content, and dissolution rate according to the procedure described as earlier.

RESULTS AND DISCUSSION

Pre-compression parameters

The Tenatoprazole powder blend was prepared and evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio (Table 6).

Table 6: Precompression parameters of Tenatoprazole blend:

Parameters	F1	F2	F3	F4	F5	F6
Angle of repose	33.93±0.54	36.75±0.34	37.89±0.24	34.09±	28.15±0.54	34.35±0.52
Bulk density(g/cc)	0.48±0.01	0.45±0.01	0.46±0.02	0.46±0.05	0.46±0.01	0.45±0.01
Tapped density(g/cc)	0.59±0.016	0.55±0.015	0.54±0.015	0.52±0.014	0.53±0.02	0.56±0.02
Carr's index (%)	14.78±2.0	18.41±3.82	16.53±1.38	14.11± 1.6	9.21±0.73	16.4±0.6
Hausner's ratio	1.15±0.05	1.22±0.05	1.19±0.02	1.17±0.05	1.10±0.01	1.16±0.03
Flow property	**Good**	**Fair**	**Fair**	**Good**	**Excellent**	**Good**

Each value represents mean ± S.D (n=3)

The flow property of the blend was assessed by determining the angle of repose and Carr's index. The values of compressibility (9.21±0.73to 18.41±3.82%) signify good flow ability. The angle of

repose of all formulation was less than 40 º (28.15 ± 0.54 to 37.89± 0.24) also indicate the good flow ability of the prepared powder blend. The bulk densities of the blend were ranged between 0.45 ± 0.05 and 0.48. ± 0.04 g/cc and the tapped densities varied from 0.52 ± 0.014 to 0.59 ± 0.016 g/cc.

Post compression parameters of Tenatoprazole core tablet

The prepared Tenatoprazole core tablets were evaluated for their thickness, hardness, friability and weight variation, content uniformity, disintegration and *in vitro* drug release (Table 7). The thickness of the core tablets were ranged between 4.26±0.2 and 4.32±0.3 mm & the hardness of the core tablets were found between 35 ± 1.6 N and 72 ± 2.1 N . The friability of the tablets was found less than 1% w/w which indicates that the friability was with in the range and having a significant mechanical strength. The content of drug present in prepared tablets formulation ranged between 97.45 ± 0.35 and 99.76 ± 0.26%. The disintegration time varied between 3.26 ± 0.34 and 7.12 ± 0.54 and all the formulations exhibits favorable results. From the above all six formulations, F5 was selected as best formulation depends upon drug content and disintegration time, and coated with enteric polymers like Hydroxy propyl methyl cellulose phthalate (HPMCP), Eudragit L30 D55 and Hydroxy propyl methyl cellulose acetate succinate (HPMCAS) with an average weight buildup of 5%, 8% & 10% w/w and renamed F5a, F5b, F5c, F5d, F5e, F5f, F5g, F5h, F5i.

Table 07: Post compression parameters of Tenatoprazole core tablets

Parameters	F1	F2	F3	F4	F5	F6
Average weight (mg)	251.6±0.54	251.2±0.23	250.8±0.31	249.6±0.52	251.5±0.21	252.5±0.24
Hardness(N)	35±1.6	43±1.4	48±0.9	54±1.8	72±2.1	60±0.8
Friability (%)	0.33±0.02	0.28±0.01	0.25±0.03	0.23±0.02	0.17±0.02	0.21±0.03
Thickness(mm)	4.32±0.3	4.26±0.2	4.28±0.2	4.30±0.2	4.25±0.3	4.29±0.3
Drug content (%)	97.56±0.25	97.65±0.33	98.75±0.21	98.64±0.42	99.76±0.26	97.45±0.35
Disintegration time (min)	6.47±0.24	7.12±0.25	6.05±0.28	4.34±0.26	3.26±0.524	5.50±0.23

Each value represents mean ± S.D (n=3)

Physicochemical evaluation of coating films

Physicochemical evaluation of Hydroxy propyl methyl cellulose phthalate (HPMCP), Eudragit L30 D55 and Hydroxy propyl methyl cellulose acetate succinate were studied for different parameters such as film thickness, and film solubility. The thickness of the film found 0.24 ± 0.03 mm. The enteric polymer Hydroxy propyl methyl cellulose phthalate (HPMCP) and Eudragit L30 D55 were found to be completely soluble in phosphate buffer (pH 6.8) and insoluble in 0.1 N HCl .

Table 8: Physicochemical evaluation of different polymer coating films

Polymer	Parameters		
	Film solubility		Film Thickness
	0.1N HCl	Phosphate buffer (pH 6.8)	
HPMCP Eudragit L30 D55 & HPMCAS	Insoluble	Soluble	0.24±0.03

Each value represents mean ± S.D (n=3)

Physicochemical evaluation of Tenatoprazole enteric coated tablets

The enteric coated tablets of Tenatoprazole exhibit almost favorable results in disintegration and drug content. The average weight of the formulations ranged between 270 ± 0.6to 284 ± 0.1 mg and the drug content varied between 97.45 ± 0.23 to 99.76 ± 0.12 %.The thickness of the tablets lies between 4.35±0.04 and 4.39±0.01mm (Table 09).

Table 9: Physicochemical evaluation of Tenatoprazole enteric coated tablets

Parameters	F5a	F5b	F5c	F5d	F5e	F5f	F5g	F5h	F5i	Market sample
Average weight(mg)	270.6± 0.32	271.4± 0.25	270.8± 0.55	282.9± 0.65	283.4± 0.25	283.1± 0.33	284.1± 0.45	278.7± 0.52	278.1± 0.25	275.9± 0.46
Thickness(mm)	4.37±0 .05	4.39±0 .01	4.36±0 .03	4.37±0 .05	4.35±0 .04	4.38±0 .03	4.36±0 .02	4.38± 0.03	4.36±0 .02	4.37±0 .02
Drug content (%)	97.56	97.65	98.75	98.64	98.74	97.45	98.89	99.76	98.96	99.62

Each value represents mean ± S.D (n=3)

In vitro drug release of Tenatoprazole enteric coated tablets

The in vitro drug release of Tenatoprazole enteric coated tablets is shown in Figure 1. The drug release was evaluated using UV spectroscopy. The dissolution study for formulation F5a-F5c with 5% weight buildup was not performed, since they could not passed disintegration test. All the formulations (F5d-F5i) have demonstrated excellent physical resistance to the acid medium after 2H and the drug release was found to be within specified limits. In case of formulations F5d, F5e, F5f, (10% weight buildup), there was less drug release up to 15min in the phosphate buffer (pH 6.8) and at the end of 45min drug release was found to be 92.81±0.3 , 94.15±0.4, 95.32±0.2 respectively. In case of formulations F5g, F5h, F5i, (8% weight buildup), drug release in the phosphate buffer (pH 6.8) at 15min was found to be 20.42±0.3, 30.33 ±0.3, 19.83 ±0.6 respectively and at the end of 45min drug release was found to be 96.16±0.1, 99.32± 0.6 and 96.24±0.6 respectively. It was found that percentage drug release was more in formulation F5h at

the end of 45 min. Among all formulations (F5d-F5i), the formulation F5h was considered optimum because in acid medium drug release was less than 10% and drug release in the phosphate buffer (pH 6.8) was found to be almost complete. The dissolution values for market sample was found to be 31.42±0.2 at the end of 15min and 97.41± 0.4 at the end of 45min which is less than that of F5h. F5h was found to be satisfactory for F5h when compared to that of market sample.(Table 10)

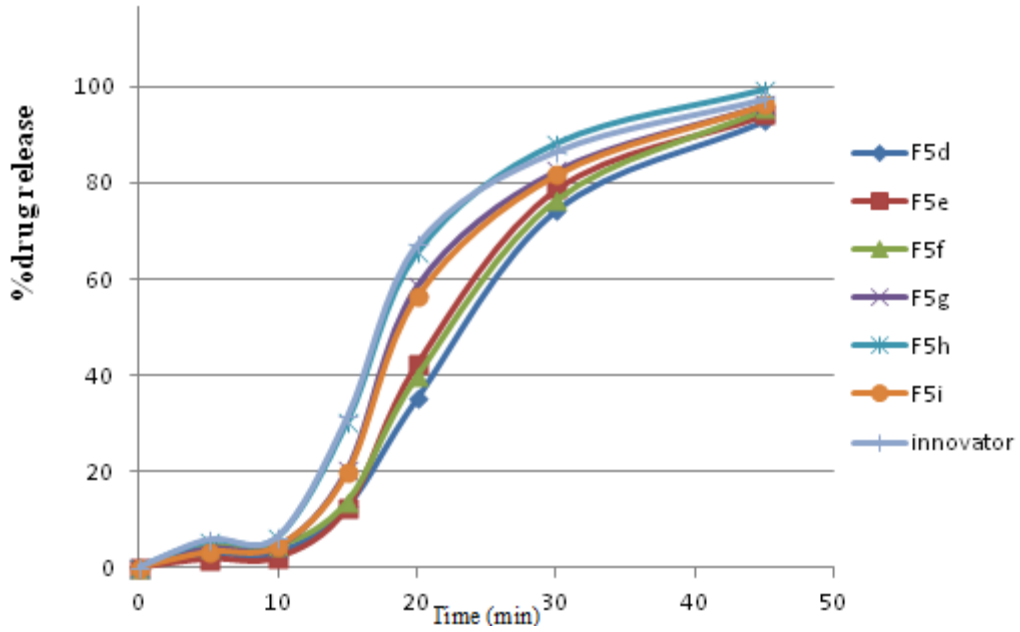

Figure 1: In-vitro release patterns of formulations F5d to market sample

Table 10:*In vitro* drug release of Tenatoprazole enteric coated tablets

Time Points	F5d	F5e	F5f	F5g	F5h	F5i	Market sample
2H(0.1NHCL)	2.4± 0.1	1.76±0.7	4.1 ±0.3	2.13± 0.2	1.56 ±0.3	1.73 ±0.3	1.59±0.4
Phosphate buffer 6.8 pH							
5min	2.7± 0.1	1.82 ±0.5	4.3 ±0.3	3.95±0.2	5.5 ±0.4	3.23 ±0.3	5.8±0.3
10min	3.1±0.2	2.1±0.7	4.5±0.5	4.31±0.4	6.3±0.4	4.4 ±0.4	6.4±0.5
15min	12.8±0.1	12.5±0.1	13.8 ±0.4	20.42±0.3	30.33 ±0.3	19.83 ±0.6	31.42±0.2
20min	35.1±0.2	42.3±0.4	39.81±0.6	58.5±0.4	65.42 ±0.4	56.35 ±0.6	67.12±0.3
30min	74.23±0.8	78.63±0.3	76.41±0.7	82.43±0.5	88.12±0.2	81.67 ±0.8	86.51±0.1
45min	92.81±0.3	94.15±0.4	95.32±0.2	96.16±0.1	99.32±0.6	96.24±0.6	97.41±0.4

Each value represents mean ± S.D (n=3)

Accelerated stability studies

Stability of a drug in a dosage form at different environmental conditions is important as it determines the expiry date of that particular formulation. Changes in the evaluation parameters of the formulation indicate the drug instability. Among all the enteric coated formulations, F5h was

selected for stability studies based on the physicochemical characterization of coating films and release characteristics. The stability studies were carried out at 40^0C ± 2^0C / 75% ± 5% RH for a period of 3 months which shown in (Table 11). There were no significant changes in their physical appearance of tablets. It was observed that the initial drug content and the drug contents of the samples analyzed after 3 month of storage were similar. The release profile also not showed any significant changes indicating that there were no significant changes in the physical as well as chemical characteristics of the formulation. Hence, it can be concluded from the results that the developed tablets were stable and retain their pharmaceutical properties over a period of 3 month.

Table 11: Accelerated stability study of optimized formulation F5h

Parameters	**Storage condition 40^0C ± 2^0C / 75% ± 5% RH**			
	Initial	**1st month**	**2nd month**	**3rd month**
Average weight (mg)	278.7±0.52	278±0.89	278±1.23	278±1.52
Thickness (mm)	4.38±0.03	4.38±0.03	4.38±0.05	4.38±0.05
Friability (%)	0.17±0.02	0.17±0.02	0.17± 0.04	0.17±0.05
Hardness (N)	72.2±0.51	72.2±0.54	72.2±0.53	72.2±0.54
Disintegration time (min)	7.32±0.03	7.44±0.05	7.50±0.06	8.20±0.03
Dissolution rate (%)	99.32±0.62	99.26±0.24	99.19±0.63	98.89±0.52

CONCLUSION

In the present study, Tenatoprazole enteric coated tablets were prepared using enteric coating polymers like Hydroxy propyl methyl cellulose phthalate, and Eudragit L30 D55 and Hydroxy propyl methyl cellulose acetate succinate. From this study it can be concluded that Tenatoprazole enteric coated tablets prepared by HPMCP and HPMCAS (i.e. F5g & F5i with 8% weight buildup) showed decreased drug release rate than the enteric coated tablets prepared by using Eudragit L30 D55 (F5h). The formulation F5h with 8% weight buildup was considered optimum because it showed negligible drug release in acidic medium and 99.76% drug release in the phosphate buffer (pH 6.8) was found to be almost complete. At the end it was found that prepared formulation gave satisfactory results compared with market sample dissolution profile. The stability studies of the selected formulation showed that the product was stable through-out the study period (3months).

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