American Journal of Advanced Drug Delivery

www.ajadd.co.uk

Original Article

Design and Characterization of Enteric Coated Delayed Release Pellets of Rabeprazole Sodium

Y. Surekha*, P. Venugopalaiah, K. Gnan Prakash and M. Gobinath

Ratnam Institute of Pharmacy, Nellore, Andhra Pradesh, India

Date of Receipt- 01/09/2013
Date of Revision- 02/09/2013
Date of Acceptance- 06/09/2013

Address for Correspondence
Department of Phrmaceutics Ratnam Institute of Pharmacy, Nellore, Andhra Pradesh, India
E-mail: surekhaakanksha054@gmail.com

ABSTRACT

Oral modified release multiple unit dosage forms have always been more effective therapeutic alternative to conventional or immediate release single unit dosage forms. The present study is to prepare Rabeprazole sodium delayed release pellets by using HPMC based sub coating and Methacrylic acid copolymer based enteric coating and to target the release of drug in intestine and to avoid stability related problems. Different batches of pellets were prepared by using drug suspension method. Comparative study of dissolution profile of final batch with market preparation was conducted and it was concluded that final batch shown good similarity with market product. The results of the accelerated stability of final formulation revealed that storage conditions were excellent.

Keywords: Rabeprazole sodium, delayed release, enteric coating.

INTRODUCTION

Proton pump inhibitors[1] (PPIs) are widely used for the treatment of esophageal reflux disease, treatment and prophylaxis of (NSAID-associated) duodenal and benign gastric ulcers and relief of dyspeptic symptoms. Rabeprazole sodium[2] is the member of a new class of substituted benzimidazoles. Chemically it is a 2-[[[4-(3-methoxypropoxy) -3-methyl-2-pyridinyl]-methyl] sulfinyl] -1H–benzimidazole sodium. H^+ /K^+ Adenosine Tri Phosphate (ATP) is an enzyme present in the secretory surface of the gastric parietal cells which is regarded as the acid (proton) pump within the parietal cell. So, Rabeprazole sodium has been characterized as a gastric proton-pump inhibitor. Rabeprazole sodium blocks the final step of gastric acid secretion in gastric parietal cells. Rabeprazole sodium is protonated, accumulated and transformed to an active sulfenamide.

Delayed release[3] systems release a bolus of the drug after a predetermined time in a predetermined location, i.e. they do not release the drug immediately after ingestion. Delayed release dosage forms are best formulations which are used for drugs that are destroyed in the gastric fluids or cause gastric irritation or absorbed preferentially in the intestine. Such preparations contain an

alkaline core material comprising the active substance, a separating layer and enteric coating layer[4,5].

The purpose of designing multiparticulate dosage form is to develop a reliable formulation that has all the advantages of a single unit formulations and yet devoid of the danger of alteration in drug release profile and formulation behavior due to unit to unit variations, change in gastro luminal pH and enzymes. Multiparticulate systems[6,7,8] perform better in vivo than single unit system, as they spread out through the length of the intestine, cause less irritation, enjoy a slower transit through the colon and give a more reproducible drug release.

MATERIALS

Rabeprazole sodium, Sugar spheres, Light Magnesium oxide, Mannitol, HPMC, Magnesium stearate, Disodium hydrogen phosphate, Sodium hydroxide, Polyethylene glycol, Polysorbate 80, Triethyl citrate, Ferric oxide red. Materials obtained from Hetero Pharma, Hyderabad.

EXPERIMENTAL
PREFORMULATION STUDIES

Preformulation studies were carried out for appropriate selection of excipients in view of Rabeprazole Sodium delayed release pellets[9].

Micromeritic properties of Rabeprazole Sodium

1. Angle of repose

The angle of repose of Rabeprazole powder was determined by the funnel method. The accurately weight powder blend 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.

2. Bulk Density and tapped Density

Both Bulk density (BD) and tapped density (TD) was determined. A quantity of 2 gm of Rabeprazole sodium powder from each formula, previously shaken to break any agglomerates formed, was introduced in to 10 ml 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 continued until no further change in volume was noted. Bulk density and Tapped density were calculated using the following equations.

Bulk density = weight of the powder blend/untapped volume of the packing

Tapped density = weight of the blend/Tapped volume of the packing

3. Compressibility Index

The compressibility Index of the powder blend was determined by Carr's compressibility index. The formula for Carr's Index is as below;

Carr's Index (%) = {(TD – BD) x 100} / TD

4. Hausner's ratio

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.

Hausner's ratio (H) = TD / BD

Where TD = tapped density, BD = bulk density.

Drug excipients compatibility study

Drug excipients compatibility studies were carried out by mixing the drug with various excipients in different proportions. Studies were carried out in flint vials at Accelerated conditions, 40±2^{0}C/75%RH±5% RH. The studies were conducted for 4 weeks and compared with control at 2 - 8^{o}C. Physical observations of the blend were recorded at regular interval of one week

Estimation of Rabeprazole sodium

Two different solutions of Rabeprazole sodium were prepared in 0.1 N HCl and 7.6 pH phosphate buffer respectively. The UV spectra were taken using spectrophotometer. The UV maxima of Rabeprazole sodium in 0.1 N HCl and 7.6 pH phosphate buffer were found to be 273 and 283 nm respectively.

Formulation development

FORMULATION OF CORE PELLETS

Preparation of Binder Soluton

●Take purified water in the hot water kettle heat up to bubbling point and transfer into a solution tank.

●Add disodium hydrogen phosphate, HPMC slowly and simultaneously under stirring. Continue stirring for another 15 min or until to form a uniform solution.

Preparation of Corepellets

●Charge sugar spheres (#24/#30) into the conventional coating pan.

●Spray the binder solution to sucrose and add the blended materials including rabeprazole sodium, light magnesium oxide, magnesium stearate and mannitol (lot I) by dusting slowly and simultaneous mixing the sucrose occasionally by hand.

●Add the sifted mannitol (lot II) to above as outer layer.

●Check the size pellets through the sieve no. #18/#22.

●Unload the wet core pellets into HDPE container lined with double polyethylene bags.

Core Pellets Drying

●Load the wet core pellets into the fluid bed coater which was warmed to 40ºC±5ºC for drying.

●Air dry for 1hour excluding occasional mixing.

●Then dry at temperature 46ºC±5ºC for 4 to 6 hours (excluding mixing time) till to get moisture content less than 2%. Mix the pellets every 1 hour for effective drying.

Core Pellets Sifting

●Sift the dried pellets through sieve no. #18. Collect passed pellets and retained pellets separately.

●Sift passed pellets through sieve no. #22. Collect passed pellets and retained pellets separately.

●Collect the retained core pellets i.e., #18 passed and #22 retained.

FORMULATION OF SUBCOATING

Preparation of Subcoating Solution

●Take purified water in hot water kettle heat up to bubbling point and transfer into a solution tank.

●Add HPMC, mannitol slowly and simultaneous to hot water under stirring. Continue stirring for another 15 min by using stirrer (or) until to form a uniform solution.

●Add propylene glycol, sodium hydroxide pellets slowly and simultaneous to above solution under stirring. Continue stirring for another 5 min or until to form a uniform solution.

●Add remaining quantity of purified water slowly under stirring. Continue stirring

for another 10 min or until to form a uniform solution.

Subcoating

●Charge core pellets into the clean fluid bed coater which was warmed to 40ºC±5ºC. Warm the pellets to reach temperature of 40ºC±5ºC.

●Start spraying the sub coating solution at the rate of 0.072 to 0.108 kg per hour with the following parameters.

●Continue the coating till to complete the solution or until the target weight build up obtained.

●Reduce the fluidization air flow to suitable level and stop guns air flow. Dry the sub coated pellets at temperature of 45ºC±5ºC for 30 min.

●Allow the sub coated pellets cool to room temperature.

●Unload the sub coated pellets into tarred HDPE container lined with double polyethylene bags. Weigh and label the container.

FORMULATION OF ENTERIC COATING

Preparation of Enteric Coating Solution

●Take Methacrylic acid copolymer (L30D) into the solution tank.

●Take purified water into the solution tank. Add sodium hydroxide pellets slowly into purified water under stirring for 5 min by using manual SS padal/ SS stirring rod.

●Add L30D55 solution under stirring. Continue stirring for another 10 min or until to form a uniform suspension.

●Add polysorbate 80 slowly under stirring. Continue stirring for another 10 min or until to form a uniform suspension.

●Add polyethylene glycol and triethyl citrate slowly under stirring until to form a uniform suspension.

●Add ferric oxide red, add remaining quantity of purified water slowly under stirring. Continue stirring for another 10 min or until to form a uniform suspension.

Enteric Coating

●Charge sub coated pellets into the fluid bed coater which was warmed to reach 40ºC±5ºC.

●Warm the pellets to reach temperature of 40ºC±5ºC.

●Start spraying the enteric coating suspension at the rate of .072 to 0.108 kg per hour with the following parameters.

●Continue the coating till to complete the solution or until the target weight build up obtained.

●Reduce the fluidization air flow to suitable level and stop guns air flow. Dry the enteric coated pellets at 45ºC±5ºC temperature for 2 hours.

●Allow the enteric coated pellets cool to room temperature.

●Unload the enteric coated pellets into tarred HDPE container lined with double polyethylene bags. Weigh and label the container.

Enteric Coated Pellets Sifting

●Sift the enteric coated pellets through sieve no #14. Collect passed pellets and retained pellets separately.

●Sift passed pellets through sieve no. #20. Collect passed pellets and retained pellets separately.

Sifted Pellets Blending

●Load the sifted pellets into a double cone blender and blend for 15 min.

●Unload the blended pellets into HDPE container lined with double polyethylene bags. Label the container.

●Send the enteric coated pellets sample for analysis.

EVALUATION[10]

Description

Examine the sample visually and record the observation.

Identification

The retention time of the principal peak in the chromatogram of the sample solution corresponds to that of the standard peak in the chromatogram of the standard solution as obtained in the assay.

Moisture content

Take about 3.0g of the pellets crushing, weigh accurately and transfer about 0.20 g of the test sample (W) into titration vessel of Karl Fisher titrator and titrate with Karl Fisher reagent to end point.

Calculate the moisture content of the test sample by the following formula

Moisture content (%w/w)= (F-I) K.F. Factor x 100/W x 1000

F= Final burette reading

I= initial burette reading

W= weight of test sample

Bulk density

Weigh and transfer around 30g of the sample into a 100 ml measuring cylinder, tap the measuring cylinder 10 to 15 times and record the volume occupied by the sample. Calculate the bulk density by using the formula.

Bulk density= weight of the sample (g)/ volume occupied by sample (ml)

Assay

Buffer

Accurately weigh and transfer about 6.80g of potassium dihydrogen orthophosphate into a beaker containing 1000ml of water and dissolve completely. Adjust the pH of the solution to 7.0±0.05 with triethylamine. Filter through 0.45µ membrane filter.

Mobile phase

Prepare a filtered and degassed mixture of buffer, acetonitrile and methanol in the ratio of 500:300:200 v/v.

Diluent

Use filtered and degassed methanol as diluent.

Chromatographic conditions

Column	:	Grace Smart RP 18, 250 x 4.6 mm, 5 µm or equivalent
Flow rate	:	1.0 mL/min
Detector	:	284 nm
Column temperature	:	Ambient
Injection volume	:	20 µL
Run time	:	12 minutes

Preparation of standard stock solution

Weigh and transfer accurately about 40mg of Rabeprazole sodium working standard into a 50 mL volumetric flask, add 30 mL of diluent and sonicate to dissolve. Make up the volume with diluent.

Preparation of standard solution

Dilute 5 mL of standard stock solution to 50 mL and make up the volume with diluent. Filter the solution through 0.45µ nylon membrane filter.

Preparation of test solution

Weigh about 470mg of Rabeprazole sodium pellets powder and transfer into a 100 mL volumetric flask, add 70 mL of diluent and sonicate for 10 min with occasional swirling, cool to room temperature and make up to volume with diluent.

Dilute 5mL of this solution to 25 mL and make up the volume with diluent and filter the solution through 0.45 µ nylon membrane filter.

Procedure

Equilibrate the column for 30 minutes with mobile phase at the flow rate of 1.0mL/min. separately inject 20µL of blank(mobile phase), standard and sample solution into the chromatograph. Record the chromatograms and measure the peak areas.

Calculate the Rabeprazole sodium content using the formula-

$$\frac{A_T \times Ws_X \times 5 \times 100 \times 25 \times P}{A_S \times 50 \times 50 \times W_T \times 5 \times 100} \times 100$$

A_T = Area of Rabeprazole sodium peak in sample solution

A_S = Average Area of Rabeprazole sodium peak in standard solution

W_S = Weight of Rabeprazole sodium working standard taken in mg

W_T = Weight of Rabeprazole sodium sample taken in mg.

P = Assay of Rabeprazole sodium working standard

Dissolution

Acid resistance (drug release in 0.1 N HCl)

Parameters

Medium	:	900 mL of 0.1 N HCl
Apparatus	:	USP type-II (paddle)
Speed	:	100 rpm
Temperature	:	37± 0.5°C
Time	:	2 hours

Preparation of sample solutions

Take 900 mL of 0.1 N HCl previously adjusted to the temperature 37±0.5°C in six dissolution bowls. Weigh and transfer about 470 mg of Rabeprazole sodium pellets in each bowl and run the apparatus for 2 hours. After the specified time drain the medium, take out the pellets and observe visually. Transfer the pellets in each bowl as completely as possible into a 100 mL volumetric flask, add about 70 mL of diluent and sonicate to dissolve and make up to volume with diluent. Dilute 5 mL of the filtrate to 25 mL volumetric flask and make up to volume with diluent. Filter through 0.45µ membrane filter.

Procedure

Inject immediately 20µL of the sample solutions into the chromatographic system. Record the chromatograms and measure the peak areas.

Calculate the Rabeprazole sodium content release using the following formula

$$\frac{[\text{Sample area} \times \text{std. wt} \times 5 \times 100 \times 25 \times P \times 100}{\text{Avg. std. area} \times 50 \times 50 \times \text{sample wt} \times 5 \times 100 \times \%\ \text{assay}] \times 100}$$

P = assay of Rabeprazole sodium working standard.

Calculate the content in 0.1 N HCl as follows:

% release in 0.1 N HCl = 100 - % value obtained from the above result.

Dissolution in buffer

Parameters

Medium	:	900 mL of dissolution medium
Apparatus	:	USP type-II (paddle)
Speed	:	100 rpm
Temperature	:	37± 0.5°C
Time	:	1 hour

Preparation of dissolution medium

Take about 40.8g potassium dihydrogen orthophosphate and 6.8 g sodium hydroxide dissolve in 6000 mL of water. Adjust the pH of the solution to 7.6 ± 0.05 with sodium hydroxide. After that prepare a mixture of pH 7.6 buffer and IPA in the ratio of 800:200 v/v.

Preparation of standard stock solution

Weigh and transfer about 40mg of Rabeprazole sodium working standard into a 100 mL of volumetric flask and add 70 mL of dissolution medium and sonicate to dissolve. Make up the volume with dissolution medium.

Preparation of standard solution

Dilute 5 mL of standard stock solution to 50 mL volumetric flask and make up the volume with dissolution medium. Filter the solution through 0.45µ nylon membrane filter.

Preparation of test solution

Take 900 mL of 0.1 N HCl previously adjusted to the temperature 37± 0.5°C in six dissolution bowls. Weigh and transfer about 470 mg of Rabeprazole sodium pellets in each bowl and run the apparatus for 2 hours. After the specified time drain the medium. Add 900 mL dissolution medium of 7.6 phosphate buffer in each bowl and run the apparatus for 60 minutes. Filter the solution through 0.45 µ nylon membrane filter.

Procedure

Separately inject 20µL blank (dissolution medium), standard solution and sample solution into the chromatographic system. Record the chromatograms and measure the peak.

Calculate the % labeled amount of Rabeprazole sodium dissolved using the following formula

= AT/AS x WS/100 x 5/50 x 900/WT x p/100 x 100/% assay x 100

Where,

AT = Area of Rabeprazole sodium peak in sample solution.

AS = Average area of Rabeprazole sodium peak in standard solution.

WS = Weight of Rabeprazole sodium working standard taken in mg.

WT = Weight of Rabeprazole sodium sample taken in mg.

P = Assay of Rabeprazole sodium working standard.

RESULTS AND DISCUSSION

Preformulation studies

From the results of micromeritic studies of the Rabeprazole sodium it was concluded that Rabeprazole sodium has poor flow property and compressibility property. From the physical observation, no significant drug- excipient interaction was noticed. So it was concluded that drug and other excipients were compatible with each other.

Evaluation parameters of the optimized batch of Rabeprazole sodium

From the results of comparative study of dissolution profile of final batch with market preparations. It was concluded that final formulation was shown good similarity with market product.

Accelerated stability[11] study of the optimized batch

From the results of the accelerated stability of the final formulation for 3 months, it was concluded that storage conditions were not found any significant changes in final formulation dissolution profile with market sample.

Selected formulation (F5) was kept for stability studies and observed that assay, acid resistance and drug release at the end of 1, 2 and 3 months. There was no significant change in i*n-vitro* release profile. It shows that formulation F5 was stable.

SUMMARY AND CONCLUSION

The aim of the present study was to formulate and evaluate delayed release pellets of Rabeprazole sodium by enteric coating. It is an acid labile drug so it is degraded at

acidic pH of stomach so an attempt was made to bypass the stomach; formulation was made by giving enteric coating. The main challenge in the formulation of Rabeprazole sodium was its degradation upon exposure to acidic environment which results into high impurity level. Thus to prevent exposure of Rabeprazole sodium in gastric environment, enteric coating was done and to prevent interaction between drug and acidic enteric coating material, seal coating was done over the core pellets.

The different batches of pellets were prepared by using drug suspension layering and were developed using fluid bed layering and coating techniques. Five formulations having alkalizing, solubilizing agents, polymers at different concentration levels were prepared in subcoating as well as enteric coating. The enteric coating was carried out by using enteric polymer Methacrylic acid copolymer L30D55. Thus study includes preformulation of drug and excipients, formulation, evaluation and stability studies of delayed release pellets. Among all formulations F5 batch showed superior properties along with excellent drug release when compared to other formulations. It showed better stability and can be the good way to improve the bioavailability of Rabeprazole sodium.

REFERENCES

1. Goodman and Gilman: The pharmacological basis of therapeutics, 10th edition. 2003,1007-1008.
2. www.drugs.com/monograph/rabeprazole sodium.
3. Chein W. Novel drug delivery systems, 2nd Edition, Marcel Dekker, Newyork, 2000: 43-135.
4. Leon Lachman, Herbert A. Lieberman and Joseph L. Kanig. The Theory and Practice of Industrial Pharmacy, 3rd Bombay: Varghese. 331-332, 364-368.
5. Cole G.C. Pharmaceutical Coating Technology, Taylor and Francis Ltd; 1998, 46-52.
6. Olsen K. Fluid bed equipment. In: Ghebre Sellassie I. Pharmaceutical Pellatization Technology. New York: Marcel and Dekker.39-69.
7. Tang ESK, Chan LW, Heng PWS. Coating of Multiparticulates for Sustained Release Technology. 2000: 473.
8. A flexible technology for modified release drugs: Multiple unit pellet system: *Journal of controlled release*, vol. 147, Issue 1, Oct 2010, 2-16.
9. Aulton. Pharmaceutics-Science and Dosage Form Design. 2nd ed: 213-227 & 204- 206.
10. Leon Lachman, Herbert Libermann Josphp L-Kanig. Theory and Practice of Industrial Pharmacy, 3rd ed: 293-329.
11. International conference on harmonization (ICH) harmonized tripartite guideline for stability testing of new drugs substances and products Q1A (R2) aug-2003. Q1A (R2) Mar 2004.

Table 1. Formulation of different batches of Rabeprazole sodium core pellets

Ingredients	F1	F2	F3	F4	F5
Rabeprazole sodium	85.00	85.00	85.00	85.00	85.00
Sugar spheres	269.10	269.10	269.10	269.10	269.10
Light magnesium oxide	34.69	60.98	60.00	62.00	62.00
Mannitol	104.08 & 69.38	104.08 & 69.38	104.08 & 69.38	104.08 & 69.38	104.08 & 69.38
HPMC (E5)	4.16	2.80	---	---	4.16
HPMC (E15)	---	---	4.16	4.16	---
Disodium hydrogen phosphate	0.86	0.92	1.00	1.00	1.00
Magnesium stearate	52.04 & 34.69	52.04 & 34.69	52.04 & 34.69	52.04 & 34.69	52.04 & 34.69
Distilled water	Q.S	Q.S	Q.S	Q.S	Q.S

Table 2. Process parameters to be maintained during preparing Rabeprazole sodium core pellets

PROCESS PARAMETER	SET PARAMETER	OBSERVED PARAMETER
Number of gun(s)	1	1
Material nozzle insert diameter	0.8 mm	0.8 mm
Atomized air pressure	0.5 to 2 bar	0.8 to 1.8 bar
Conventional coating pan rpm	8	8
Peristaltic pump speed	3-9 rpm	4-8 rpm
Spray rate	5-10 g/min/gun	6-9 g/min/gun

Table 3. Formulation of different batches of Rabeprazole sodium sub-coated pellets

Ingredients	F1	F2	F3	F4	F5
Core pellets	654.03	654.03	654.03	654.03	654.03
Sodium hydroxide	0.24	0.24	1.00	1.50	1.50
HPMC (E5)	58.42	---	---	65.00	65.00
HPMC (E15)	---	59.90	---	---	---
HPMC (K4)	---	---	20.00	---	---
Mannitol	5.84	5.84	5.00	10.00	10.00
PEG 6000	5.25	5.25	5.00	5.00	5.00
Distilled water	Q.S	Q.S	Q.S	Q.S	Q.S

Table 4. Process parameters to be maintained during preparing sub coated pellets of Rabeprazole sodium

PARAMETER	SET PARAMETER	OBSERVED PARAMETER
Number of gun(s)	1	1
Material nozzle insert diameter	0.8 mm	0.8 mm
Inlet air temperature	30ºC -70ºC	30ºC -70ºC
Product temperature	45ºC±5ºC	45ºC
Atomized air pressure	1-2 bar	1.2 – 1.8 bar
Peristaltic pump speed	3-9 rpm	4-8 rpm
Spray rate	15-20 g/min/gun	16-18 g/min/gun

Table 5. Formulation of different batches of Rabeprazole sodium enteric coated pellets

Ingredients	F1	F2	F3	F4	F5
Methacrylic acid copolymer	742.09	742.09	742.09	742.09	742.09
Sodium hydroxide	1.74	1.07	1.00	1.00	1.00
Poysorbate 80	5.30	5.00	30.00	10.00	20.00
Polyethylene glycol	22.00	22.00	---	10.00	---
Triethyl citrate	---	---	15.00	25.00	30.00
Ferric oxide red	10.00	10.00	10.00	10.00	10.00

Table 6. Process parameters to be maintained during preparing enteric coated pellets of Rabeprazole sodium

PARAMETER	SET PARAMETER	OBSERVED PARAMETER
Number of gun(s)	1	1
Material nozzle insert diameter	0.8 mm	0.8 mm
Inlet air temperature	30ºC -70ºC	30ºC - 70ºC
Product temperature	45ºC±5ºC	45ºC
Atomized air pressure	1-2 bar	1.2 – 1.8 bar
Peristaltic pump speed	3-9 rpm	4-8 rpm
Spray rate	15-20 g/min/gun	16-18 g/min/gun

Table 7. A.P.I characterization

S.No.	Characteristics	Results
1.	Physical appearance	A off-white powder
2.	Bulk density	0.53gm/ml
3.	Tap density	0.69gm/ml
4.	Compressibility index	32.1%
5.	Hausner's ratio	1.47
6.	Melting point	140-141^{0}C
7.	Molecular weight	381.43

Table 8. Observation for Drug-excipient compatibility test

S. NO	Drug-Excipients combination	D:E Ratio	Final description 1M(40°C/75%RH 7 days)
1	RS	-	No color change
2	R S+Mannitol	1:10	No color change
3	RS+ Light MgO	1:10	No color change
4	R S+ HPMC (E5)	1:1	No color change
5	RS+ HPMC (E15)	1:1	No color change
6	RS+ HPMC (K4)	1:1	No color change
7	RS+Magnesium stearate	1:0.5	No color change

RS=Rabeprazole sodium

Table 9. Comparative study of dissolution profile of optimized batch with market sample

S. NO.	Time (min)	Market sample	F5
1	10	20.6	24.8
2	20	52.4	63.8
3	30	72.3	79.2
4	40	87.9	89.8
5	50	92.7	93.2
6	60	98.4	99.5

Table 10. Comparison of Assay, Moisture content, Bulk density and Drug release of enteric coated pellets with innovator

S. No	Test %	Market sample	F1	F2	F3	F4	F5
1	Assay	8.38	8.22	8.17	8.23	8.35	8.41
2	Moisture content	3.2	6.5	4.7	3.66	3.4	3.19
3	Bulk density	0.85	0.77	0.73	0.81	0.82	0.86
4	Drug release	98.4	87.25	88.23	91.2	93.5	99.5

Table 11. Stability data of optimized batch (F5)

Duration	Description	Water content	Dissolution		Related substances	Assay	remarks
			Acid resistance(drug release in 0.1N HCl)	Buffer stage			
Initial	A dark brown colored spherically uniformed enteric coated pellets	3.19	Nil	99.5	1.63	8.41	Passes
1st month	A dark brown colored spherically uniformed enteric coated pellets	3.19	Nil	97.85	1.82	8.39	Passes
2nd month	A dark brown colored spherically uniformed enteric coated pellets	3.24	Nil	96.68	2.05	8.35	Passes
3rd month	A dark brown colored spherically uniformed enteric coated pellets	3.29	Nil	96.15	2.19	8.35	Passes

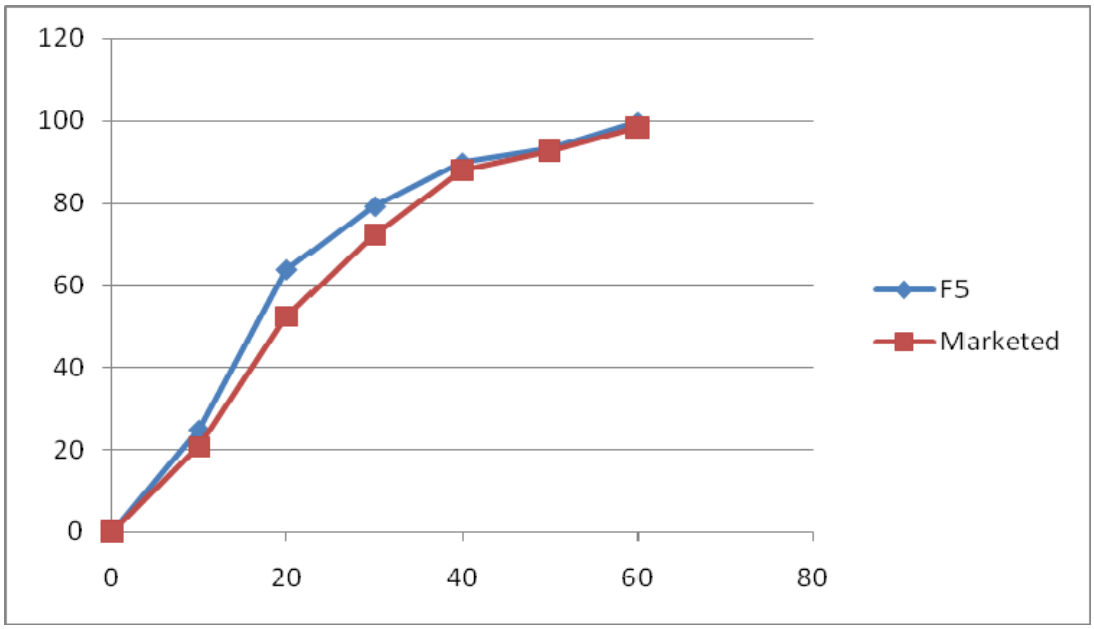

Figure 1. *In Vitro* dissolution profile in buffer stage of optimized batch and market sample

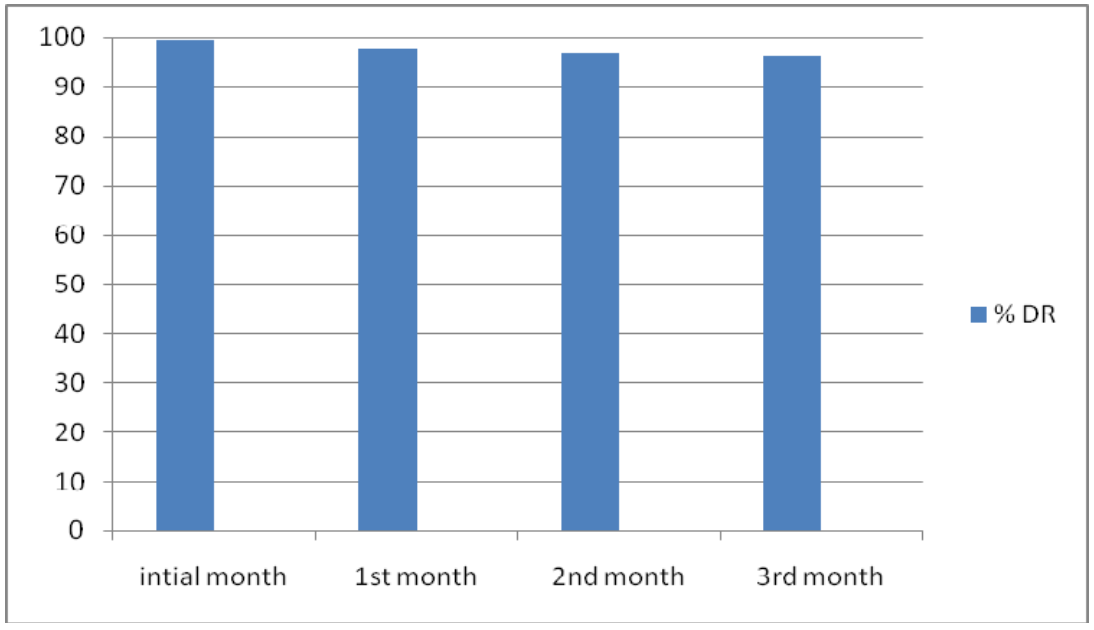

Figure 2. Dissolution profile of selected stability sample