RESEARCH ARTICLE

Design, Development and Physicochemical Evaluation of Formulation for Gastroesophageal Reflux Disease

Ghugarkar Prasad Gorakshanath*, Kadam Pallavi Kanifnath

Dr. N. J. Paulbudhe College of Pharmacy, Ahmednagar, India

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ABSTRACT

The present study mainly involves the targeting the gastro intestinal ulcer by using Rabeprazole formulation. In this main strategy contains the formulation and optimisation of Rabeprazole pellet formulation. The stomach is the primary acidic environment in which nearly all drugs that inhibit proton pumps breakdown. The strategy involve is to coat the Rabeprazole pellet formulation with polymer coat which release the formulation in appropriate site only. Pre formulation date of material detected. Compatibility study of drug with selected excipients was analysed by using Fourier Transform Infrared Spectroscopy. Thermal study of the Rabeprazole was analysed by using differential scanning calorimetry instrument. Purity of the Rabeprazole was detected by using different physical and chemical characters as well as by using ultra violet spectrometry. For core pellet formulation of Rabeprazole, Extruder and Spheroniser method was used. After core pellet formulation it was seal coated with Opadry seal coat material. Lastly seal coated pellet of Rabeprazole was coated by using Eudragit polymer for site specific drug delivery. Eudragit inhibits the release of formulation in acidic condition. Evaluation parameters detected on optimised batch. Stability study was performed as per International Council for Harmonisation guideline.

Keywords: Peptic Ulcer, Stomach, Dissolution, Intestine.

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INTRODUCTION

Solid oral dosage forms are widely prescribed over other type of formulations because of their patient compliance, better acceptability and due to cost effective formulation. Peptic ulcer which is common dieses in which ulcer was occurred in upper part of the small intestine and below the stomach.Peptic ulcer mainly occurred due to infection of H. pylori in stomach[1]. Peptic ulcer mainly occurs below the stomach region and in upper part of the small intestine. Proton pump inhibitors are the drug which is used to cure the peptic ulcer. Proton pump inhibitor results the maximum absorption in basic pH condition. Hence the main strategy to deliver the proton pump inhibitor is to formulate such formulation which consist of enteric coating or site-specific drug delivery system [2]. Such formulation protects the drug degradation from acidic condition which is present in gastrointestinal tract and it delivers the formulation in given site or in basic pH condition. This type of formulation increases the bioavailability of drug by targeting the site specificity[3].

MATERIALS AND METHODS

Materials

Rabeprazole, Sorbitol, Starch, Sodium Starch Glycolate, Calium Stearate, Opadry coat, Eudragit S-100, Polyethylene Glycol obtained from Modern manufacturer.

Methods

Determination of Melting Point

Capillary Tube method was used to determine melting point of material.

Pre Formulation Study

Pre formulation study of the selected drug as well as formulation was carried out. Initially For API physical characteristics was carried out in pre formulation study.

FTIR Spectroscopy

FTIR study of the selected API as well as API & excipients was carried out. Initially FTIR spectra. Of plain API was studied to check the purity of selected API. Mixture of selected al excipients and API was also scanned under IR spectroscopy and it was studied to check the compatibility of API and excipients [4].

UV Analysis

0.1 N HCL used to mix drug material so as to make the standard stock solution. Final volume of the solution was adjusted with solvent. From this solution 10 ml of aliquot mixed in another volumetric flask with selected solvent. From this solution different aliquots were prepared and scanned under UV spectrophotometry. From the obtained data calibration graph was plotted.

DSC Study

Initially selected API was pressed under DSC instrument, with increasing temperature condition. From the obtained thermogram purity as well as thermal effect of the API studied [5].

Pellet Preparation Procedure

**Author for Correspondence: ghugarkarp@gmail.com*

Extruder and spheroniser method was selected for the pellet preparation of Rabeprazole. Efficiency of the Extruder and spheroniser method higher than other pellet formulation techniques. Initially Rabeprazole and all selected excipients were transferred from sieve no. 40 so as to avoid segregation in blend. After that Rabeprazole was mixed with sorbitol followed by starch with selected solvent.

Mixture was mixed thoroughly and dried to reduce moisture effect. Then Sodium Starch Glycolate and calcium stearate was mixed in blend. After all excipients added with Rabeprazole, it was mixed thoroughly. Then the blend was introduced in to Extruder. The main mechanism of the extruder is to form a cylindrical shape long particle which is known as extruder. After preparation of extrudes from all prepared blend, the extrudes were transferred to spheroniser. The main mechanism of the spheroniser is to convert cylindrical shape extrudes to uniform sphere shape particle. Hence all the extrudes of the formulation were formulated as a uniform spherical shape pellet by using spheroniser[6]. Opadry coat polymer was selected for initial coat. MDC and IPA solvents were used for seal coating. The proportion of the MDC and IPA was taken as 1:1 ratio. Seal coat was completed in Glatt instrument. This seal coated pellet was used for polymer coat. For polymer coat Eudragit S-100 polymer was used. Polyethylene Glycol used as a plasticizer. Polymer coat was completed in Glatt instrument.

Table 1: Formulation of Pellet

Ingredient	Quantity (mg)					
	F1	F2	F3	F4	F5	F6
Rabeprazole	20	20	20	20	20	20
Sorbitol	8	8	9	12	14	16
Starch	2	3	4	6	8	10
Sodium Starch Glycolate	3	4	5	6	7	8
Calium Stearate	2	2	3	3	4	4
Alcohol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

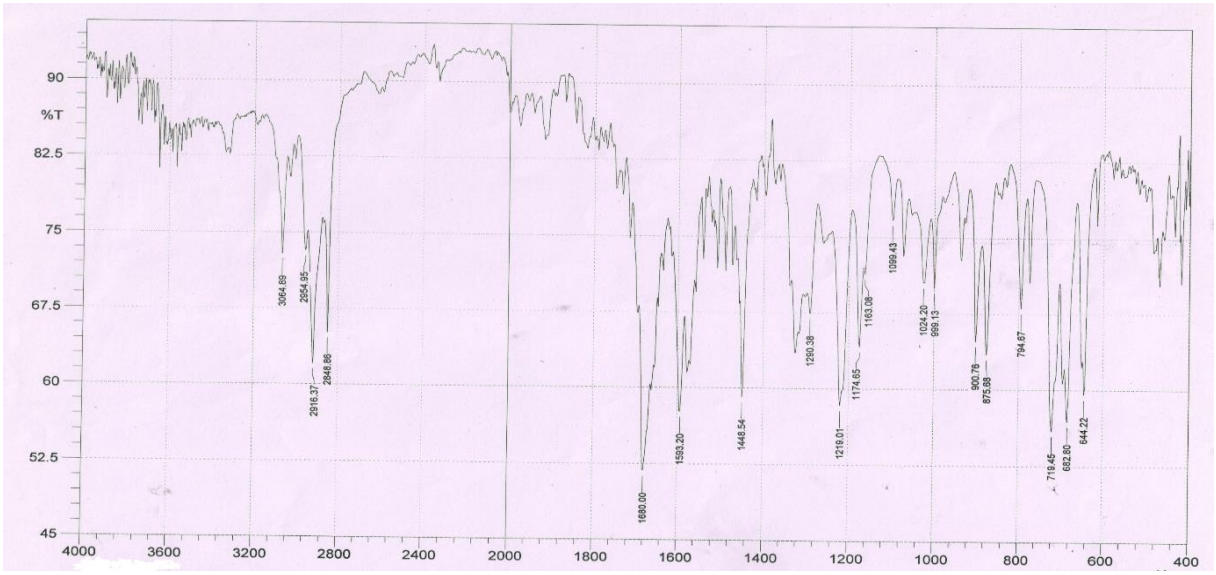

Figure 1 : FTIR Study of Drug Material

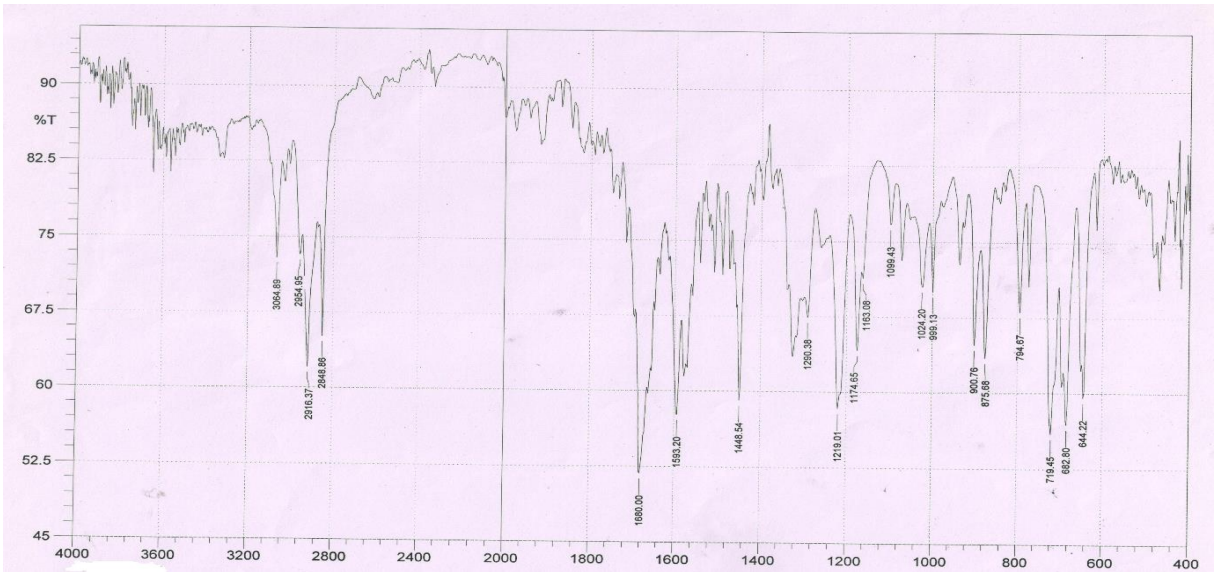

Figure 2 : FTIR Study of Mixture

RESULTS AND DISCUSSION

Physicochemical Property

Physicochemical properties of the API studied. Appearance, Colour, Odour and Melting point was determined[7].

Pre Formulation Study

Pre formulation characteristics of the prepared mixture was studied.

FTIR Spectroscopy Study

FTIR Spectra of Plain Rabeprazole as well as the for the combination of API and Excipients was studied. From the obtained FTIR spectra it was observed that there was no any major deviation in the spectra hence selected excipients can be used with the API [8].

Ultraviolet Analysis

Different aliquots and solution was scanned under UV spectrometry. Lambda max of the API was shown at 291 nm. So, at this range aliquots of the Rabeprazole were analysed. The obtained data was plotted on graph as mean absorbance vs. concentration of solution. Calibration curve was showing a linear result and R^2 value was within the acceptable range.

DSC Analysis

Optimised formulation was analysed for thermal study by Differential Scanning Calorimetry instrument. From the obtained thermogram, the highest peak on the thermogram shows at 221.28^{0}C. *In-vitro* dissolution test: It was performed in 0.1 N HCL medium followed by 6.8 Phosphate Buffer. Total 2 hrs dissolution time wa taken and it shows zero drug release in 0.1 N HCL. Same formulation was studied for dissolution profile in 6.8 phosphate buffer. Optimisedformulation shows best result among all formulations [9].

Stability Test

Table 2: Composition of pellet primary coat

Material	Quantity
Opadry coat	22 %
Methylene Dichloride	50 %
Iso Propyl Alcohol	50 %

Table 3: Composition of Polymer coating

Ingredient	Quantity (mg)
Eudragit S-100	44
Polyethylene Glycol	11.20
Talc	08

Table 4: Organoleptic characterisation

S. No.	Particular	Inferance
1	Appearance Test	Amorphous
2	Colour Test	White to pale white
3	Odour	Characteristic
4	Melting Point	137-140^{0}C.

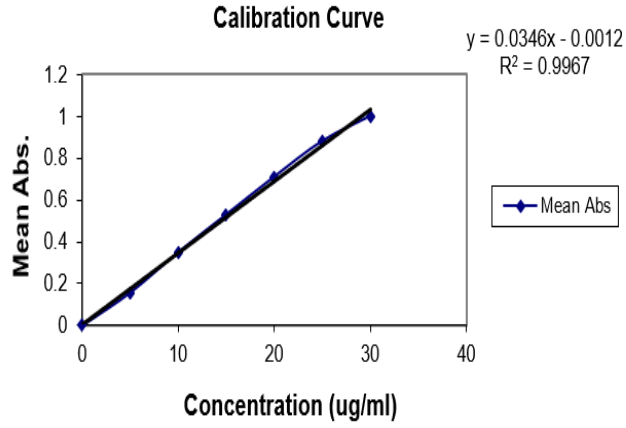

Figure 3 : Calibration curve of Rabeprazole

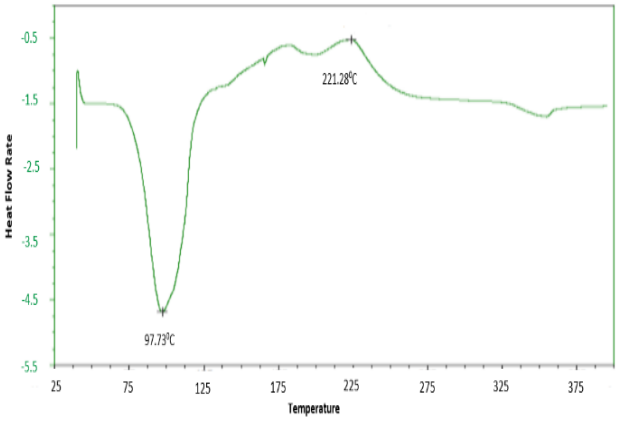

Figure 4: DSC study of Product

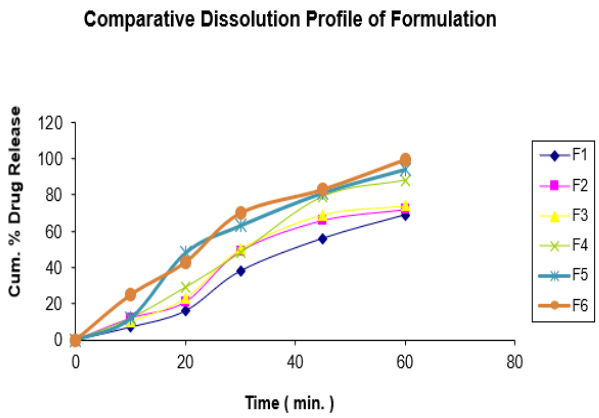

Figure 5: Comparitive study of In-vitro

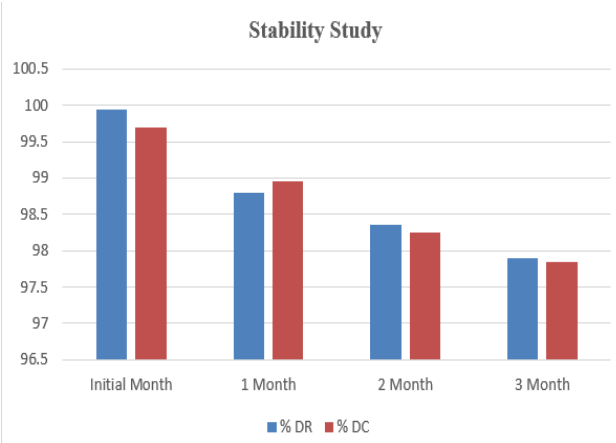

Figure 6 : Stability Test

Table 5: Pre formulation result

Batch	Angle of repose	Bulk density	Tapped density	Compressibility index	Hausnar's ratio
1	21.40±0.08	0.74	0.84	11.90	1.13
2	41.31±0.10	0.77	0.84	08.33	1.09
3	25.36±1.11	0.75	0.87	13.79	1.16
4	27.37±0.07	0.78	0.85	08.23	1.08
5	32.48±0.07	0.73	0.84	13.09	1.15
6	33.11±0.09	0.71	0.83	14.45	1.16

Stability study was performed on the optimised formulation. Selected formulation was kept in stability chember at condition of 25°C/60% RH, 30°C/65% RH and 40°C/75% RH condition. Total 4 different samples were withdrawn for analysis purpose at Initial mont, 1 month, 2 month and 3 month respectively. From the obtained data of % drug release and % drug content are with in limit [10].

Response Surface Plot and Overlay Contour Plot

Factors which are dependent in nature then this type of factore is known as response and the factors which are independent in nature is known as predictable variable. F6 was selected for optimisation. For response surface plot and overlay contour plot, % drug release, % polymer coat and % plastiizer in coat these factores were selected. From the obtained graph and result it was observed that factors are optimised in selected batch [11].

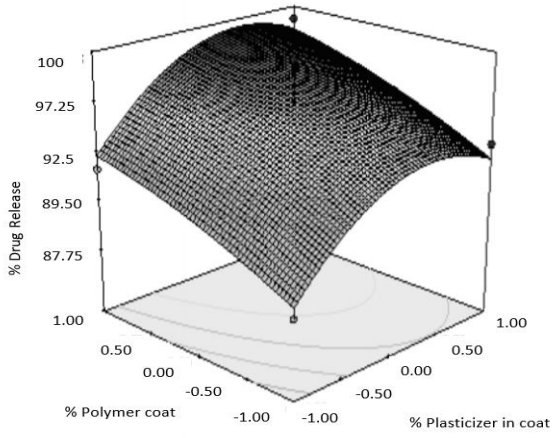

Figure 7 : Response surface plot

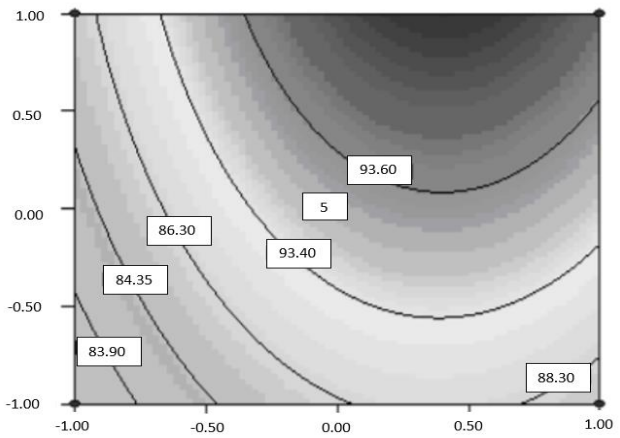

Figure 8 : Overlay Contour Plot

CONCLUSION

Most of proton pump inhibitors shows activity in basic pH condition hence it degrades in acidic condition in stomach. Polymer coat helps to deliver formulation directly in to selected site ad it protects formulation from acidic envirnment. Pellet formulation was then coated with seal coating material to protect the formulation from other coating material and from different enviormental conditions like temperature, humidity. Then seal coated formulation then finally coated with polymer coat i.e. Eudragit S-100. Polymer coated pelletes shows good result in 6.8 phosphate buffer. All evaluation parameters shows acceptable results.

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