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Research Paper

FORMULATION AND EVALUATION OF ENTERIC COATED TABLET OF RABEPRAZOLE SODIUM

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Formulation and Evaluation of enteric coated tablets of Rabeprazole sodium for the effective treatment of duodenal ulcer was successfully carried out by performing the preformulation studies,formulation of Rabeprazole sodium enteric coated tablets, evaluation parameters, *in vitro* drug release studies and stability studies.

The preformulation studies and drug excipientscompatibility studies were carried out with aid of IR spectroscopica nalysis of drug with excipients which showed that the drug was compatible with excipients which were further used in the formulation.The prepared powder blend was evaluated for precompression parameters like a ngle of repose, bulk density, tapped density, compressibilityindex and Hausner ratio. The obtained results indicated that it has good flow property.

Rabeprazole Sodium enteric coated tablets were prepared by wet granulation method.The prepared tablets were evaluated for hardness, thickness, weight variation,friability, assay and disintegration time.All these parameters were found to be within the pharmacopoeial limits in F-V formulation. Rabeprazole Sodium enteric coated tablets were coated with Cellulose acetate phthalate and Diethyl phthalate in different concentrations.

Key Words: Hausnerratio, Diethyl phthalate,enteric coated tablets, tapped density, compressibility index .

INTRODUCTION

Oral route is the most acceptable route of drug administration among all routes that have been explored for the systemic delivery of drug via various pharmaceutical products of different dosage form. Solid medicaments may be administered orally as powders, pills, sachets, capsules or tablets. These dosage forms contain a quantity of drug which is given as a single unit and they are known collectively as solid unit dosage forms, even in the case of sustained action preparations which, technically, contain the equivalent of several normal doses of drug.

The stringent formulation requirements of modern medicaments, the many advantages of tablet and capsule medication, coupled with expanding health services and the commitment need for large scale economic manufacture, have led to a steady decline in the prescribing of powders and pills. Tablets and capsules, on the other hand, currently account for well over two third of the total number and cost of medicines produced all over the world[1].

Oral site-specific drug delivery systems have attracted a great deal of interest recently for the local treatment of a variety of bowel diseases and also for improving systemic absorption of drugs, which are unstable in the stomach. However, the micro environment in the gastrointestinal tract and varying absorption mechanisms generally causes

hindrance for the formulation scientist in the development and optimization of oral drug delivery. Delivery of therapeutic agent into the intestinal region could be accomplished by the application of an enteric coating on a solid dosage form. Several approaches have been attempted and reported during the last decade to develop new methodologies for site-specific drug release, including pH-sensitive drug release and time-controlled drug release. Among these, the time-controlled release systems such assustained or delayed-release dosage forms are very promising. Nevertheless, due to the p large variation of gastric emptying time of dosage forms in humans, these dosage form may show high inter patient variability in the site of drug delivery.

On the other hand, pH-sensitive delivery systems such as enteric-coated dosage forms offer a simple and practical means for intestinal drug delivery. Esomeprazole magnesium trihydrate, is a classical example of proton pump inhibitors and is approved by FDA for the treatment of symptomatic gastroesophageal reflux disease, short-term treatment and maintenance of erosive esophagitis.

METHODS

1. Preformulation Studies

Preformulation studies were carried out for appropriate selection of excipients in view of Rabeprazole sodium delayed release tablet.

Organoleptic Properties

The organoleptic studies of Rabeprazole sodium like general appearance like nature, colour, odour etc. were performed and observed.

- **Colour:** Small quantity of Metoprolol Succinate was taken in butter paper and viewed in well illuminated place.
- **Odour:**Very less quantity of drug was smelled to get the odour.

Solubility Study

Solubility is determined in different solvents like Freely Soluble in water, soluble in Ethanol and methanol. An excess amount of the drug was added to 10 ml volumetric flask containing various aqueous media at different temperature and pH conditions. The samples were allowed to shaken for 48 hours and finally filtered through Whatman's filter paper. After 48 hours, the drug concentration was determined spectrophotometrically.

Identification by Infrared Spectrophotometry

Sample Preparation: Asmall amount of finely ground powder of Rabeprazole Sodium mixed with 100 times its weight of Potassium bromide (KBr) and compressed into a thin transparent pellet using a hydraulic press. These pellets are transparent to Infra-Red radiation and its used for analysis.

Calibration Curve: Calibration curve was performed with 0.1N HCl and Phosphate buffer (pH6.8). The results show good Correlation coefficient with both the solvents.

Estimation of Rabeprazole sodium

Two different solution of Rabeprazole sodium were prepared in 0.1 N HCL (8.5 mL of Conc. Hydrochloric Acid in 1000 mL of water.) and phosphate buffer pH 6.8 (6.8 gm of Potassium di

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Hydrogen Orthophosphate in 1000 mL of water) respectively. The UV spectrums were taken using Shimadzu UV-1800 UV/Visible spectrophotometer.

1.1 Evaluation of Powder Blend

Powder blend was evaluated for Angle of repose, Bulk density and Tapped density, Compressibility Index, Hausner's ratio as described above. Additionally, Blend Uniformity was calculated by following procedure:

Micromeritic Properties of Powder Blend

- **Angle of Repose**

The angle of repose of powderwas 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 angleof repose was calculated using the following equation.

$$\tan \theta = \frac{h}{r}$$

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

Bulk Density and Tapped Density

Both Bulk density (BD) and tapped density (TD) was determined. A quantity of 2 gm of API 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 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TDB were calculated using the following equations.

BD= Weight of the powder blend/Untapped Volume of the packing

TD=Weight of the powder blend/Tapped Volume of the packing

Table 1: Flow Properties and Corresponding Angles of Repose

Flow Property	Angle of Repose
Excellent	25-30
Good	31-35
Fair	36-40
Passable	41-45
Poor	46-55
Very poor	56-65
Very very poor	>66

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2. Result and Discussion:

Preformulation Studies

2.1 Description

Table 2: Description of Rabeprazole Sodium

S. No.	Test	Result
1	Colour	White
2	Odour	Unpleasant
3	Nature	Crystalline
4	Taste	Bitter

Discussion: The colour, odour, nature and taste of the API were evaluated. It was found to be as per the monograph.

2.2 Solubility

Table 3: Solubility of drug

Material	Solubility
Rabeprazole Sodium	Soluble in Ethanol
	Soluble in Methanol
	Soluble in Water

Discussion: Thus the results revealed that the drug was soluble in water, methanol and ethanol.

2.3 Identification

Infrared spectrophotometry

Identification of Rabeprazole sodium was carried out with the help of IR spectrophotometry. The Sample Infrared of Rabeprazole sodium was compared with the Reference Infrared of Rabeprazole sodium as per Indian Pharmacopoeia 2018.

Discussion

In FTIR spectra the peaks of Rabeprazole Sodium were compared with the Indian Pharmacopoeia 2018 reference spectra. Same peaks were observed. Thus Identification of Rabeprazole Sodium was confirmed

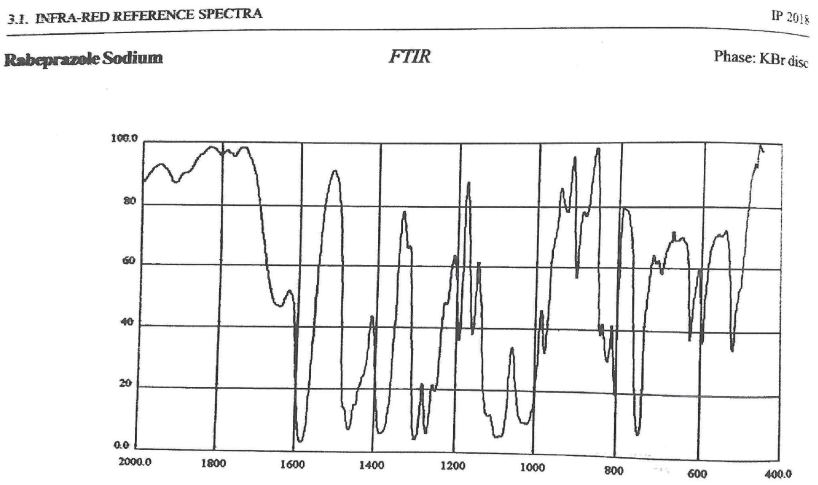

Figure 1: Infra-Red of Rabeprazole Sodium (Reference)

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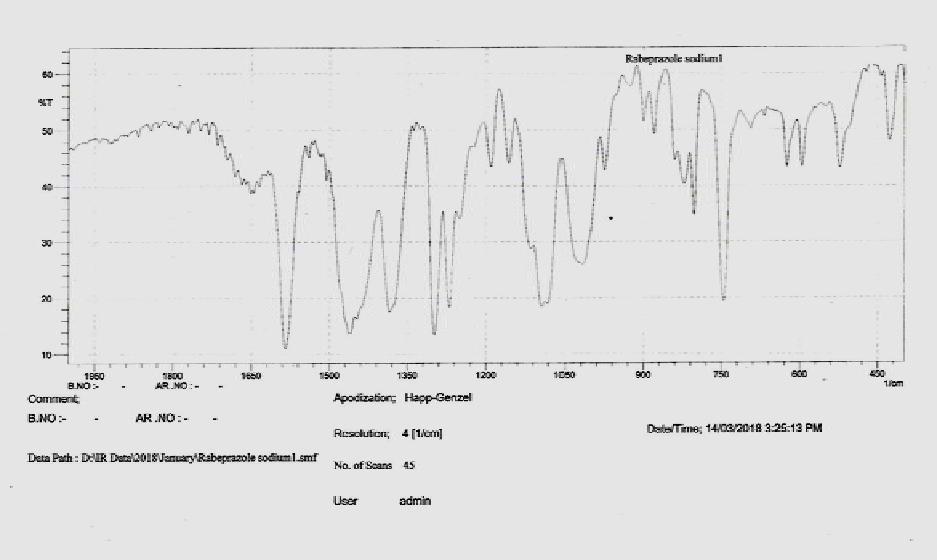

Figure 2: Infra-Red of RabeprazoleSodium(Sample)

Table 4: Flow properties of different formulations

Blend Property						
Formulations	**B.D (gm/mL)**	**T.D (gm/mL)**	**C.I. (%)**	**H.R.**	**Angle of Repose**	**Property**
F1	0.580	0.679	14.58	1.275	42	Passable
F2	0.612	0.750	18.40	1.225	37	Fair
F3	0.658	0.810	18.76	1.231	36	Fair
F4	0.630	0.720	12.50	1.145	33	Good
F5	0.667	0.730	8.630	1.094	29	Excellent
F6	0.648	0.780	16.92	1.203	38	Fair

2.4 Micromeritic Properties

Discussion:

The angle of repose was found to be in the range of 29 to 42 for all formulations.If the angle of repose was within 30°, it shows excellent flow properties. The result proved that F5 formulations showed excellent flow properties as compared to other formulation.

The bulk density of all formulations was measured by using bulk density apparatus. The bulk density was in the range 0.580 to 0.667 gm/mL.

The tapped density of all formulations was measured by using tapped density apparatus. The tapped density was found in the range of 0.679 to 0.810± 0.3 gm/mL.

The compressibility index was in the range of

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8.630 to 18.76%. It proved that the flow behaviors and compressibility of the granules are good.

The hausner's ratio lies in the range of 1.094 to 1.275. Hence the flow properties of all formulations were good.

2.5 Drug Excipients Compatibility Study

Table 5: Drug-excipient compatibility study

S.No.	Composition	Description		
		Initial Time	2nd Week	4th Week
1	Rabeprazolesodium	WhitetoOffwhitepowder	NCC	NCC
2	Rabeprazolesodium+Magnesium oxide light	WhitetoOffwhitepowder	NCC	NCC
3	Rabeprazolesodium+Colloidal silicon dioxide	WhitetoOffwhitepowder	NCC	NCC
4	Rabeprazolesodium+ Microcrystalline cellulose	WhitetoOffwhitepowder	NCC	NCC
5	Rabeprazolesodium+Sodium starch glycolate	WhitetoOffwhitepowder	NCC	NCC
6	Rabeprazolesodium+P.V.P.K. 30	WhitetoOffwhitepowder	NCC	NCC
7	Rabeprazolesodium+Croscarmellose sodium	WhitetoOffwhitepowder	NCC	NCC
8	Rabeprazolesodium+Ethyle cellulose	WhitetoOffwhitepowder	NCC	NCC
9	Rabeprazolesodium+Cellulose acetate phthalate	WhitetoOffwhitepowder	NCC	NCC
10	Rabeprazolesodium+ Diethyl phthalate	WhitetoOffwhitepowder	NCC	NCC

NCC* No Characteristics Change

Discussion:

From the drug excipients compatibility study , it was observed that there was no change between drug and excipients.Thus it was concluded that the excipients selected for the formulation were compatible with Rabeprazole sodium.

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6 Drug excipients compatibility study by FT-IR

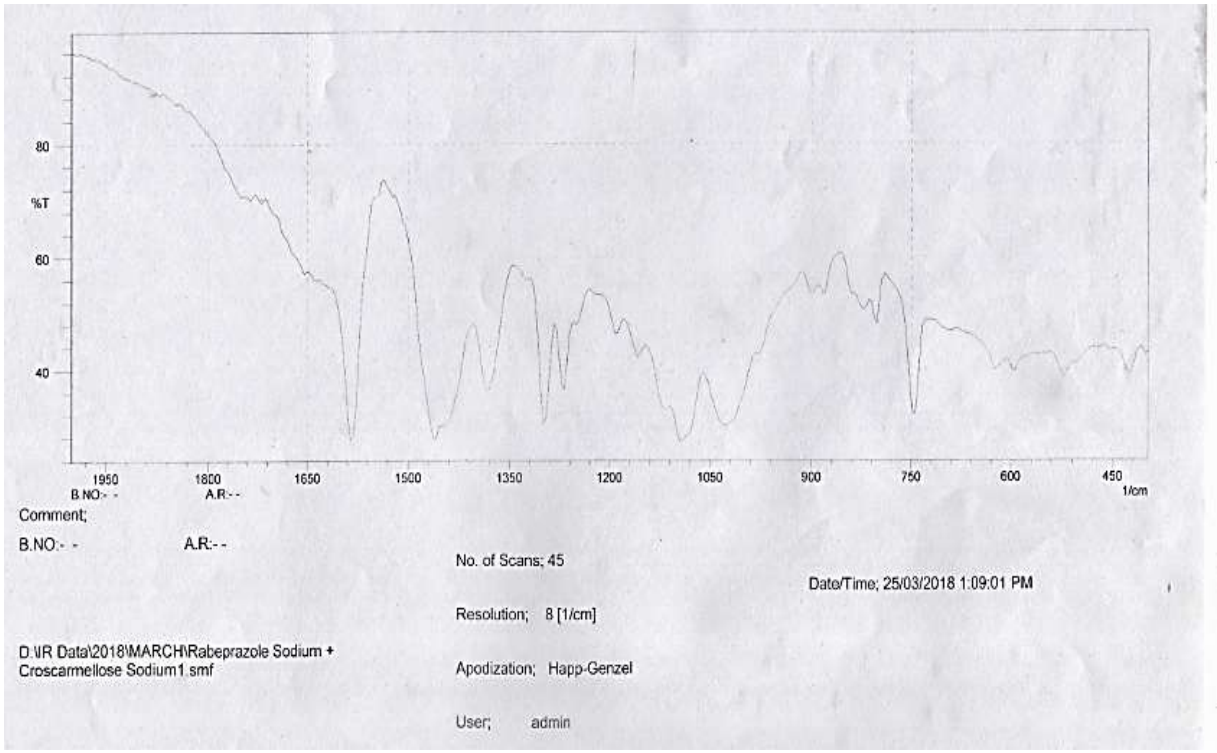

Figure 3: Rabeprazole Sodium + Croscarmellose

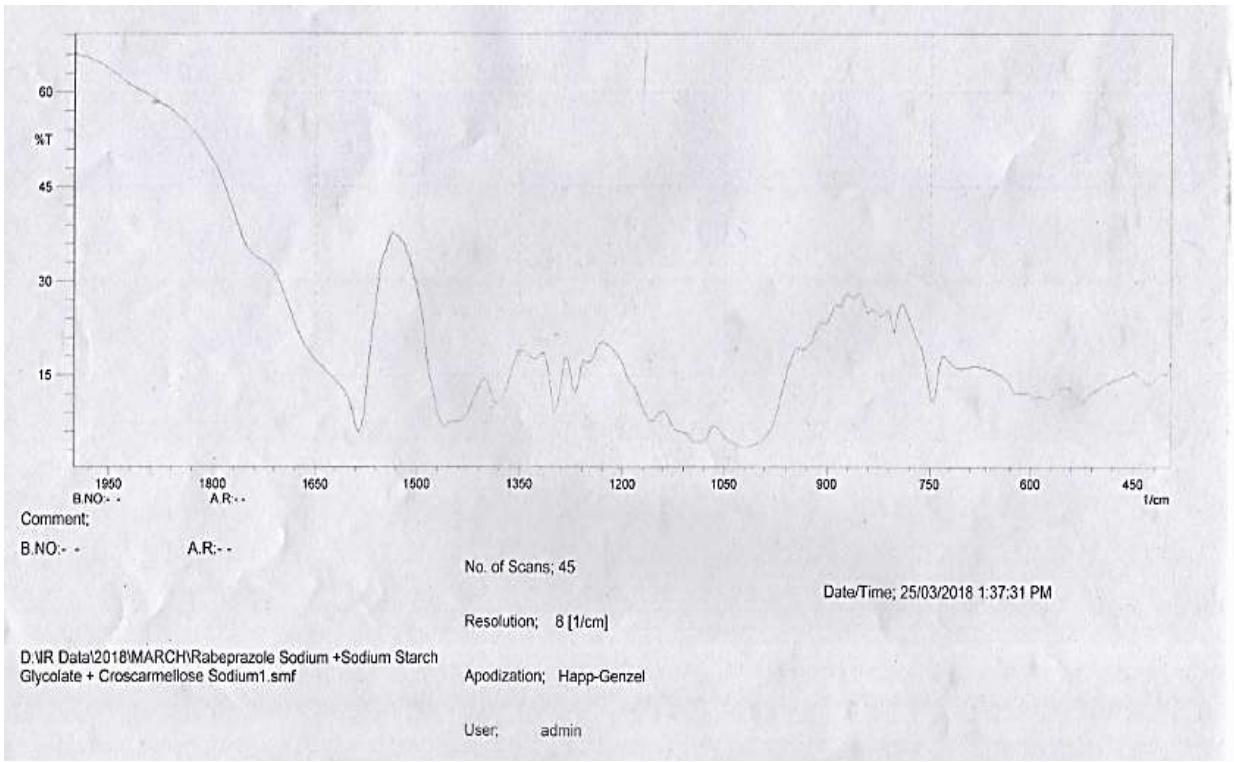

Figure 4: Rabeprazole Sodium + Sodium Starch Glycolate + Croscarmellose

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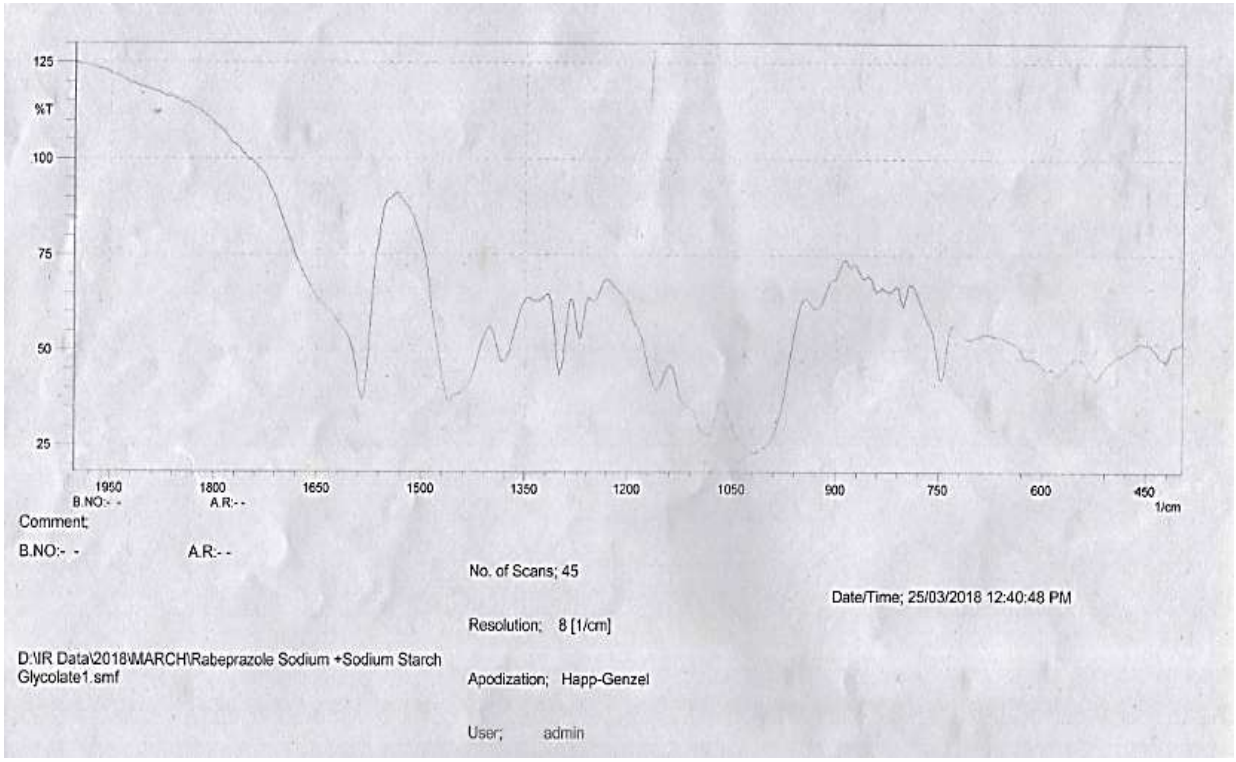

Figure 5: Rabeprazole Sodium + Sodium Starch Glycolate

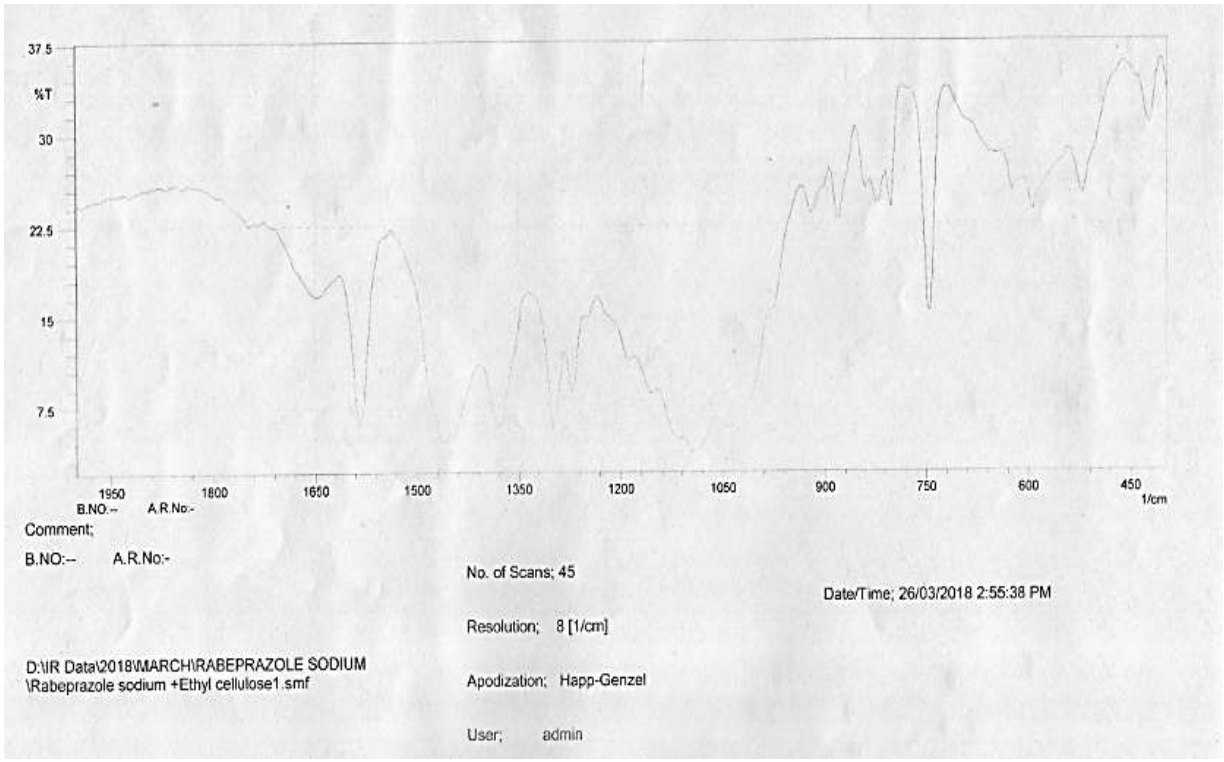

Figure 6: Rabeprazole Sodium + Ethyl Cellulose

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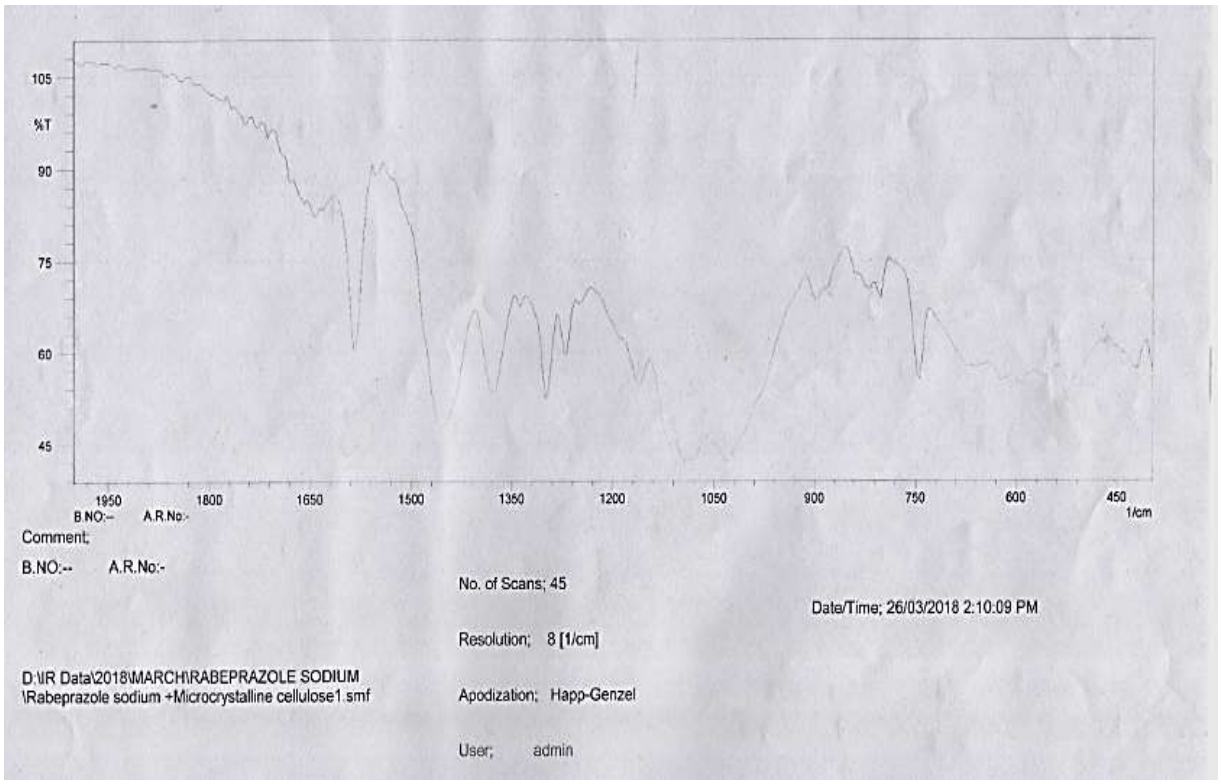

Figure 7: Rabeprazole Sodium + Microcrystalline Cellulose

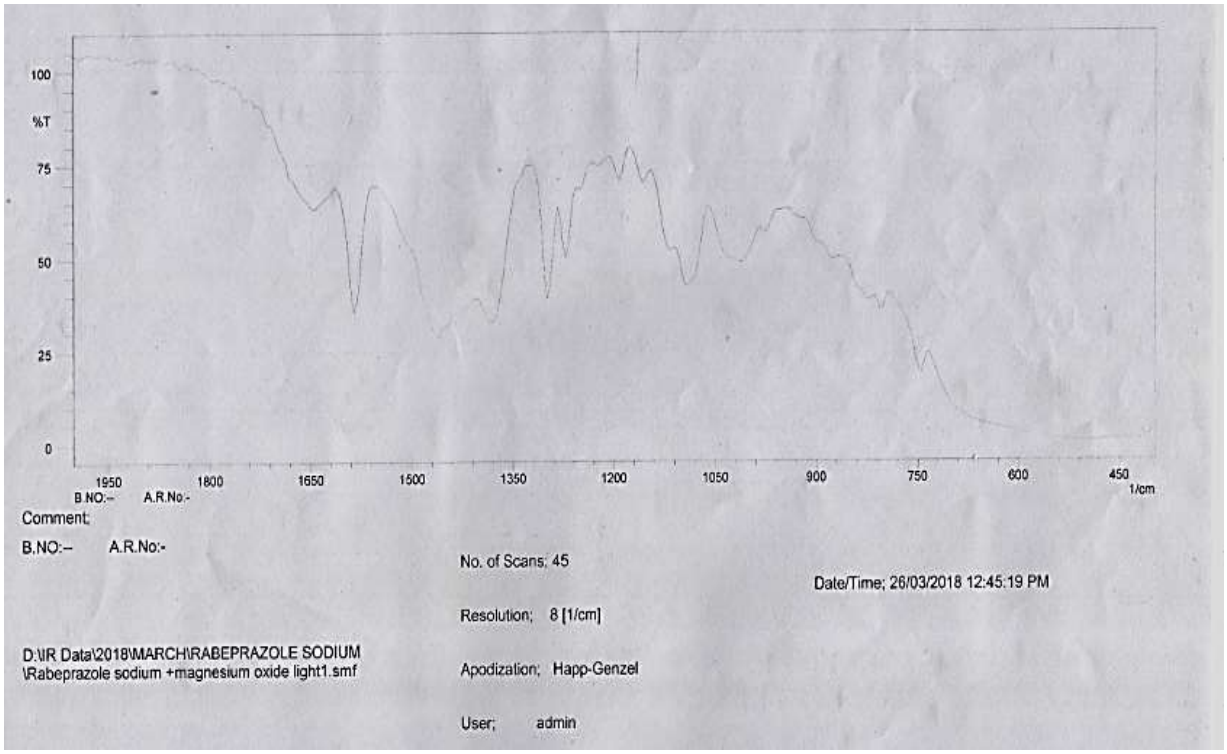

Figure 8: Rabeprazole Sodium + Magnesium Oxide Light

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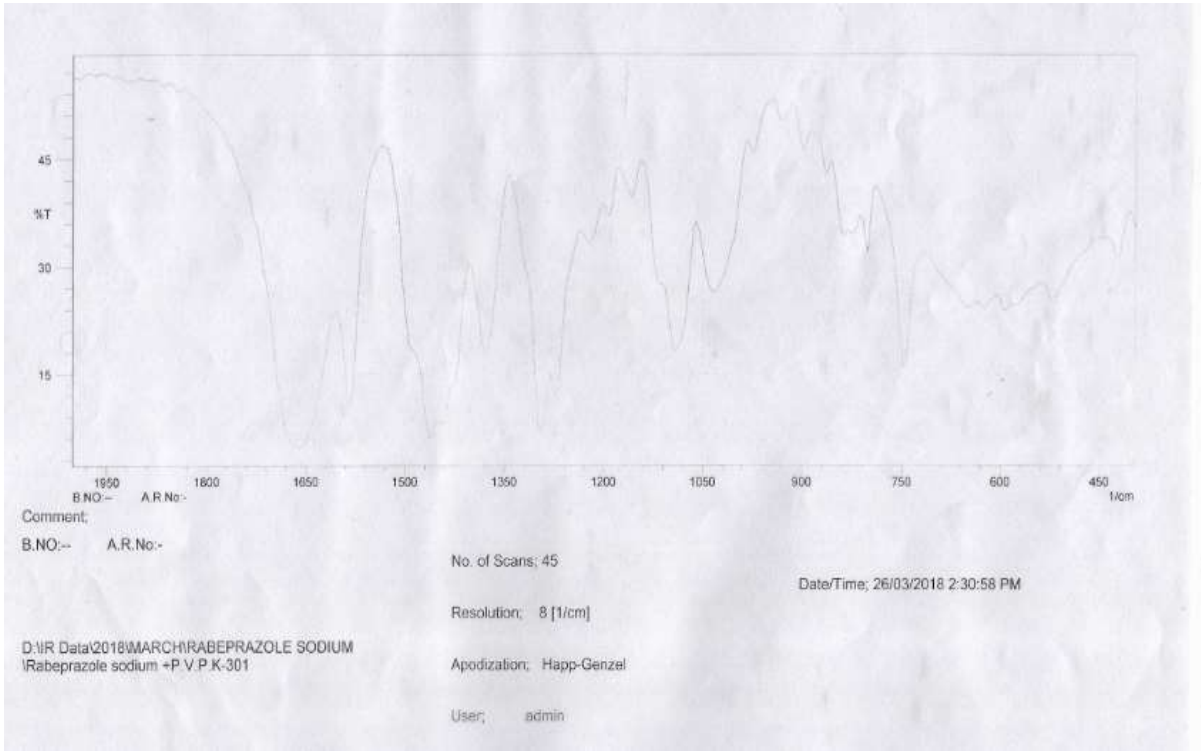

Figure 9: RabeprazoleSodium + Polyvinylpyrrolidone K-30

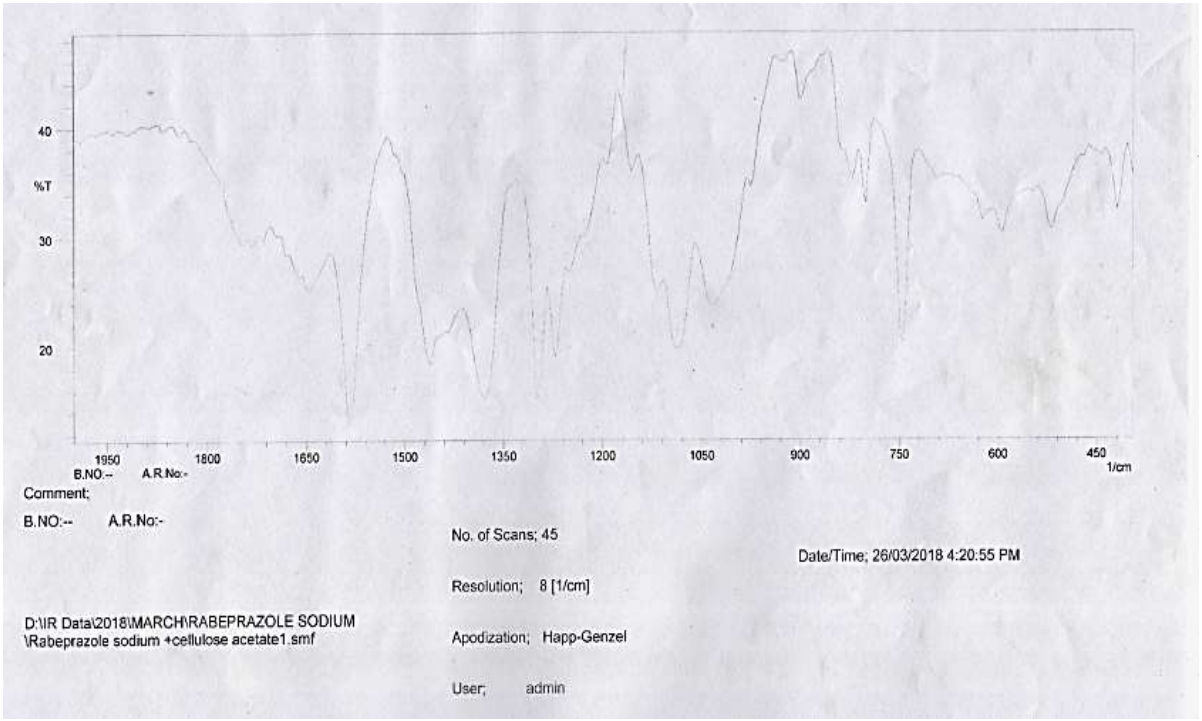

Figure 10: Rabeprazole Sodium + Cellulose Acetate Phthalate

Estimation of Rabeprazole sodium

Calibration Curve: Calibration curve was performed with 0.1N HCl and Phosphate buffer (pH6.8). The results show good (R^2= 0.999) Correlation coefficient with both the solvents.

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Table 6: Calibration Curve of Rabeprazole in 0.1N HCl

S. No.	Conc. (µ/mL)	Absorbance
1	10	0.282
2	15	0.418
3	20	0.559
4	25	0.692

Table 7: Calibration Curve of Rabeprazole in Phosphate Buffer (pH 6.8)

S. No.	Conc. (µ/mL)	Absorbance
1	10	0.305
2	15	0.456
3	20	0.612
4	25	0.760

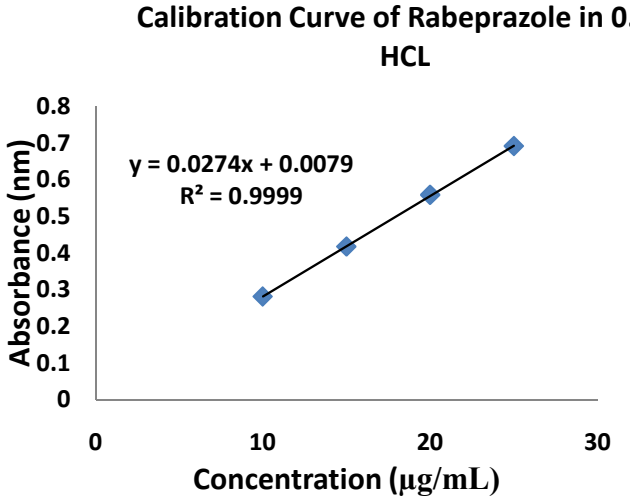

Figure 11: Calibration Curve of Rabeprazole in 0.1N HCl

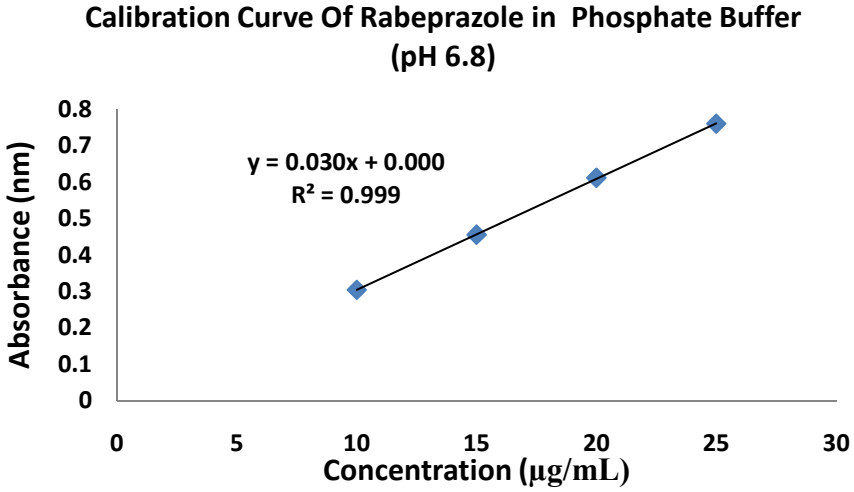

Figure 12:Calibration Curve of Rabeprazole in Phosphate Buffer (pH 6.8)

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3. EVALUATION OF CORE TABLETS

Table 8: Evaluation of Rabeprazole sodium Uncoated Tablet

Formulation	Average Weight (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Disintegration Time (min)	Drug Content (%)
F-I	171	7.5	2.90	0.95	12	97.82
F-II	169	6.5	2.80	0.73	16	97.66
F-III	171	8.0	2.88	0.69	13	92.00
F-IV	170	6.5	2.95	0.48	10	95.48
F-V	170	5.0	2.80	0.35	7	98.80
F-VI	171	6.0	2.89	0.40	9	98.78

Discussion:

GeneralAppearance

Theformulatedtabletswereevaluatedfortheirorganolepticcharacters.Thetablets arecircular, biconvexinshapeandoff whiteincolour. Allthetablets showedeleganceinappearance.

Average Weight

Twenty tablets of each formulation were selected for weight variation test. The accepted percentage deviation was±7.5 for 130-324mg weight tablets. The results showed that weight variation was ranging from 169 to 171 mg. It was within the I.P. limit and all the tablets passed the weight variation test.

Hardness

The hardness of the tablets was measured by Monsanto hardness tester. The hardness of all the formulations was found to be in the range of 5 to 8 kg/cm^2. It indicates all the tablets have adequate mechanical strength.

Thickness

Thickness of the tablets was found to be in the range of 2.80mm to 2.95mm. The results showed that the thickness of all formulated tablets was found to be uniform.

Friability Test

Friability test was carried out by Roche friabilator. The maximum weight loss should be not more than 1 %. The maximum and minimum friability values among 6 formulations were found to be in the range of 0.35 to 0.95 % respectively. Hence all the tablets passed the friability test.

Disintegration Test

The disintegration test was carried out according to IP procedure on six tablets using disintegration test apparatus with discs in water maintained at 37 °C ± 2 °C. Disintegration of tablet was found to be in the range of 7 to 16 min.

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Conclusion: Formulation and Evaluation of enteric coated tablets of Rabeprazole sodium for the effective treatment of duodenal ulcer was successfully carried out by performing the preformulation studies, formulation of Rabeprazole sodium enteric coated tablets, evaluation parameters, *invitro* drug release studies and stability studies.

The preformulation studies and drug excipients compatibility studies were carried out with aid of IR spectroscopic analysis of drug with excipients which showed that the drug was compatible with excipients which were further used in the formulation.

The prepared powder blend was evaluated fo rpre compression parameters like angle of repose,bulk density, tapped density, compressibility index and Hausner ratio. The obtained results indicated that it has good flow property.

Rabeprazole Sodium enteric coated tablets were prepared by wet granulation method. The prepared tablets were evaluated for hardness, thickness, weight variation, friability, assay and disintegration time. All these parameters were found to be within the pharmacopoeial limits in F-V formulation.

Rabeprazole Sodium enteric coated tablets were coated with Cellulose acetate phthalate and Diethyl phthalate in different concentrations.

Selection of the best formulation based on disintegration time. Croscarmellose and Sodium starch glycolate were used in the formulation as a super disintegrant. The disintegration time of best formulation (FV) was found 14 minute (buffer medium), while the disintegration time of Market sample was found 19 minute in buffer medium.

Invitro dissolution study was carried out for F-V formulation showing better drug release than the marketed product.The drug release was found tobe 99.12% at 60 minute The accelerated stability studies of F-V formulation at 40 ºC/75 % RH for a time period of 3 months indicated that there was no significant change in description, disintegration time, drug content and in vitro dissolution profiles. The result shows that the F-V formulation was stable for 3 months.

From all the above observations the study concluded that the enteric coated tablets of Rabeprazole sodium (F-V) formulation was better one compared to the other formulations.

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