CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com *Research Article*

FORMULATION, OPTIMIZATION AND EVALUATION OF IN-SITU RAFT-FORMING SUSPENSION OF RABEPRAZOLE SODIUM USING GUAR GUM.

Jayesh M. Rajput
Department of Pharmaceutics, JIIU's Ali-Allana College of Pharmacy and Research center, Akkalkuwa, Dist- Nandurbar, Maharashtra-425415, India.

Article Received: October 2022 **Accepted:** October 2022 **Published: October** 2022

Abstract:
Rabeprazole Sodium belongs to a class of Anti-Secretory compounds (substituted benzimidazole proton-pump inhibitors) that do not exhibit anticholinergic or histamine H2-receptor antagonist properties, used to prevent production of acid in the stomach, it reduces symptoms and prevents injury to the oesophagus or stomach in patients with gastroesophageal reflux disease (GERD). It has a daily dose of 10 mg minimum and 20 mg maximum. In this formulation Rabeprazole Sodium is used as an active pharmaceutical ingredient (API), and excipients such as Sodium Alginate, Guar Gum, Sodium Bicarbonate, Calcium Carbonate, Methyl Paraben, Propyl Paraben are used. In this study FTIR was done for evaluation of pure drug and to evaluate between the API and excipients, all the results were within its standard ranges. Many tests such as In-Vitro gelation time/Floating lag time, Floating time, Raft weight, Raft volume, Content uniformity, Viscosity of suspension and raft, Micromeritic study and In-Vitro drug release study was conducted and all the obtained results were within the standard ranges. Formulation SA3 and GG5 due to their linear drug release they were selected for Stability Study. 2 Months Stability Study were conducted and on each 1-Month interval readings were taken, no major difference in formulation and readings were observed after 3rd month study But, Further Long-Term stability study and In-Vivo study was recommended.

Keywords: *Rabeprazole Sodium, Oesophagitis, Gerd, Gastroesophageal Reflux Disorder, Raft-Forming Suspension.*

Corresponding author:
Jayesh M. Rajput,
Postal address- 29/B,
Matoshree residency, Dahindule street,
Patonda. Dist- Nandurbar, 425412, Maharashtra, India.
Mail: rajputjayesh533@Gmail.com
Mob: (+91) 8010358128

QR code

Please cite this article in Jayesh M. Rajput, ***Formulation, Optimization And Evaluation Of In-Situ Raft-Forming Suspension Of Rabeprazole Sodium Using Guar Gum****., Indo Am. J. P. Sci, 2022; 09(10).*

INTRODUCTION:

According to a study done by the Department of Gastroenterology, Coimbatore medical college and hospital published in 2004, cancer of the oesophagus is common in India. The risk of oesophageal cancer is 3.5 times higher with alcohol consumption, 2.5 times higher for tobacco users and 2.8 times higher each for betel nut chewers and smokers. [19] In another study conducted by AIIMS, published in 1999, it was concluded that this devastating disease is associated with significant morbidity rate and mortality rate. The tumour has a relative resistance to chemotherapy and radiotherapy so, surgery remains the best form of treatment for both palliation and cure. Therefore, it is most important to detect the problem as early as possible. It has now become apparent, through studies and research in the United States and India, that people who suffers from acid reflux are likely to predisposed to carcinoma of the oesophagus are advised to undergo endoscopy on a regular basis to detect the problem in time. [11,12,13,14] Thus, it is necessary to detect this problem earlier and treat it by using a suitable treatment. Although, 90% of the patient with this disorder get treated and cured medicines itself, while in severe cases other mode of treatment are applied such as surgery or endoscopy. Mode of medication involves the use of medicines and formation of mechanical barrier. So, that the reflux rate can't be refluxed back in oesophagus. The formation of mechanical barrier is the most common amongst medication mode of treatment and comes under the category of over-the-counter drugs. Such formulations are known as Anti-reflux formulations.

[7,8,9,10] Gastroesophageal reflux disorder or (GERD) is one of the gastric disorders occurs due to the exposure of refluxate of stomach on the wall of oesophagus. The content of the stomach is known as "Chymes". The Chymes get mixed thoroughly with gastric acid secretion of stomach and becomes mixture of low pH below 3. The pH of the cell lining of oesophagus is above 6 and almost near to neutral range. Thus, on exposure to Chymes of stomach to oesophagus there is a sudden change in pH environment of the cell lining which causes burning sensation. Thus, this disorder is also known as "Heart Burn" or "Oesophagitis". It is characterized by burning sensation behind the sternum bone and hoarse or raspy sound. This disorder also leads dangerous to asthmatic patients. [1,2,3,4,5,6] The Aim of formulation or dosage form development is to deliver drug at specific body site in desired concentration in therapeutic range. To achieve such objectives, extensive research had been carried out by various scientists. Now, from past few decades the controlled or sustained release formulations have been developed. This formulation is intended for maximum therapeutic efficacy and reduction in side effects of drug. Also, these formulations have an advantage of more patient compliance due to reduced dosing frequency and dose dumping. Also, drug loss is prevented conventional drug delivery such as Tablets, Capsules, etc. is old and comes along with so many limitations. Conventional dosage forms provide drug in specific concentration in blood circulation without any control over drug delivery. This uncontrolled manner of drug delivery by conventional formulations causes fluctuation in blood plasma concentration. [15,16,17,18] This problem induces the need of controlled release and sustained release of drug delivery. Therefore, the drug release from the formulation is largely independent of external factors. The absorption of drug from oral delivery gets varied from person to person. The major issue due to which these variations occur are gastric retention or gastric transit time of drug, which is due to the physiological variations. Also, the main issue of the oral drug delivery is that the drug must be delivered in the absorption window, after passing the absorption window, the drug may not be utilized and this may cause either drug wastage or toxicity. This problem is due to GRT of the dosage form is less than 12 Hrs. This makes researchers to overcome such a problem and increase the retention time of drug in GIT for prompt and predictable time. Dosage forms which retained in the stomach is known as "Gastro Retentive drug delivery system" or "GRDDS" over the past few years devices and system designed to retain the dosage form in the dosage form in the upper part of GIT such floating system, expanding system, bio-adhesive system, low density system, high density system and raft forming system. Attempts are being made to develop a drug delivery system which can provide therapeutically effective plasma concentration for longer period of time. Thereby this reduces the dosing frequency and minimizing fluctuations of drug concentration in plasma to maintain it in steady state by delivering drug in controlled and reproducible manner. GRDDS can improve control delivery of the drugs that have an absorption window by continuous releasing the drug for prolong period of time before it reaches the absorption site. Prolonged retention of dosage form is sometimes desirable for achieving therapeutic benefit of drug that absorbed from specific part of GIT and also useful for targeting in desired site in GIT. Also, GRDDS formulation are used to improve the drug performance which are pH sensitive and their activity or inactivity depends upon pH of the GIT where drug is administered. The drugs that are easily absorbed from GIT and have short half-life are eliminated quickly from systemic circulation or body.

To avoid such a limitation the controlled release formulation is an attempt to release drug that required to maintain effective drug concentration in plasma. After oral administration of such a formulation, it retains in stomach for more than a normal time and release drug in controlled manner. So, that drug could be available in desired concentration at absorption site. Prolonged gastric retention improves bioavailability and duration of drug release that minimizes the drug dose. The increased GRT in stomach required for local treatment on stomach and upper part of intestine.

[18,19] The drug Rabeprazole Sodium is used as an API in the formulation. Rabeprazole Sodium belongs to a class of Anti-Secretory compounds (Substituted Benzimidazole Proton-Pump inhibitors) that do not exhibit anticholinergic or histamine H2-receptor antagonist properties, but suppress gastric acid secretion by inhibition the gastric H^+/K^+ ATPase (Hydrogen-potassium adenosine triphosphatase) at the secretory surface of the gastric parietal cell. Because this enzyme is regarded as the acid (Proton) pump within the parietal cell, Rabeprazole Sodium has been characterized as a gastric proton-pump inhibitor. Rabeprazole Sodim blocks the final step of gastric acid secretion. In gastric parietal cells, Rabeprazole sodium is protonated, accumulates and is transformed to an active Sulfenamide. When studied in-vitro, Rabeprazole Sodium is chemically activated at pH 1.2 with a half-life of 78 Seconds. It has an oral bioavailability of 52%, T_{Max} of 2 to 5 Hrs. there is no appreciable accumulation when doses of 10 mg to 40 mg are administered every 24 Hours. Following a single 20 mg oral dose of ^{14} C- labelled Rabeprazole, approximately 90% of the drug was eliminated in the urine, primarily as thioether carboxylic acid, its glucuronide, and mercapturic acid metabolites. Rabeprazole Sodium prevents the production of acid in the stomach. It reduces symptoms and prevents injury to the oesophagus or stomach in patients with Gastroesophageal reflux disease (GERD) or ulcers. Rabeprazole Sodium is also useful in conditions that produce too much stomach acid such as Zollinger-Ellison syndrome. Rabeprazole Sodium may also be used with antibiotics to get rid of bacteria that are associated with some ulcers. Rabeprazole Sodium is a selective and irreversible proton pump inhibitor, suppresses gastric acid secretion by specific inhibition of the H^+, K^+ ATPase, which is found at the secretory surface of parietal cells. In doing so, it inhibits the final transport of hydrogen ions (via exchange with potassium ions) into the gastric lumen. It has a daily dose of 10 mg minimum and 20 mg maximum. Conventional dosage forms have many disadvantages so, In-Situ raft forming suspension of Rabeprazole Sodium with Guar Gum was formulated. Rabeprazole Sodium was used as an API, and other excipients such as Sodium alginate, Guar gum, Calcium carbonate, Sodium bicarbonate, Methyl paraben and Propyl paraben were used in the formulations.

MATERIALS AND METHODS:

Rabeprazole Sodium was the gift sample of pure API from "Micro. Labs, Bengaluru", Guar Gum, Calcium Carbonate, Sodium Bicarbonate, Methyl Paraben, Propyl Paraben were purchased from "Research Fine-Chem, Mumbai", rest of the lab chemicals were provided by college of pharmacy, Dept. of Pharmaceutics, Akkalkuwa, and all the chemicals used during the study were of Analytical grade.

- **FTIR Analysis:** - The gift sample of Rabeprazole Sodium received from Micro labs, Bengaluru was subjected for its standardization and so, FTIR analysis were performed for that 1 mg of API was accurately weighed on a digital weighing balance and triturated with approximately 300 mg of dry, finely powdered KBr (IR). A transparent thin pellet was prepared by using compression mould. The KBr pellet was placed in a sample holder of the IR spectrophotometer and scanned through the frequency 4000^{-1} wave number to 400^{-1} wave number and the IR spectrum so obtained was observed.
- **Solubility Study:** - Solubility of Rabeprazole Sodium was determined by adding an excess amount of drug in 5ml of water to obtain a saturation and stirred for 24 Hrs. by using magnetic stirrer. After stirring the resultant solution was filtered and kept a side for 1 Hr. then, supernatant obtained was diluted properly and absorbance was taken by UV Spectrophotometer at 272 nm. The unknown concentration of the sample was determined by using equation obtained from standard calibration curve.
- **Melting Point:** - Capillary Tube method was used to detect the melting point of sample. The method was performed twice and average value (range) was noted.
- **Loss on Drying:** - 1 gm of drug sample was weighed accurately and placed in a dried porcelain dish. The dish weight with drug and placed in a hot air oven and measured the weight after 10 Min interval until the constant weight was obtained and the percentage LOD were calculated by using the following equation. LOD = Initial Wt. – Final Wt./ Initial Wt.× 100
- **X-Ray Diffraction study:** - XRD was used to determine the polymorphism of the compound. It

was used to determine whether the compound is crystalline or amorphous in nature.

- **Preparation of Suspension:** -Raft forming suspension of Rabeprazole Sodium was prepared by using a magnetic stirrer and final volume was made by using citro-phosphate buffer 7.0 initially, 525 mg of Citric acid was taken in 25 ml of volumetric flask and dissolved in sufficient quantity with distilled water and filled upto mark with distilled water to produce 2.1% W/V solution and named as "A" in another 100 ml volumetric flask 7.15 gm of Disodium Hydrogen phosphate was taken and dissolved in distilled water and filled with it up to the mark to produce 7.15% solution and named as "B". then to produce CPB 7.0, 17.6 ml of A and 87 ml B are taken in 1000 ml volumetric flask and mix properly and diluted upto mark with distilled water. To make suspension according to batch design accurately weighed quantity of Sodium Alginate, Guar Gum was taken and added very slowly to 50 ml of CPB 7.0 with continuous stirring by using magnetic stirrer rotated at 600 rpm for 1 Hr. then with continuous stirring accurately weighed quantity of Sodium Bicarbonate, Methyl Paraben and Propyl Paraben was added and again mixed for 15 Minutes. Finally, accurately weighted quantity of Calcium Carbonate was added and volume was made upto 100 ml by using CPB 7.0 composition of batch was given in the table below. All the quantities were taken in milligram (mg).

Table 1: -Formulation Batch Scheme

Ingredients [Batches]	RPS (API)	Sodium Alginate	Guar Gum	Sodium Bicarbonate	Calcium Carbonate	Methyl Paraben	Propyl Paraben	
SA 1	200	600	-	400	800	180	20	CPB 7.0 Upto 100 ml
SA 2	200	800	-	400	800	180	20	
SA 3	200	1000	-	400	800	180	20	
SA 4	200	1200	-	400	800	180	20	
SA 5	200	1400	-	400	800	180	20	
GG 1	200	-	600	400	800	180	20	
GG 2	200	-	800	400	800	180	20	
GG 3	200	-	1000	400	800	180	20	
GG 4	200	-	1200	400	800	180	20	
GG 5	200	-	1400	400	800	180	20	

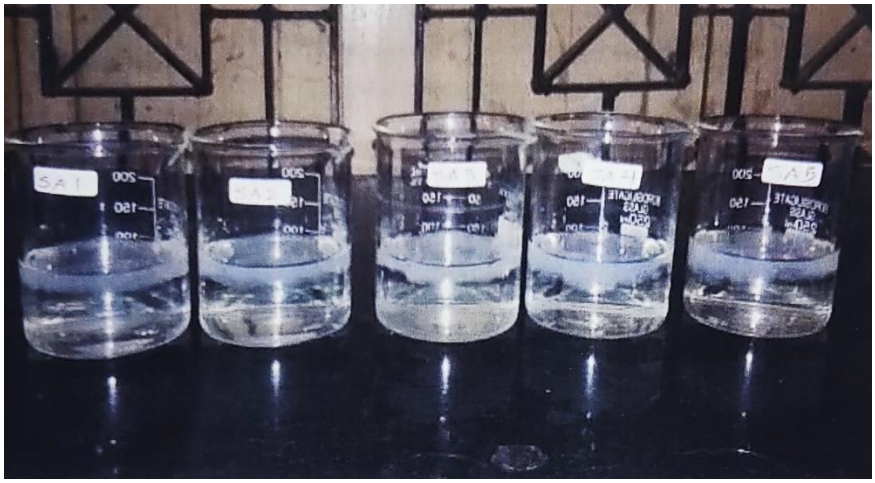

Fig 1: - Raft formed by Sodium Alginate batches

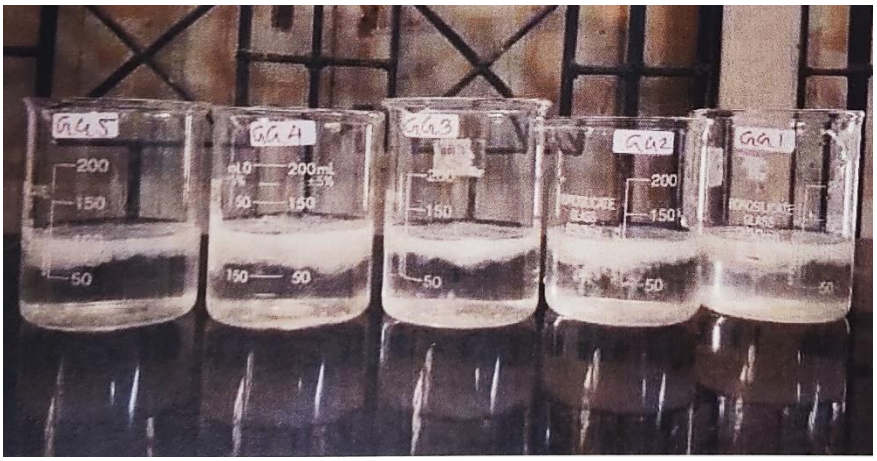

Fig 2: - Raft formed by Guar Gum batches

- **Analytical Study: -** The Calibration curve of Rabeprazole Sodium was taken at 272 nm in 0.1 N HCL against blank containing 0.1 N HCL. For Calibration Curve the concentration was kept in 0.2 µg/ml, 0.4 µg/ml, 0.6 µg/ml, 0.8 µg/ml and 1 µg/ml. All the volumes were made in triplicates to minimize the error and validate the process.
- **Evaluation Parameters: -**

I. Physical Appearance: - The Physical appearance of the formulation was the Colour, Odour and Appearance of the suspension.

Fig 3: - Physical Appearance of Suspension

II. **In-Vitro Gelation time/ Floating lag time: -** 10 ml of suspension was added to 250 ml beaker containing 100 ml of 0.1 N HCL and time required to clear lower portion of beaker was used to describe gelation time.

III. **Floating time: -** 250 ml of beaker was used in which 100 ml of 0.1 N HCL was added. 10 ml of raft forming suspension was added to it and time to which raft remain on the liquid was noted.

IV. **Raft weight: -** 250 ml beaker was used containing 100 ml of 0.1 N HCL. To this, 10 ml of suspension was added, raft was allowed to develop completely. For complete raft development, the beaker was remained for 30 min without disturbing. After raft development, the remaining liquid was decanted carefully then place the raft on a butter paper and the liquid was soaked by using towel paper. Then dry raft was weighed directly.

V. **Raft volume: -** Initially beaker used for raft development was washed and dry completely and weighed and noted as W1. Then to such a dry beaker, 100 ml of 0.1 N HCL was added carefully that it does not expel out, then again beaker with raft developing liquid was weighed and noted down as W2. At this point the level to which raft developing liquid was added was marked. To this beaker 10 ml of raft developing suspension was added and remains for 30 mins undistributed for complete raft development. Then, remaining liquid was decanted and raft was dried by using towel paper. The dry raft was weighed and noted down as W3. This dried raft was added to a beaker used for raft development and filled with a purified water upto the mark made while 100 ml of raft developing liquid was added. After filling with water, beaker was again weighed and down as W4. After noting all four weights, the raft volume was calculated by using following formula

Raft Volume = [W4-W1] – [W2-W1-W3]

VI. **Content Uniformity: -** 10 ml of suspension which believed to be contained 20 mg of Rabeprazole Sodium in 100 ml volumetric flask and dilute upto the mark with 0.1 N HCL. Then from this solution 0.1 ml was pipette out in 10 ml volumetric flask and diluted upto the mark with 0.1 N HCL. Then absorbance was taken at 272 nm against the blank containing 0.1 N HCL.

VII. **Viscosity of Suspension: -** The viscosity of the suspension was determined by using Brookfield Viscometer. For determination of viscosity, spindle of various number is used and rotated at different speed in ascending order. Then, torque experienced by the spindle was used as a function to determine the viscosity.

VIII. **Viscosity of Raft: -** The viscosity of raft was determined by using Brookfield Viscometer. For determination of viscosity of raft spindle of various number was used and rotated at different speed in ascending order. Then, torque experienced by the spindle was used as a function to determine the viscosity. For determination of viscosity of raft, 10 ml of suspension was mixed and diluted upto 100 ml with 0.1 N HCL and mixed well and viscosity was determined.

IX. **Micromeritic Study: -** The appearance of the suspension at micron level was observed and its particle size was determined.

X. **In-Vitro drug release studies: -** The In-Vitro dissolution study was determined by using USP dissolution testing apparatus. The paddle shaft was used which was rotated at 50 rpm and system was maintained at 37^0 C. for this study 500 ml of 0.1 N HCL was added to the beaker. The paddle shaft was moved down and 10 ml of raft forming suspension was added to beaker and raft was allowed to develop for 5 mins. Then shaft was started to rotate at 50 rpm and 1 ml of sample was withdrawn in 10 ml volumetric flask at interval of 1 Hr. To maintain sink condition 1 ml of 0.1 N HCL was added after sampling. The volume was made upto mark with 0.1 N HCL. Then absorbance was taken at 272 nm by UV visible spectrophotometer to determine the concentration. By, applying dilution factor concentration in mg/ml was obtained.

XI. **Stability Studies: -** The Stability Study of suspension was performed at room temperature. Initially the suspension was observed daily for a week, then observations noted down for at an interval of 1 month for 2 months' time period.

RESULTS AND DISCUSSION:

A. **Description: -** Rabeprazole Sodium was Pale Yellowish powder. It has characteristic irritating odour. The powder was crystalline in nature which was very sensitive to the moisture and lights.

B. **Solubility: -** Solubility of Rabeprazole Sodium was found to be 99.97 mg/ml in distilled water.

C. **Melting Point: -** Melting Point was detected by Capillary Tube method and was found within range of 139.8^0 C to 141.6^0 C and were within its standard range.

D. **Loss on Drying (LOD): -** LOD of Rabeprazole Sodium was found to be 5.85%

Table 2: - LOD of Rabeprazole Sodium

Weight of Empty Crucible	Initial Weight	Final Weight	Difference	% Loss
24.86 gm	26.860 gm	26.743 gm	1.883 gm	5.85 %

E. **Standard Calibration Curve of Rabeprazole Sodium: -** The standard calibration curve is prepared in 0.1 N HCL. The concentration and their respective absorbance are given in the table below.

Table 3: - Standard calibration curve of Rabeprazole Sodium in 0.1 N HCL

Concentration in µg/ml	Absorbance at 272 nm			Average
	A	B	C	
0.2	0.052	0.046	0.046	0.048
0.4	0.078	0.083	0.093	0.085
0.6	0.127	0.121	0.131	0.126
0.8	0.187	0.155	0.155	0.166
1.0	0.198	0.184	0.233	0.205

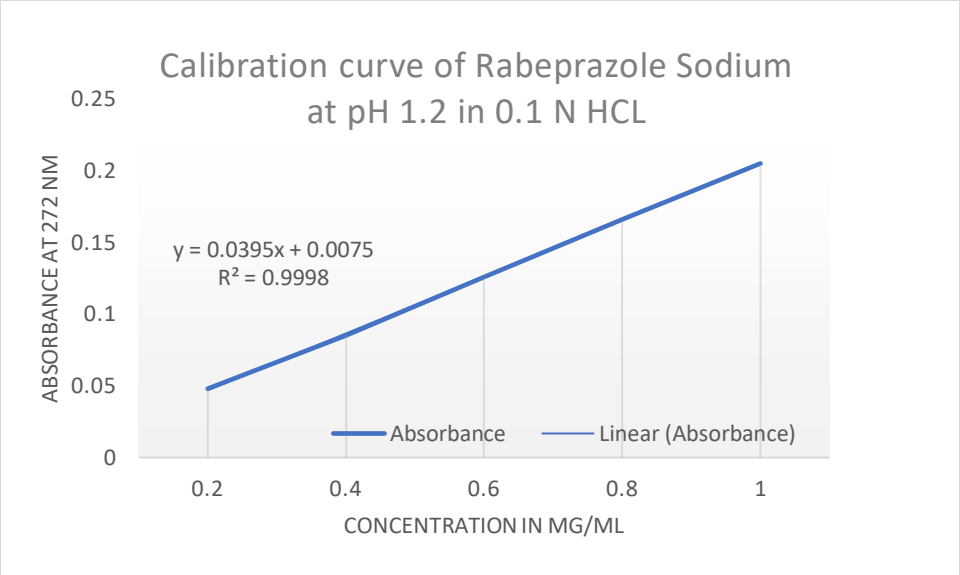

Fig 4: - Standard Calibration Curve of Rabeprazole Sodium in 0.1 N HCl (pH 1.2)

F. Evaluation of Suspension: -

- **Physical Appearance: -** Sodium alginate formed light yellowish brown while Guar Gu formed cream coloured suspension. Suspension formed by Guar Gum was more viscous than suspension formed by sodium alginate. Both have characteristic colour of the substance used as raft forming agent.

Table 4: - In-Vitro Gelation time

Batch	Floating Lag Time (In sec)	Batch	Floating Lag Time (In sec)
SA 1	29	GG 1	181
SA 2	22	GG 2	42
SA 3	18	GG 3	24
SA 4	24	GG 4	9
SA 5	19	GG 5	8

Table 5: -Floating Time

Batch	Floating Time	Batch	Floating Time
SA 1	More than 24	GG 1	More than 24
SA 2	More than 24	GG 2	More than 24
SA 3	More than 24	GG 3	More than 24
SA 4	More than 24	GG 4	More than 24
SA 5	More than 24	GG 5	More than 24

Table 6: - Raft Weight

Batch	Raft Weight (In Gram)	Batch	Raft Weight (In Gram)
SA 1	1.3	GG 1	1.27
SA 2	1.86	GG 2	1.65
SA 3	2.26	GG 3	2.19
SA 4	2.78	GG 4	2.6
SA 5	3.35	GG 5	3.12

Table 7: - Raft Volume

Batch	Raft Volume (In ml)	Batch	Raft Volume (In ml)
SA 1	2.26	GG 1	2.15
SA 2	2.68	GG 2	2.49
SA 3	3.05	GG 3	2.89
SA 4	3.47	GG 4	3.21
SA 5	3.99	GG 5	3.68

Table 8: - Acid Neutralizing Capacity

Batch	Acid Neutralizing Capacity (ml)	Batch	Acid Neutralizing Capacity (ml)
SA 1	6.55	GG 1	4.53
SA 2	5.84	GG 2	4.77
SA 3	6.67	GG 3	5.72
SA 4	5.13	GG 4	5.01
SA 5	6.08	GG 5	5.96

Table 9: - Content Uniformity

Batch	Content Uniformity	Batch	Content Uniformity
SA 1	97.54	GG 1	98.41
SA 2	99.23	GG 2	99.06
SA 3	100.81	GG 3	100.49
SA 4	98.65	GG 4	98.54
SA 5	101.32	GG 5	99.01

G. FTIR Studies: -

I. FTIR of Rabeprazole Sodium: -

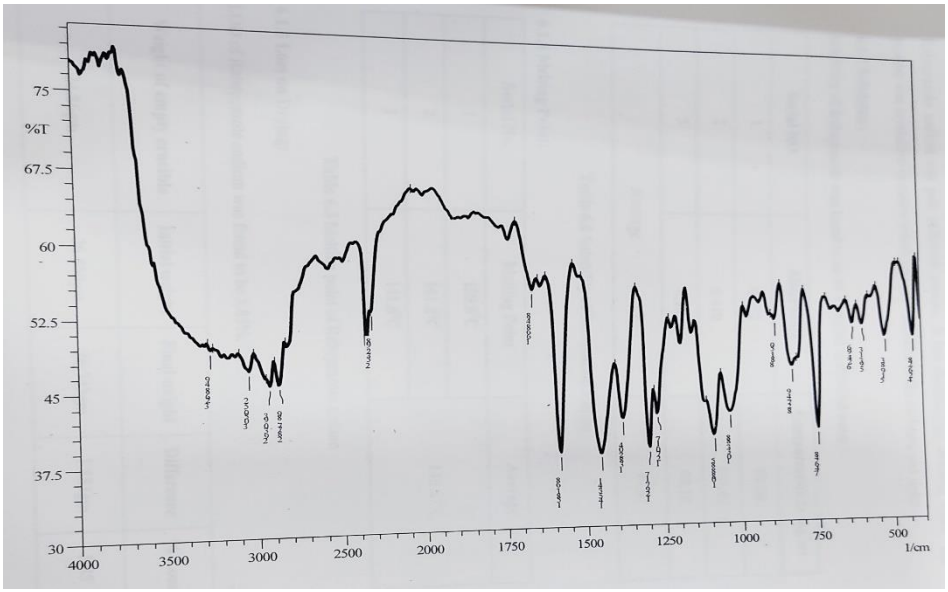

Fig 5: - FTIR of Rabeprazole Sodium

Table 10: - FTIR analysis of Rabeprazole Sodium

Functional Group	Characteristic Peaks cm^{-1}
C-N Stretching	1297.17
C=N Stretching	1581.68
C-H (Aromatic) Stretching	2930.93
C-H (Aliphatic) Stretching	2877.89
$O=CH_3$ Stretching	2332.98

II. FTIR of Sodium Alginate

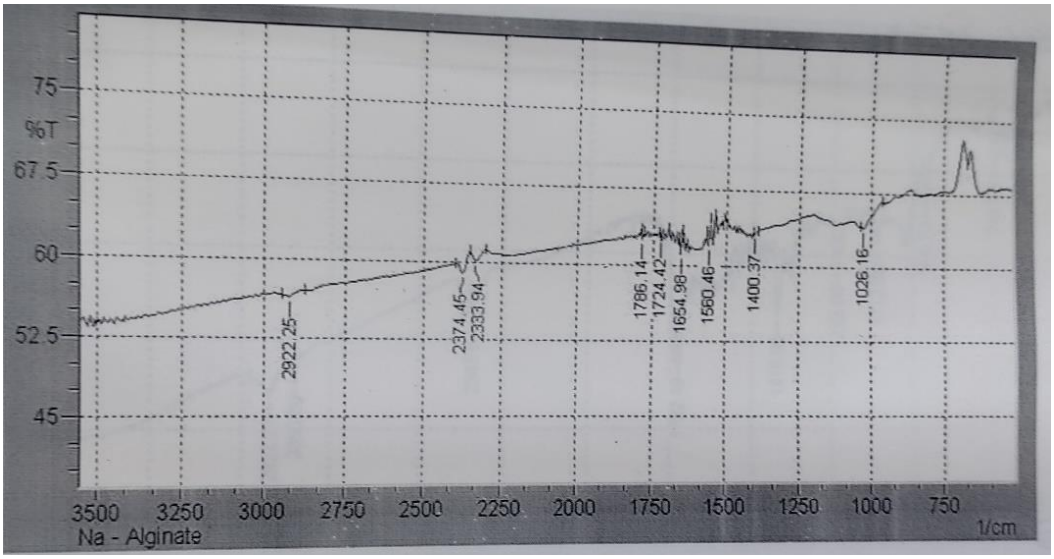

Fig 6: - FTIR of Sodium Alginate

III. FTIR of Guar Gum

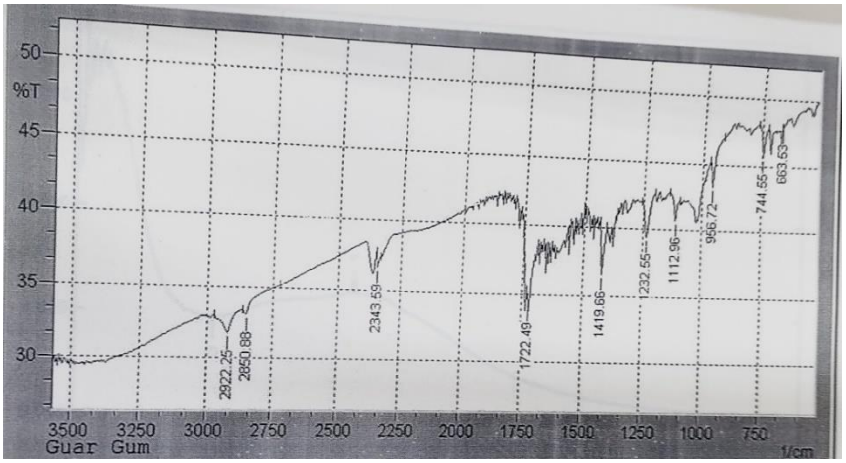

Fig 7: - FTIR of Guar Gum

IV. FTIR of Rabeprazole Sodium with Sodium Alginate

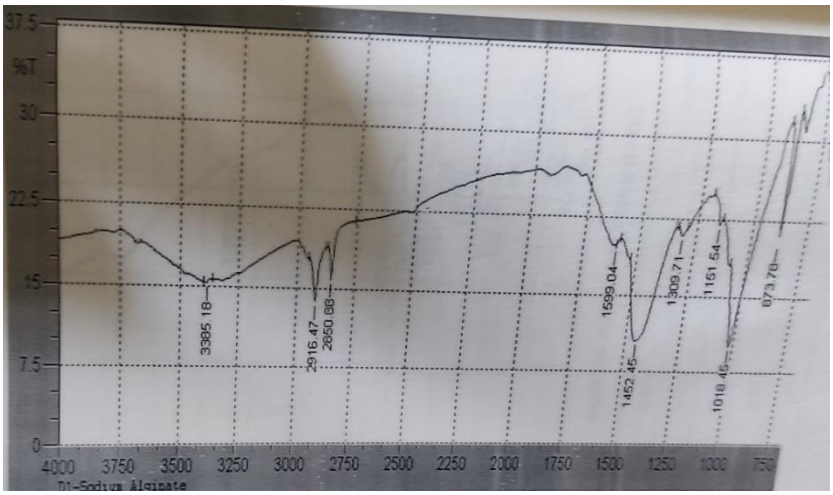

Fig 8: - FTIR of Rabeprazole Sodium + Sodium Alginate

V. FTIR of Rabeprazole Sodium with Guar Gum

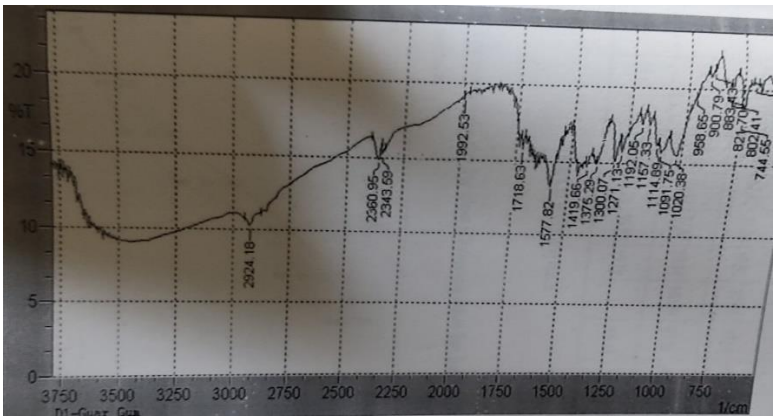

Fig 9: - FTIR of Rabeprazole Sodium + Guar Gum

Table 11: - FTIR analysis of Rabeprazole Sodium + Guar Gum

Functional Group	Characteristic Peaks cm^{-1}
C-N Stretching	1300.07
C=N Stretching	1577.82
O-CH3 Stretching	2360.95
C-H (Aromatic Stretching)	2924.18

H. X-Ray Diffraction Study: -

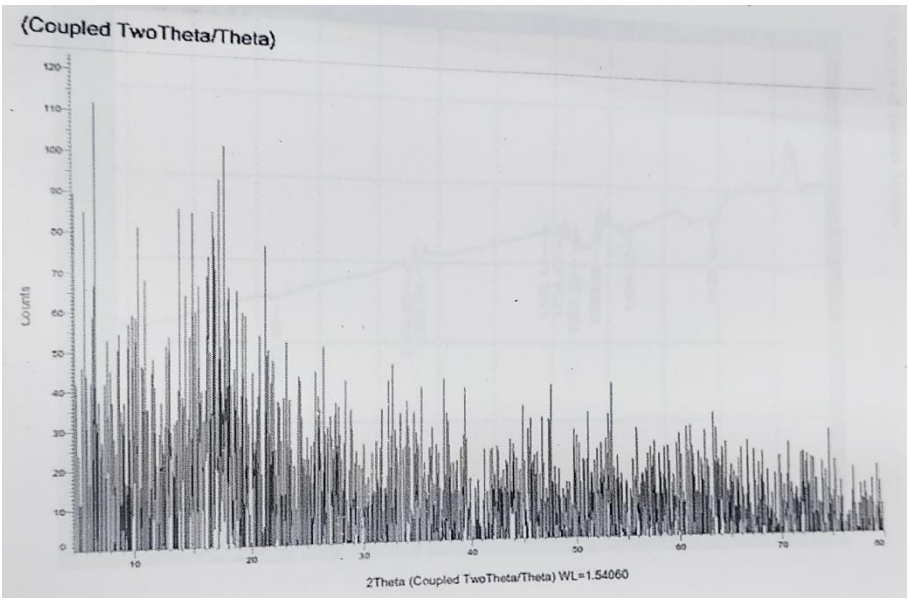

Fig 10: - X-Ray Diffraction of Rabeprazole Sodium

I. Scanning of Rabeprazole Sodium in 0.1 N HCL: -

The Rabeprazole Sodium shows maximum absorbance at wavelength of 272 nm.

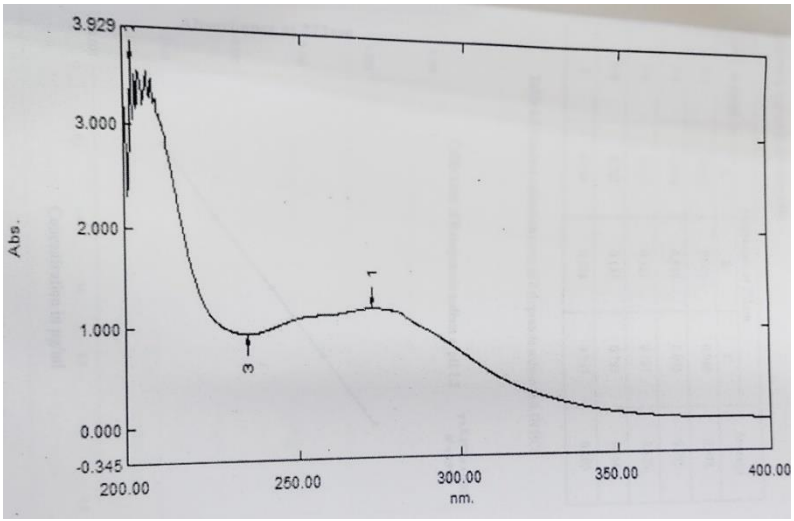

Fig 11: - λ-Max of Rabeprazole Sodium

J. Micromeritic Study: -
[Scanning Electron Microscopy (SEM)]

1) SEM of Sodium Alginate Suspension

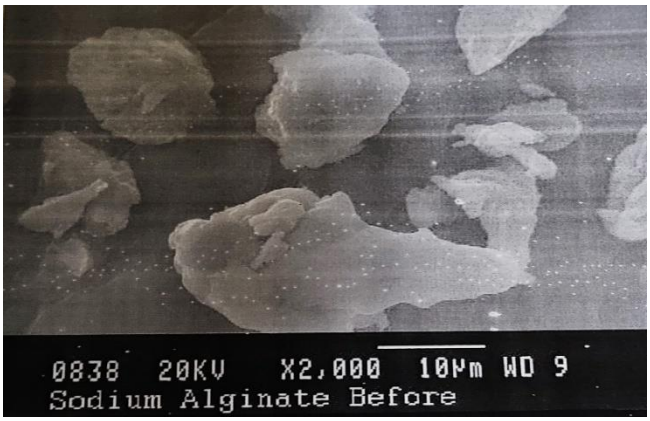

Fig 12: - SEM of Sodium Alginate Suspension

2) SEM of Sodium Alginate Raft

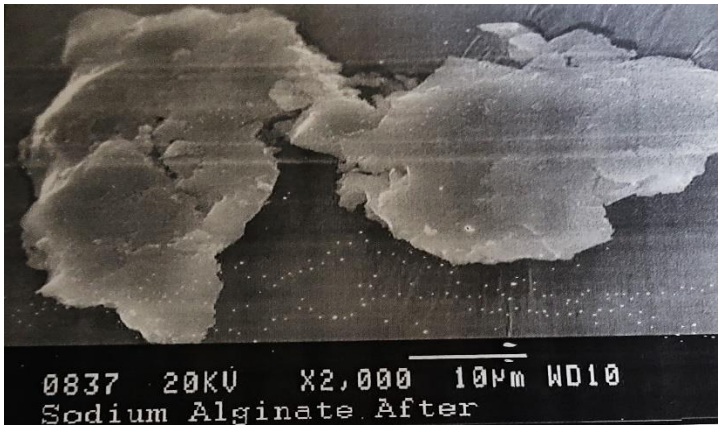

Fig 13: - SEM of Sodium Alginate Raft

3) SEM of Guar Gum Suspension

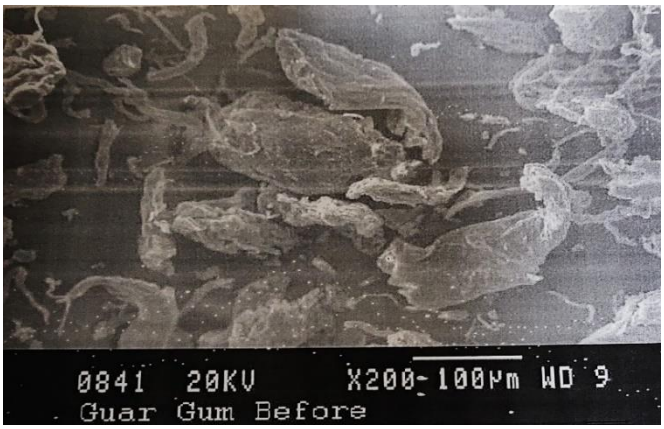

Fig 14: - SEM of Guar Gum Suspension

4) SEM of Guar Gum Raft

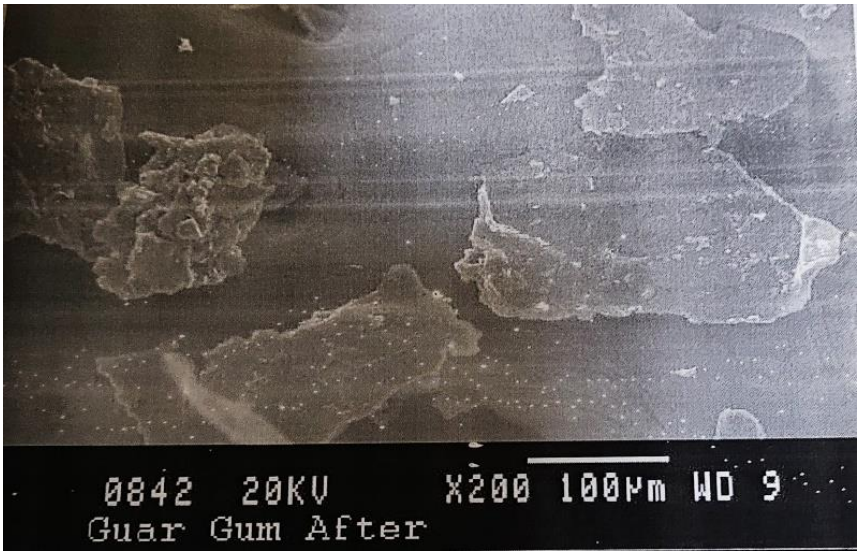

Fig 15: - SEM of Guar Gum Raft

K. Viscosity Studies: -

a. Viscosity of Suspension: - The viscosity of the suspension is given in poise. The details are given below.

Table 12: - Viscosity of Suspension

RPM	BATCH									
	SA 1	SA 2	SA 3	SA 4	SA 5	GG 1	GG 2	GG 3	GG 4	GG 5
5	1.95	2.25	2.69	3.21	3.56	3.29	3.49	3.77	5.63	5.86
10	4.8	5.1	5.8	6.45	7.12	5.42	5.91	6.28	8.74	10.06
20	6.8	6.69	8.29	9.12	10.01	7.36	8.22	9.35	12.89	14.66
50	11.79	11.84	12.73	13.18	13.85	12.5	12.89	13.74	16.46	17.85
100	13.65	14.02	14.9	15.32	16.13	14.36	14.96	16.62	18.85	19.96

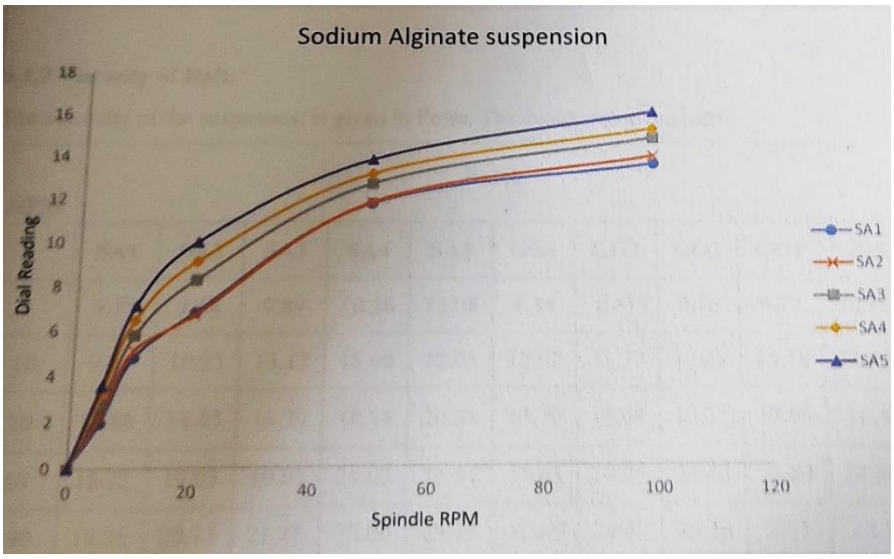

Fig 16: - Thixotropy of Sodium Alginate Suspension

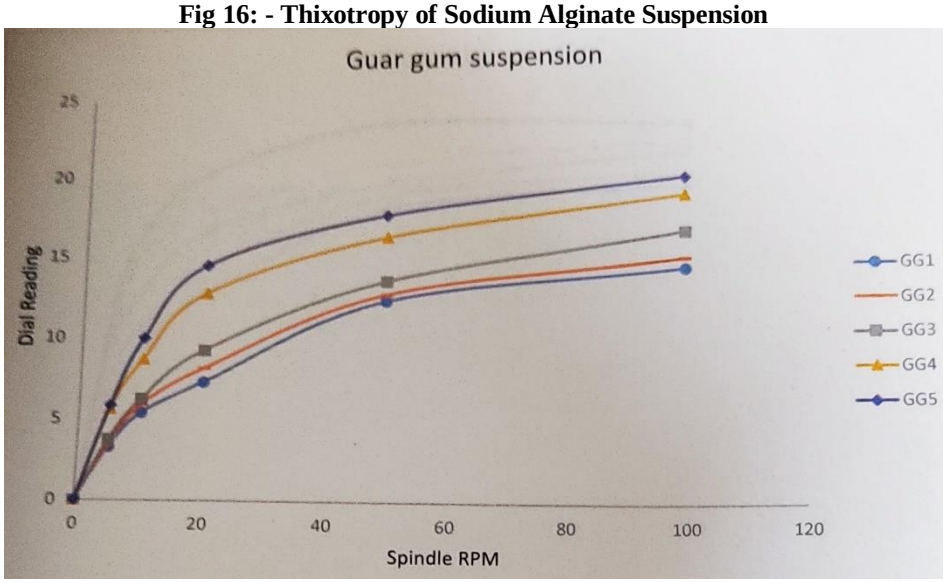

Fig 17: - Thixotropy of Guar Gum Suspension

b. Viscosity of Raft: - The Viscosity of the Suspension is given in Poise; the details are given below.

Table 13: - Viscosity of Raft

RPM	BATCH									
	SA 1	SA 2	SA 3	SA 4	SA 5	GG 1	GG 2	GG 3	GG 4	GG 5
5	6.35	7.68	9.89	10.56	12.08	8.34	8.61	9.16	9.77	10.16
10	9.71	10.95	13.12	15.68	17.05	12.02	12.77	13.85	15.18	16.45
20	12.88	14.45	16.79	18.14	20.51	13.79	14.44	16.31	17.96	18.4
50	18.22	19.03	19.85	21.03	23.51	18.63	19.75	21.42	23.84	24.68
100	19.36	20.13	21.45	22.06	23.14	23.84	24.47	26.46	27.1	28.7

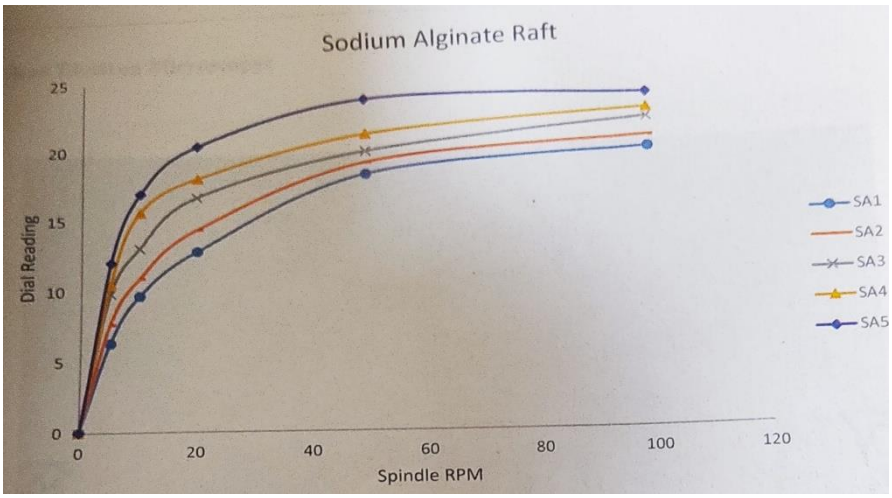

Fig 18: - Thixotropy of Sodium Alginate Raft

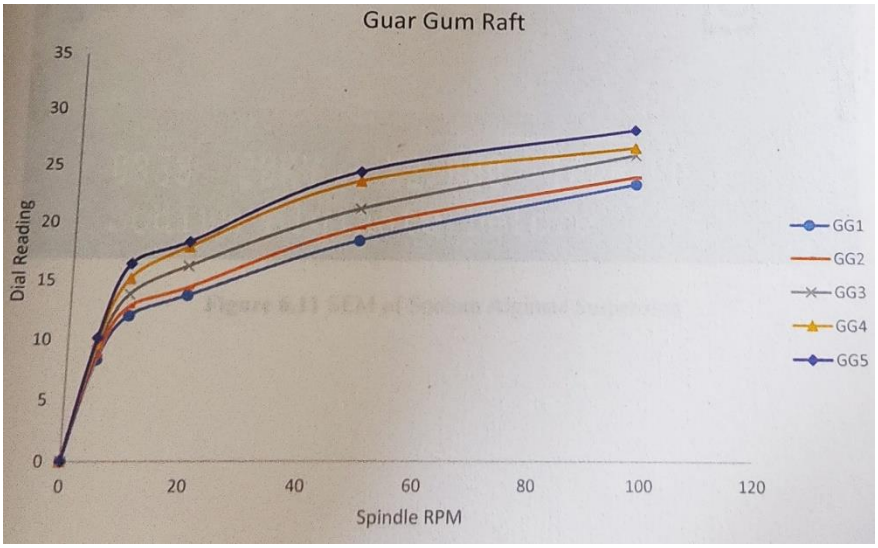

Fig 19: - Thixotropy of Guar Gum Raft

L. In-Vitro Drug Release Profile: -

Table 14: - In-Vitro Drug Release Study Profile

Time (In Hrs.)	SA 1	SA 2	SA 3	SA 4	SA 5	GG 1	GG 2	GG 3	GG 4	GG 5
1	20.46	15.14	13.24	13.87	8.81	18.30	22.48	15.52	11.97	11.09
2	34.76	30.71	27.92	33.24	18.81	38.18	48.05	25.77	36.03	21.34
3	58.43	59.57	48.94	55.01	38.68	57.54	64.00	53.87	52.35	43.49
4	82.35	79.95	67.04	67.42	74.00	69.95	77.92	67.54	87.16	59.82
5	95.14	99.49	87.16	93.11	77.67	95.14	100.84	89.06	98.09	82.99
6	98.62	-	99.95	97.29	99.82	96.12	-	95.12	-	97.29

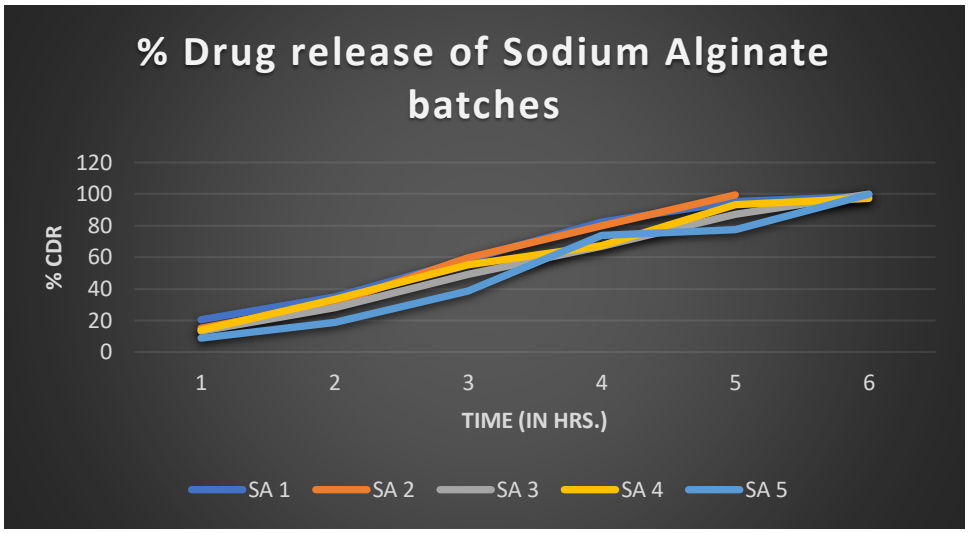

Fig 20: - Drug release of Sodium Alginate batches

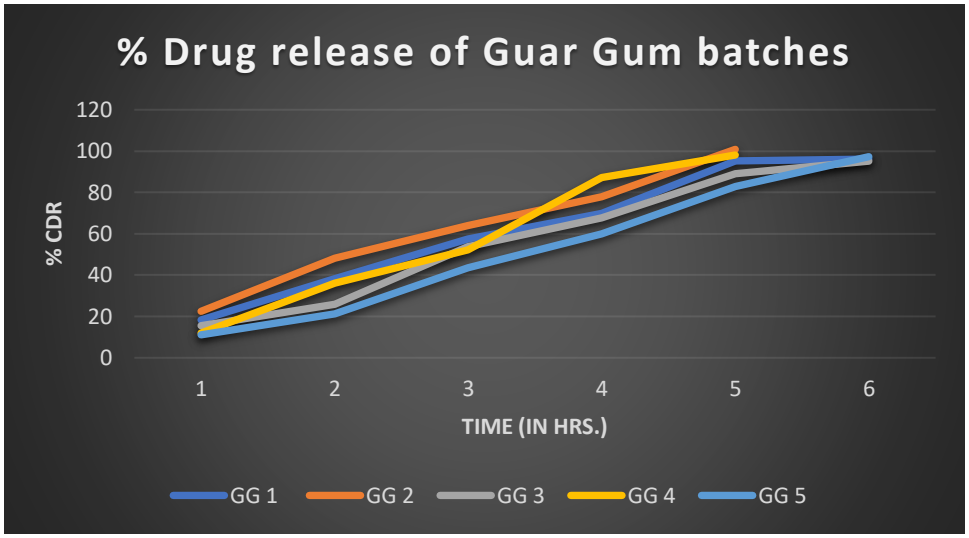

Fig 21: - Drug release of Guar Gum batches

M. Statistical Analysis of data: -

Table 15: -Release Kinetics of SA 3

Batch	Zero Order		First Order		Matrix		Korsmeyer-peppas		Hixson-Crowel	
SA 3	R	Slope	R	Slope	R	Slope	R		R	Slope
							0.9980	0.7114		
	0.9989	0.7052	0.9989	0.0072	0.9372	1.4407	n	k	0.9989	0.0024
							0.9920	0.7114		

N. Zeta Potential Study: -

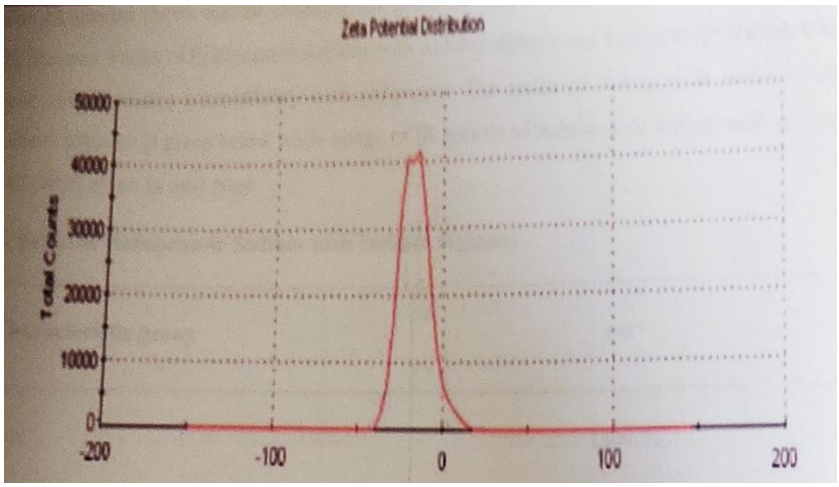

Fig 22: - Zeta Potential of Suspension SA 3

O. Stability Study: - Batches SA 3 and GG 5 were selected for Stability Study due to its linear drug release in In-Vitro drug dissolution study.

Table 16: - Stability Study of SA 3 and GG 5 batch at room temperature

Batch	Duration (Month)	At Room Temperature		
		Floating lag time (Sec)	Acid Neutralizing Capacity (ml)	% Content
SA 3	0	21	6.67	100.81
	1	20	7.1	99.63
	2	23	6.9	100.2
GG 5	0	7	5.96	99.01
	1	8	5.85	101.12
	2	10	5.88	99.64

CONCLUSION:

The main aim of the study was to formulate, Optimize and Evaluate In-Situ Raft-Forming suspension of Rabeprazole Sodium using Guar Gum. This formulation was formulated by using excipients such as Sodium Alginate, Sodium Bicarbonate, Calcium Carbonate, Methyl Paraben, Propyl Paraben. In this study formulation SA 3 and GG 5 showed satisfactory results in the release of drug in a linear form. The studies of FTIR shows that all the above characteristic peaks of Rabeprazole Sodium were observed near their respective standard values. So, it has been concluded that there is no incompatibility between polymers and pure drugs. The preliminary examination of Rabeprazole Sodium like its Melting point obtained in the range from 139.8^0 C to 141.6^0 Cand were within its standard range. The solubility of Rabeprazole Sodium was found to be 99.97 mg/ml in distilled water. Rabeprazole Sodium was pale yellowish powder. It has characteristic irritating odour. The powder was crystalline in nature which was very sensitive to the moisture and lights. Loss on Drying of Rabeprazole Sodium was found to be 5.85%. The Standard Calibration Curves of Rabeprazole Sodium was taken in 0.1 N HCL (pH 1.2) and the R^2 obtained were R^2= 0.9997. the suspension was evaluated after its formulation in that Sodium Alginate formed light yellowish brown while Guar Gum formed cream coloured suspension, the suspension formed by Guar Gum was more viscous than suspension formed by Sodium Alginate. Both have characteristic odour of the substance used as Raft forming agent. Many of the other parameters such as Floating Time, Raft Weight, Raft Volume, Acid Neutralizing capacity, Content Uniformity, X-Ray Diffraction Study, Scanning Electron Microscopy studies, Viscosity studies were done.

The In-Vitro Drug release study were done in 0.1N HCL (pH 1.2) and batches SA 3 and GG 5 were selected for further Stability Studies, because they released drug in a linear form. The Stability Studies were done for 0-2 Months and 1-Month interval readings were taken for the parameters such as Floating Lag Time, Acid Neutralizing Capacity and % Content. Not much of variations were seen in results after 2- Months of Stability period. But the author recommends future Long-Term Stability studies and In-Vivo studies were recommended.

ACKNOWLEDGEMENTS

The Author is thankful to "Micro labs, Bengaluru" for providing gift sample of Rabeprazole Sodium, thanks to JIIU's Ali-Allana College of Pharmacy and Research Centre's Department of Pharmaceutics for providing lab chemicals and a friendly environment for study. Special thanks to Dr. G.J. Khan, Dr. Quazi Majaz, Dr. Imran Kalam for their valuable guidance

FUNDING

No Funds were provided for the Project Work.

CONFLICTS OF INTEREST

The Author Declares "No Conflict of Interest".

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ABBREVIATIONS

- AIIMS- All India Institute of Medical Science
- GERD- Gastroesophageal Reflux Disease
- GRT- Gastric Retention Time
- Hrs.- Hours
- GIT- Gastro-Intestinal Tract
- API- Active Pharmaceutical Ingredient
- Wt.- Weight
- HCL- Hydrochloric Acid
- UV- Ultra-Violet
- Rpm. – Revolutions Per Minute
- Nm- Nanometre
- SEM- Scanning Electron Microscopy
- GGS- Guar Gum Suspension
- SAS- Sodium Alginate Suspension
- GIT- Gastro Intestinal Tract