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Research Article

Formulation Development and Evaluation of Sustained Release Ranolazine Microbeads using Natural Polymer

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Abstract



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The goal of this study was to develop sustained-release microbeads containing Ranolazine. The Ranolazine was selected on the basis of its short half-life i.e., 1.5 h and used in treatment of Angina pectoris. The fundamental goal of this research is to increase duration of drug release. Ranolazine was encapsulated with natural polymers such as Hygrophila auriculata seed mucilage by an ionotropic gelation technique. The formulation batches were optimized with a 3^2 factorial design and physicochemical characteristics were also evaluated. The particle size of microbeads, entrapment efficiency of drug, surface morphology, *In-vitro* release of drug was investigated.

The *in-vitro* studies of optimized microbeads formulation batch (B2) containing 100:600 ratio of Hygrophila auriculata seed mucilage and sodium alginate exhibited as a sustained release of Ranolazine up to 12 h and. The mucoadhesion potential was found to be $97 \pm 1\%$ up to 12 h. In our perspective, the current ER pellet formulation might be the most feasible alternative to traditional pain management formulas.

All the trial's batches were shown to be suitable in extended release of a short elimination half-life medication with enhanced bioavailability, implying that it is useful for oral drug delivery.

Keywords: Design of experiment, Extrusion-spheronization, Ionic gelation, Microbeads, Ranolazine,

1. INTRODUCTION

It is necessary to administer the appropriate dose of medication for the effective medication therapy in the treatment of chronic or acute disease¹. Systemic drug delivery can be accomplished using different nasal, oral, transdermal and parenteral routes of administration¹. Among all, due to the ease of administration of medications, oral route is preferred and special attention². There are several traditional dosage forms available for oral drug delivery, such as emulsions, capsules tablets and suspensions³. Conventional treatment shows plasma concentration in peak valleys and fast metabolic clearance⁴. It includes a numbers of doses treatment, which may be controversial due to patient safety issues⁵. Controlled drug delivery has made remarkable achievements in the past 20 years because it can improve medication release and lessen unwanted effects through localisation of drug at the place of action and monitoring release of drug⁶. Furthermore, drug entrapment within polymers can protect delicate medications (for example, peptides/proteins) from chemical and enzymatic degradation⁷. Microsphere is commonly used for the controlled release of pharmaceuticals and is developed utilizing biodegradable polymers⁶. The primary advantage of employing biodegradable polymers is that they degrade in a

biologically friendly manner after performing their functions⁸. It therefore ensures a steady state plasma concentration and greater compliance with patients⁸. Oral control method of drug delivery system delivers the medication over a given time span at a fixed rate⁹⁻¹⁰. As a result, the oral controlled drug administration system may encounter issues related with traditional/conventional dose forms while increasing the therapeutic efficacy of a specific pharmaceutical^{3,9,10}. For the oral administration of pharmaceuticals, numerous controlled release methods are available, including multiple layer tablets, transformed capsules, microbeads as well as matrix tablets. Microbeads are extensively customized because to their ease of planning and administration^{3,9,10}. It is a spherical particle with a diameter ranging from 0.5 to 1000m⁵⁻⁶. Microbeads incorporate drug compounds in sphere polymeric matrix and gradually release medication over time in a regulated manner^{5-6, 11}. Natural biodegradable polymers such as starch, sodium alginate and gums pose a relatively wide area of active research in the controlled delivery of drugs¹²⁻¹³. These natural polymers have the benefit of being fragmented into physiologically suitable compounds which are metabolized and extracted from the body through normal metabolic process¹⁴⁻¹⁵. Such natural polymers are hydrophilic and are more suitable for physical and chemical modifications through

simple processes than the synthetic polymers that are commonly used¹⁶⁻¹⁷.

Herbal mucilage obtained from seeds of *Asteracantha longifolia* and Family- Acanthaceae is one of the most utilized seed mucilage distributed throughout India, Nepal, Burma, Malaysia and Srilanka¹⁸. Kokilaksha seed mucilage is a hydrophilic polysaccharide that swells in hot water. Herbal mucilage and sodium alginate have been characterized and used to form microbeads using calcium chloride as a chelating agent by an ionic gelation method¹⁹. Angina pectoris is a condition characterized by significant chest discomfort caused by a lack of blood supply to the heart. Ranolazine is an FDA approved medication for the angina pectoris treatment²⁰. Ranolazine is a novel anti-ischemic therapeutic substance that selectively inhibits cardiac sodium channel²¹. It is extensively metabolized by enzymes of the hepatic cytochrome (CYP3A4 and CYP2D6). Although about 5% of the medication is eliminated intact, intermediates are primarily excreted via urine. The biological half life of drug is 1.5 to 2 hrs for non-extended-release preparations²².

In this study, ranolazine microbeads were prepared using natural polymer (herbal mucilage) and sodium alginate to look into its possible outcomes for sustained drug delivery upon oral administration. Ranolazine was used as a model drug in the formulation used to treat angina pectoris. The ionotropic gelation process was used to create microbeads and evaluated.

2. MATERIALS AND METHODS

2.1 Materials

Ranolazine as a drug model was received as gift sample from Cipla House, Peninsula Business Park Mumbai, India. Kokilaksha seed was purchased from Shree Shail Medifarm, Nagpur, India. Sodium alginate was a gift sample from Loba Chem, (Mumbai, India).

2.2 Methods

2.2.1 Extraction of mucilage Kokilaksha seed

About 100 gm of *Hygrophila auriculata* (kokilaksha seed) seeds were immersed in distilled water and cooked at temperature of 60 °C for 1 hour before being set aside for 24 hours at room temperature. The viscous fluid that resulted was filtered via the muslin fabric. Following that, the filtrate was refrigerated until it was used. The mucilage was then precipitated by adding an equal volume of ethanol and stirring continuously at room temperature. Mucilage was removed by filtering and dried at temperature of 50°C in an oven. The dry mucilage was then ground and sieved (# 60) to generate free flowing powder²³⁻²⁴ and further mucilage powder was used in preparation of microbeads

2.2.2 Physicochemical characterization of *Hygrophila auriculata* seed mucilage

2.2.2.1 Phytochemical investigation

For research purposes, the extracted mucilage powder was submitted to several phytochemical identification assays. Tannins (Ferric chloride, lead acetate test), Carbohydrates (Molisch's test), Mucilage (Ruthenium red test) and starch (Iodine test) were all tested²⁵.

2.2.2.2 FTIR of obtained mucilage

A coarsely crushed 1% dried mucilage powder was placed in a pellet-forming die using KBr powder that was fine in size (200 mg) (KBr press, Karnavati, India). In a vacuum, a pressure is applied for five minutes of approximately 8 tons, resulting in translucent pellets. The pellet was placed on a FT-IR holder for measurements (FTIR 4800, Shimadzu, Japan). The spectra was measured in the 4000 to 400 cm⁻¹ wave number range and used to classify the functional groups and structural features of the sample mucilage²⁶.

2.2.2.3 Determination of mucilage polysaccharide content

In 100 mL of distilled water, 10 mg of the resultant mucilage was solubilized. 1 ml of separated seed mucilage solution was treated with 5% phenol and 5 ml of concentrated H₂SO₄ to estimate the polysaccharide concentration. The absorbance was measured after 10 minutes at 488 nm in comparison to a blank solution produced similarly, but without mucilage. The experiment was repeated three times. The polysaccharide content of a standard polysaccharide prepared similarly as a test solution was measured using a linear equation derived from the concentration vs. absorbance curve for varied values (50-90 g/ml of glucose)^{27,28}.

2.2.3 Preparation of microbeads

All microbead formulation batches were created using the ionotropic gelation technique and natural polymers such as herbal mucilage, calcium chloride and sodium alginate as crosslinking agents.

In preparation of drug loaded sodium alginate microbeads, initially, sodium alginate was dispersed in 20 ml of distilled water with Persistent mixing was required until a completely homogenous dispersion was attained¹. Similarly, in another phase, herbal mucilage was dissolved in 20 ml of distilled water with continuous stirring at 65°C. Mix both resultant viscous solution with each other and drug was incorporated into the polymer solutions and it was placed on a magnetic stirrer at 35°C and at 600 rpm for about 30 minutes. Now, the drug-containing polymer solution formed above was poured drop by drop through 23 gauze needles into another beaker containing calcium chloride solution (2%w/v) with continuous magnetic stirring at 300 rpm for 30 min^{15,19}. The formed microbeads were filtered, cleaned with distilled water, and were dried in a hot air oven at 40°C for 24 hours²⁹. Schematic representation of Preparation of microbeads by ionotropic gelation technique is shown in Figure 1.

2.2.3.1 Application of design experiment software

Optimization is a technique for improving and maximizing the efficiency of a product or method by identifying the most important element influencing the response and the link between that component and the response³⁰. A response surface 3 level factorial design with varying concentrations of herbal mucilage and sodium alginate polymer as independent factors and particle size (mm), entrapment efficiency of drug (%), and drug release (%) as dependent responses was employed in this study. The build information 3 level factorial design, factors for 3 level factorial design and response for 3 level factorial design are given in Table 1, Table 2 and Table 3 respectively.

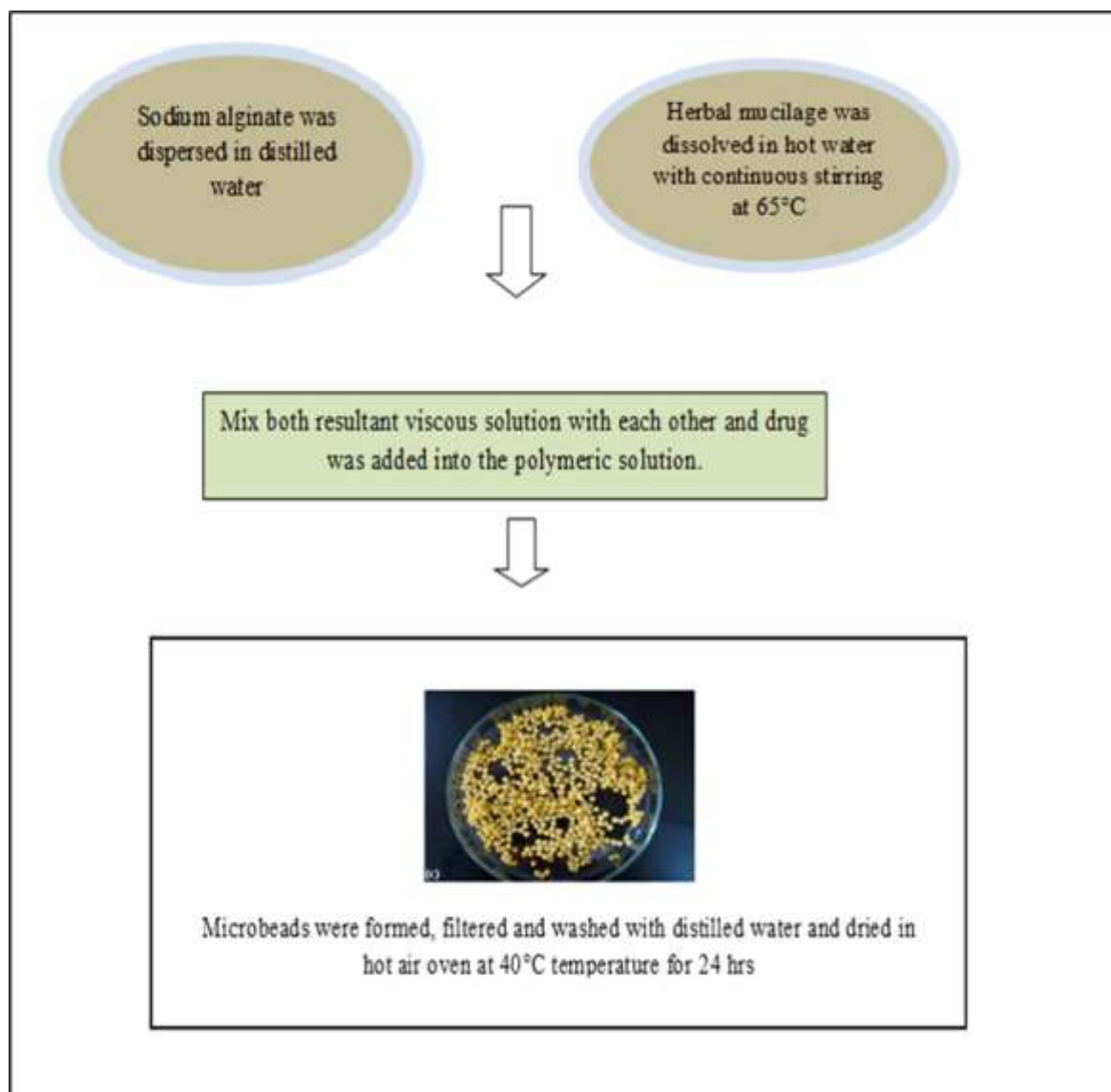


Figure 1: Preparation of microbeads by inotropic gelation technique

Table 1: Build information 3 level factorial design

File Version	12.0.1.0		
Study Type	Response Surface	Subtype	Randomized
Design Type	3 Level Factorial	Runs	13
Design Model	Quadratic	Blocks	No Blocks
Build Time (ms)	160.00		

Table 2: Factors for 3 level factorial design

Factor	Name	Units	Type	Minimum	Maximum	Coded Low	Coded High	Mean	Std. Dev.
A	HM		Numeric	50.00	150.00	-1 ↔ 50.00	+1 ↔ 150.00	100.00	35.36
B	SA		Numeric	400.00	800.00	-1 ↔ 400.00	+1 ↔ 800.00	600.00	141.42

Table 3: Response for 3 Level Factorial Design

Response	Name	Units	Analysis	Minimum	Maximum	Mean	Std. Dev.	Model
R1	R1: Particle size	mm	Polynomial	1.04	1.36	1.20	0.0796	Linear
R2	R2: Drug Release	%	Polynomial	72.67	93.16	84.89	5.56	Quadratic
R3	R3: Entrapment Efficacy	%	Polynomial	58	73.83	67.75	5.76	Quadratic

2.2.4 Characterization of microbeads

2.2.4.1 Drug entrapment efficiency

In a glass mortar, accurately weighed 10 mg of microbeads and that have been crushed. The drug was extracted over a 24-hour period by soaking the drug powder in 100 cc of phosphate buffer pH 6.8. The mixture was stirred for 15 minutes the next day before being filtering and diluting with the same buffer pH 6.8 phosphate buffer. A UV-spectrophotometer at 272nm was used to determine the content of ranolazine in the filtrate in comparison to a blank solution ⁵. The Drug entrapment efficiency were determined by the equation no 1.

$$\text{Drug entrapment efficiency} = \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \times 100 - \text{eq}(1)$$

2.2.4.2 Percent yield of microbeads

The practical yield of various batches of microbeads was calculated by comparing the weight of the end product after drying to the original total weight of the medicine and polymer used to make the microbeads ^{6,31}. The percent yield of microbeads is determined by using equation no 2

$$\% \text{ yield of microbeads} = \frac{\text{Weight of microbeads}}{\text{Total weight of drug and polymer}} \times 100 - \text{eq}(2)$$

2.2.4.3 Particle size determination

A digital microscope (DMWB2-223, Motic B1 Series System Microscope, China) set to 10X magnification and attached to a Motic M210 video camera was used to examine the particle shape and size of microbeads. Photographs of the manufactured microbeads were shot with a video camera and scaled in terms of the mean of our Feret diameters determined utilizing images in various orientations processing software i.e; Motic Photographs 2000 ver. 1.3 ^(31,32).

2.2.4.4 Scanning electron microscopy (SEM)

Scanning electron microscopy (JEOLJSM-6360, Japan) was used to study surface morphology of composite microbeads. Using a sputter coater, the Microspheres were placed in a gold/palladium plated slab ^{6,32}. The SEM image of formulation batch B2 is shown in Figure 3.

2.2.4.5 X-ray diffraction study (XRD)

The research was carried out to observe the transformation of the crystalline structure of pure drug into amorphous state ³⁰. XRD pattern was recorded on X-ray diffractometer (Rigaku, Japan). For analyzing pure drug and dried drug loaded microbeads, Cu-K was used as a radiation source with 45kV voltage and 25mA current respectively. The instrument was

worked at a phase size of 0.01° and samples were scanned with a scanning speed of 2° min⁻¹ at 2θ between 5°–6° ³⁰⁻³².

2.2.4.6 Percentage swelling index

The percentage of water absorbed by the beads was used to compute the swelling ratio. In 20 ml of pH 6.8 phosphate buffer, 50 mg of microbeads were put. The microbeads were weighed after 3 hours, and the proportion showing the weight increase of beads after swelling to the weight of dry beads was used to calculate water intake by using equation no 3 ⁵.

$$\% \text{ swelling index} = \frac{\text{Swollen weight} - \text{Initial weight}}{\text{Initial weight}} \times 100 - \text{eq}(3)$$

2.2.4.7 In-vitro drug release studies

At 37±0.5°C, an *in vitro* drug release investigation of microbeads was performed using USP dissolving apparatus I. For 2 hours, 900 cc of 0.1N hydrochloric acid buffer (pH 1.2) was used in the dissolution investigation ². After 2 hours, a dissolution study was carried out in 900 cc of pH 6.8 phosphate buffer for approximately 12 hours. At certain time intervals, 5 ml of sample volume were extracted precisely and was replaced by a fresh medium ^{5,3-32}. The absorbance of the withdrawn sample was measured using a UV-spectrophotometer at 272 nm in comparison to a blank solution.

3. RESULTS AND DISCUSSION

3.1. Phytochemical study of herbal mucilage

3.1.1 Practical yield of dry mucilage

The extracted mucilage from Hygrophilla auriculata seeds was brown-colored having non-hygroscopic nature. The yield of herbal mucilage was found to be 6.5%. However, we avoided utilizing synthetic polymers to limit degradation products because the goal of this study is to examine the potential of mucilage extracted for therapeutic purposes.

3.1.2 Phytochemical investigation

The presence of carbohydrates and mucilage in Hygrophilla auriculata seeds was confirmed by phytochemical studies on isolated mucilage. The starch, alkaloids, and tannins, on the other hand, were not found in the mucilage sample under inquiry.

Mucilage that has been isolated was found to be diffused in water and insoluble in acetone, chloroform, ethanol, and methanol in a solubility experiment. The entire phytochemical investigation tests are given in Table 4.

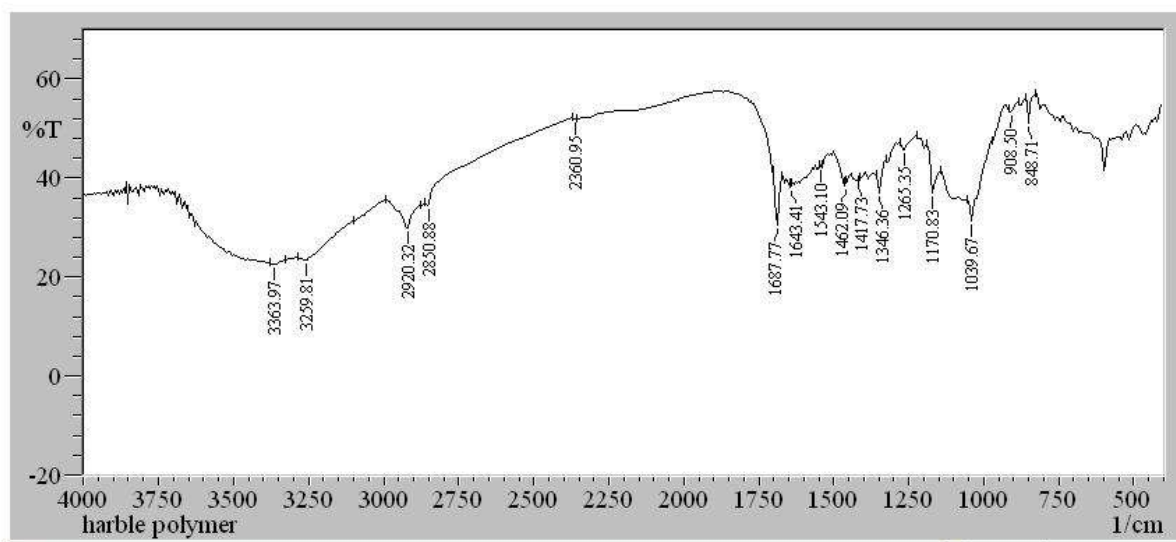
Table 4: Phytochemical investigation test

Sr. No.	Test	Observation	Inference
1.	Carbohydrates test (Molischs test): Add a few drops of alpha-naphthol + aqueous extract, agitate + conc. H ₂ SO ₄	At the intersection of two liquids, a violet ring form	Carbohydrate is present.
2.	Test for mucilage: Add powdered drug materials in water.	Powdered drug material swells in water.	Mucilage is confirmed.
3.	Iodine test: Mix. 3 mL test solution + few drops of weak iodine solution	Blue colour not appeared.	Starch is absent.
4.	Test for tannin: To 2-3 ml aqueous extract + drops of 5% FeCl ₃ solution.	Deep blue-black colour do not formed.	Tannin is absent.
5.	Dragendorffs test: To residue add dilute KCl, shake well and filter. With 2-3 ml filtrate + few drops of Dragendorffs reagent	Orange, brown ppt is not formed.	Alkaloid is absent.

3.1.3 FT-IR study of herbal mucilage

The FTIR spectrum of *Hygrophilla auriculata* seed mucilage is shown in the picture below. A broad band of absorption was discovered in the wave number range of 3572-3064 cm⁻¹, which was attributed primarily to O-H stretching of hydroxyl groups contained in mucilage sugar residues. The distinctive bands between 2920 and 2850 cm⁻¹ were caused by -C-H

stretching in the saturated moieties' -CH₂ and -CH₃ groups. The 1039 cm⁻¹ band was ascribed to vibrations such out-of-plane C-H bending (from aromatic structures). The typical peaks in the area 1249-1031 cm⁻¹ due to C-O and C-O-C stretching vibrations, which are features of natural polysaccharides, have also been identified. FT-IR spectrum of herbal mucilage is shown Figure 2.

**Figure 2: FT-IR spectrum of herbal mucilage**

3.2. Evaluation of microbeads

3.2.1 Drug entrapment efficiency

Entrapment efficiency of ranolazine loaded microbeads were found in the range of 58.00 to 73.83%. It was found that as the polymeric ratio increases, drug entrapment efficiency also increases. It is directly proportional to the polymeric ratio, as polymer concentration increases then drug entrapment

efficiency also increases. All the result of Drug entrapment efficiency is in the Table 5.

3.2.2 SEM analysis

SEM images of Ranolazine loaded microbeads were shown in following Figure 3 microbeads are spherical in shape. Figure 3A and 3B represent that microbeads are spherical and form roughness texture on their surface. Figure 3C, 3D and 3E are the cross-section images of microbeads formulation.

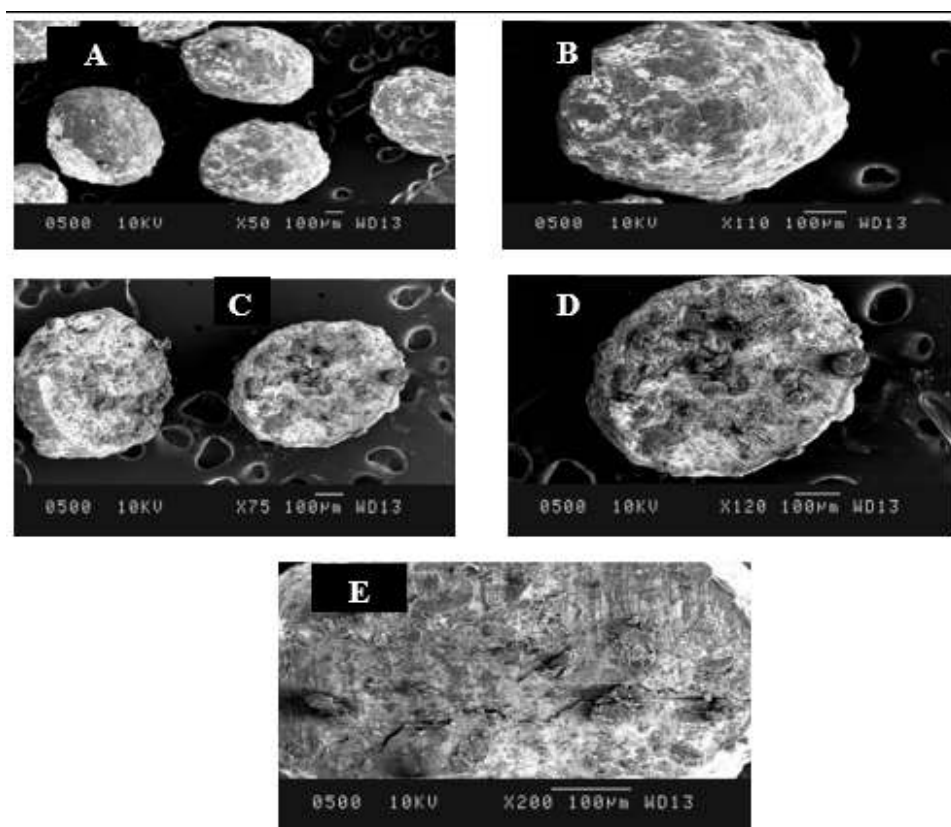


Figure 3: Scanning electron microscopy and cross section images of optimized formulation

3.2.3 Morphology studies by Motic microscopy

Photographs of microbeads were utilized to evaluate the size, diameter, and circularity of microbead compositions. Size and diameter of microbeads formulations depends on polymer concentrations. As concentration of polymer increases the size of microbead formulation also increases. Particle size of all microbead formulation lies between 1.04 to 1.36 mm is in the Table 5. The outcome of circularity was discovered to be in the range of 0.9995004 to 1.0659321.

3.2.4 Percent yield of microbeads

Percent practical yield was calculated by practical yield divide by theoretical yield multiplied by 100. Percent practical yield

of all formulation batches was found in the range between 75.7 to 90.6%. All formulation batches show increase in practical yield as increases in polymer ratio. Percent practical yield is directly proportional to polymer ratio as polymer concentration increase then percent practical yield is also increases. All the results are in the Table 5

3.2.5 Swelling index

The swelling index of microbeads was investigated in a phosphate buffer medium (pH 6.8). 50 mg of microbeads were dissolved in buffer and after 3 hrs reweighed the swollen microbeads and calculate the swelling index of microbeads. Swelling index was found to be 88.6%.

Table 5: Particle size, entrapment efficiency and drug release

Sr. No.	Formulation code	Drug dose mg	Herbal mucilage: polymer ratio	Particle size mm	Entrapment efficiency %	Drug release %	% Practical Yield
1	Batch A1	500	50 : 400	1.04	58.65	93.16	75.7
2	Batch A2	500	50 : 600	1.15	63.59	87.84	84.9
3	Batch A3	500	50 : 800	1.21	71.35	80.99	86.5
4	Batch B1	500	100 : 400	1.14	58.00	91.84	78.8
5	Batch B2	500	100 : 600	1.19	71.25	85.33	90.6
6	Batch B3	500	100 : 800	1.32	72.24	77.52	90.1
7	Batch C1	500	150 : 400	1.22	59.33	89.69	79.0
8	Batch C2	500	150 : 600	1.26	67.5	83.26	88.9
9	Batch C3	500	150 : 800	1.36	73.83	72.67	89.3

3.2.6 XRD

XRD spectrum of drug showed distinctive 2 θ peaks at 10.31°, 12.19°, 14.92°, 15.98°, 16.45°, 21.36°, 23.38°, 24.63° and several minor peak up to 30°. The presence of sharp peaks

clearly showed that crystallinity occurs in pure drug (Figure 4), in case of microbeads formulation (Figure 5), only broad and diffused peaks appeared indicating the change of crystalline drug into an amorphous state when incorporated into microbeads formulation.

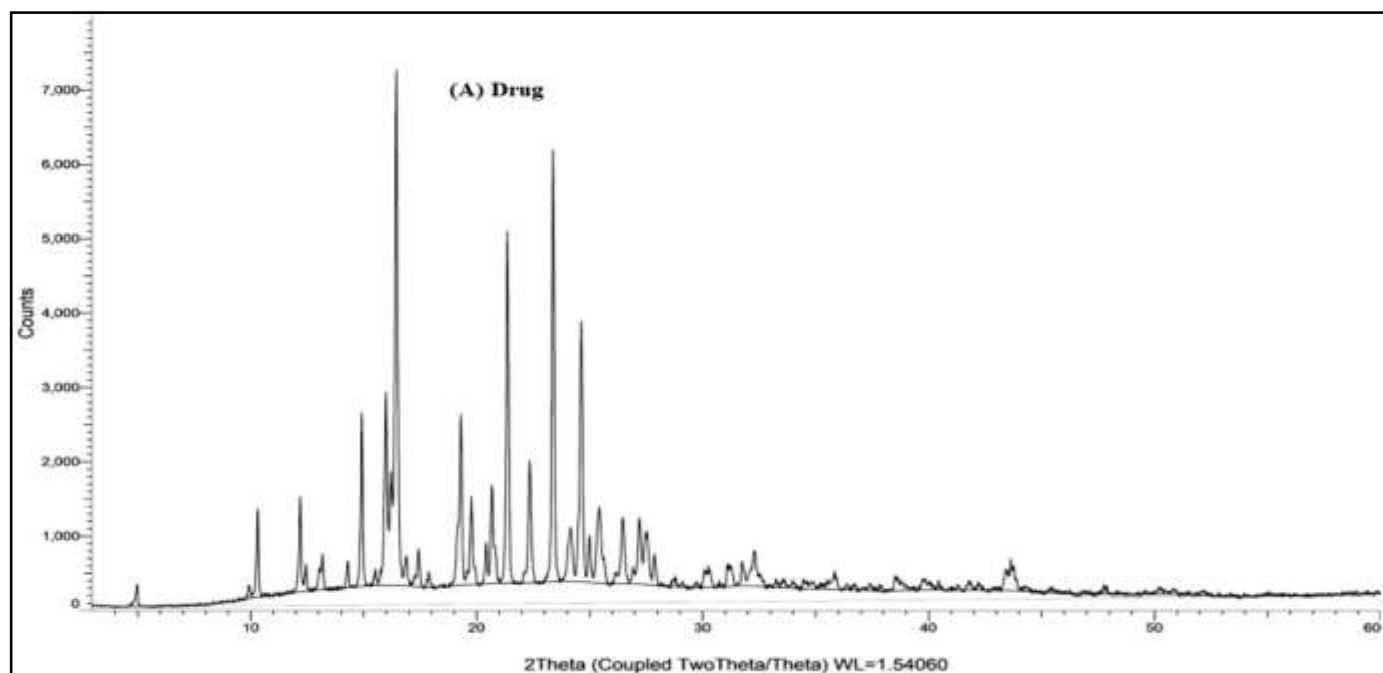


Figure 4: XRD spectra of drug

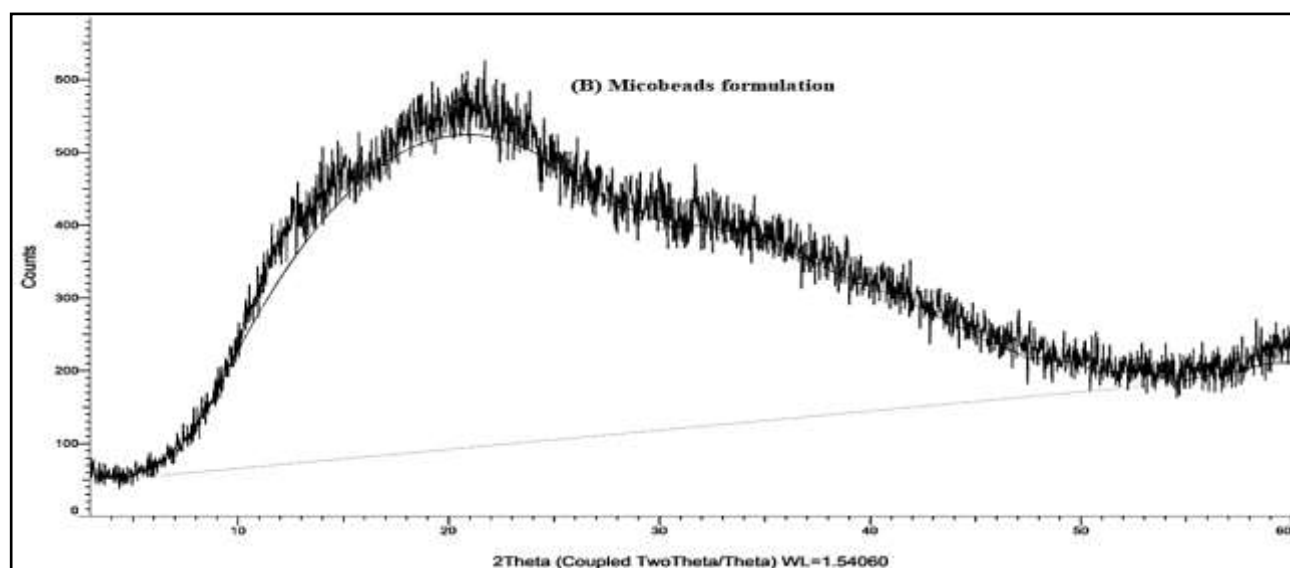


Figure 5: XRD spectra of optimized formulation

3.2.7 In vitro drug release studies

Using simulated gastric fluid of pH 1.2 (0.1N HCl) and simulated intestinal fluid (pH 6.8) to imitate physiological settings, the drug-release pattern was studied for up to 12 hours. All formulations batches show few amount release of drug into the gastric fluid; however, a an alteration in media indicates greater difference in drug release. As polymer concentration increases the drug release decreases.

3.2.8 Optimization of Formulation Batch

The table 6 summarizes the analysis of variance table for response parameters. After examining the P values for the parameters of response, the model was found to be significant. Non-significant terms ($p > 0.05$) were removed from polynomial equations to simplify the models. The P values for particle size, entrapment efficiency, and cumulative drug release in 12 hours were determined to be 0.0001, 0.0008, and 0.0001, respectively, all of which are less than 0.0500, showing that model terms are significant.

Table 6: ANOVA table for response parameters for 3 level factorial design for microbeads**Response 1: Particle size**

Source	Sum of square	Df	Mean Square	F-value	P-value	
Model	0.0723	2	0.0361	94.50	<0.0001	Significant
A-HM	0.0323	1	0.0323	84.37	<0.0001	
B-SA	0.0400	1	0.0400	104.64	<0.0001	
Residual	0.0038	10	0.0004			
Lack of fit	0.0038	6	0.0006			
Pure Error	0.0000	4	0.0000			
Cor Total	0.0761	12				

Response 2: Drug entrapment efficiency

Source	Sum of square	Df	Mean Square	F-value	P-value	
Model	367.50	5	73.50	17.16	0.0008	significant
A-HM	8.33	1	8.33	1.95	0.2057	
B-SA	286.21	1	286.21	66.84	<0.0001	
AB	0.8100	1	0.8100	0.1892	0.6767	
A ²	19.07	1	19.07	4.45	0.0728	
B ²	25.73	1	25.73	6.01	0.0440	
Residual	29.97	7	4.28			
Lack of Fit	29.97	3	9.99			
Pure Error	0.0000	4	0.0000			
Cor Total	397.47	12				

Response 3: Drug release

Source	Sum of square	Df	Mean Square	F-value	P-value	
Model	369.90	5	73.98	511.13	<0.0001	Significant
A-HM	44.66	1	44.66	308.57	<0.0001	
B-SA	315.52	1	315.52	2179.92	<0.0001	
AB	5.88	1	5.88	40.63	<0.0004	
A ²	0.0646	1	0.0646	0.4463	0.5255	
B ²	2.89	1	2.89	19.97	0.0029	
Residual	1.01	7	0.1447			
Lack of Fit	1.01	3	0.3377			
Pure Error	0.0000	4	0.0000			
Cor Total	370.92	12				

3.2.8.1 Effect of independent variables on particle size of microsphere

The particle size was observed to be in the ranges of 1.04 to 1.36 mm. R² was found to be equal to 0.9498. Model F-value of 94.50 implies the model is significant. The difference between “Pred R-Squared” and “Adj R Squared” value was found to be

less than 0.2, which is desirable. “Adeq Precision” measures the signal to noise ratio. Here, ratio of 32.998 indicates an adequate signal. This approach is useful for navigating the design space. Contour plots revealed the link between the independent and dependent variables. The Counter Plot (A) and 3D Surface (B) of particle size of microbeads is shown in Figure 6.

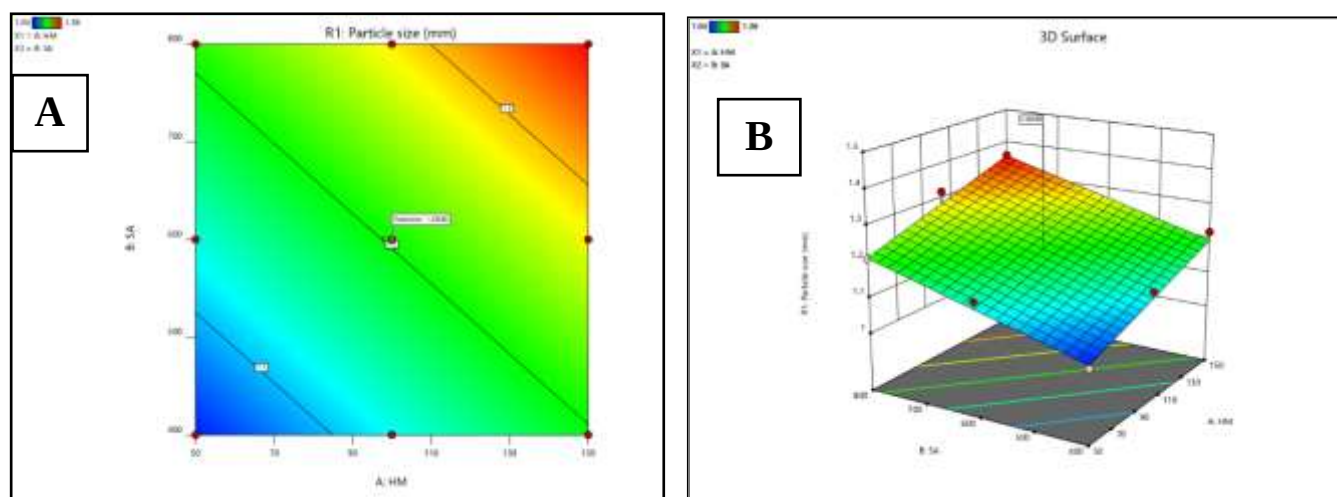


Figure 6: Counter Plot (A) and 3D Surface (B) of particle size of microbeads

3.2.8.2 Effect of independent variable on entrapment efficiency

The percent entrapment efficiency was discovered to be between 58.00 to 73.83%. R^2 was calculated to be 0.9246. The model's F-value of 17.16 suggests that it is significant. The "Adeq Precision" metric assesses the signal-to-noise ratio. A

ratio greater than 4 is preferred. A ratio of 12.213 shows a sufficient signal in this case. This paradigm is useful for navigating the design space. Contour plots revealed the link between the dependent and independent variables. The Counter Plot (A) and 3D Surface (B) of entrapment efficiency of microbeads shown in Figure 7.

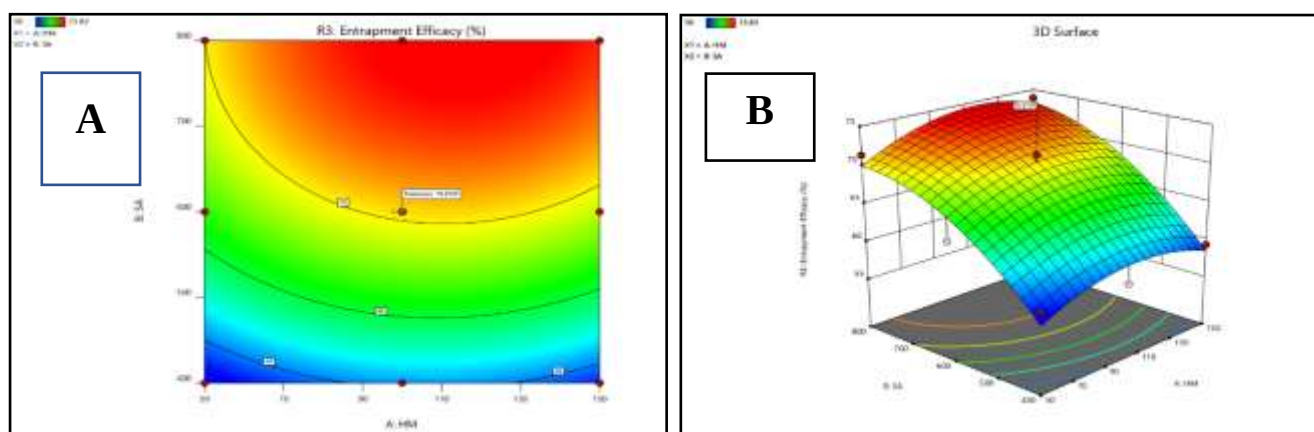


Figure 7: Counter Plot (A) and 3D Surface (B) of Entrapment Efficiency of microbeads

3.2.8.3 Effect of independent variables on drug release

The % CDR was determined to be between 72.67 to 93.16. R^2 was discovered to be 0.9973. The model's F-value of 511.13 indicates that it is significant. The difference in values between "Pred R-Squared" and "Adj R Squared" was discovered to be less than 0.2, which is ideal. The "Adj Precision" metric assesses the signal-to-noise ratio. A ratio greater than 4 is

preferred. The ratio of 77.226 suggests a sufficient signal in this case. This paradigm is useful for navigating the design space. Contour plots revealed the link between the independent and dependent variables. The Counter Plot (A) and 3D Surface (B) of drug release shown in Figure 8 and *In-vitro* drug release profile of all batches of microbeads shown in Figure 9.

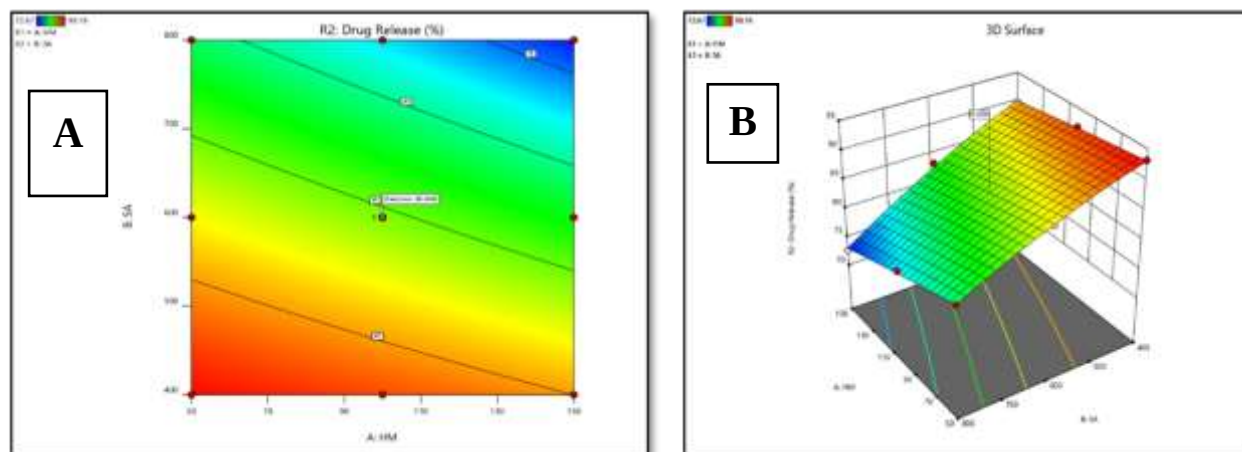


Figure 8: Counter Plot (A) and 3D Surface (B) of Drug Release

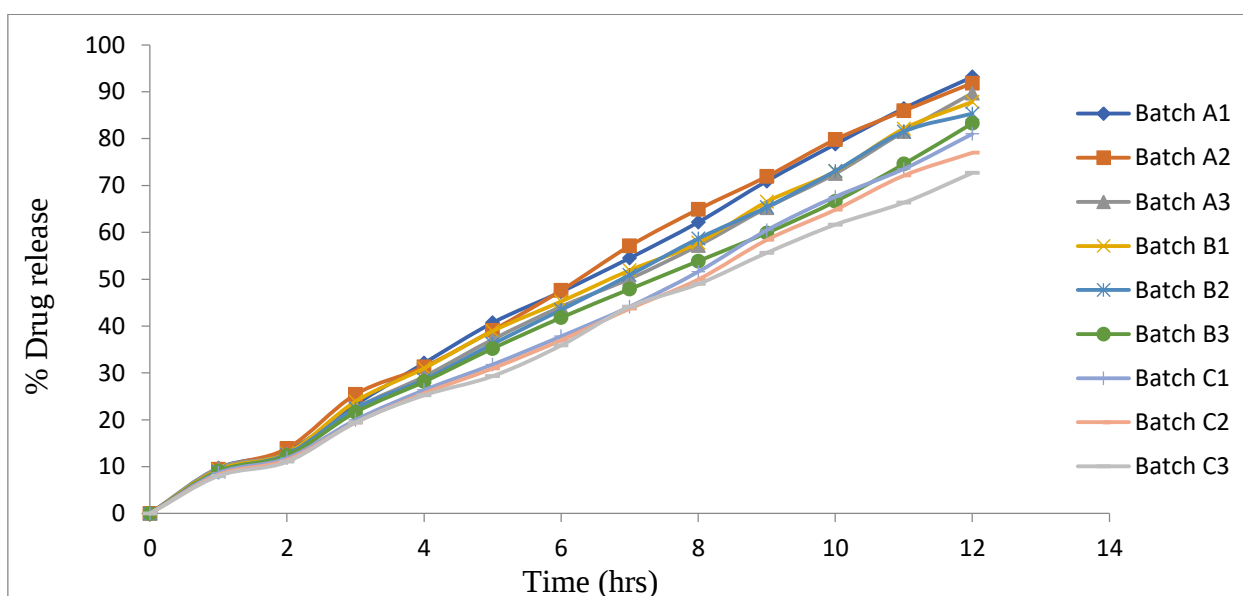


Figure 9: *In-vitro* drug release profile of all batches of microbeads at different pH conditions (1-2 hrs) at pH 1.2; 3-12 hrs at pH 6.8.

4. CONCLUSION

Ranolazine microbeads were formulated using different ratio of herbal mucilage and sodium alginate polymer in simulated physiological condition evaluated for drug release. The polymer composition has been found to influence the physical properties as well as the medication release pattern of microbead formulations. Based on these results, it can be concluded that product yield often increases as the drug polymer ratio increases. The actual drug loading rose as the predicted drug loading increased. Because of the rise in relative viscosity, the mean particle size increases as the polymer concentration increases in our study. All formulation shows particle size in the range of 1.04 to 1.36 mm. The Batch A1 have maximum drug release, whereas the minimum drug release was for Batch B2. As polymer concentration increases the drug release decreases. This could be explained according to the distribution of particle size. Increased polymer content increases particle size, thereby reducing the effective surface area.

With the highest formulation Batch B2, we obtained acceptable entrapment efficiency with adequate practical yield.

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