FORMULATION AND EVALUATION OF OMEPRAZOLE MAGNESIUM LOADED MICROSPONGES

Ramandeep Kaur[1], Chamanpreet Kaur[2], Shailesh Sharma[3]

[1]Pharmaceutical Research Division, Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial College of Pharmacy, (An Autonomous College) Bela-140111., Ropar, Punjab, India.
E-mail: raman1604503017@gmail.com, Chamanpreetmann495@gmail.com

ABSTRACT

The main aim of research work was to develop the microsponge of omeprazole magnesium to measure the gastroretentive efficacy via optimization of targeted floating microsponges for improved site specific absorption of gastric ulcer. Modified quasi emulsion solvent diffusion method was utilised for the encorporation of microsponge. The effect of different composition of ethyl cellulose and polyvinyl alcohol concentration selected as independent variables was determined on the % entrapment efficiency, % buoyancy and % cumulative drug release. The USP (type II) apparatus was used for in vitro release and the release data best fitted zero order models and mechanism of drug release is independent of concentration. The optimized formulation (F9) demonstrated the favourable % entrapment efficiency (72.5), % buoyancy (78.3±3.0) and % cumulative drug release (72.4±0.1). FTIR spectroscopy was used to check the compatibility properties of drug with excipients. Scanning electron microscopy revealed porous and spherical microsponge shape. This study presents the new and highly patented approach based on floating ability of microsponge for treatment of gastric ulcer.

KEYWORDS: Floating microsponge, Omeprazole magnesium, Gastroesophageal reflux disease, Quasi-emulsion solvent diffusion method, FTIR, SEM.

1. INTRODUCTION

Microsponge delivery system are very similar to the polymeric microspheres which are also called the" solid phase porous microbeads". This technology is highly patented and crosslinked having a large porous surface with preserved spherical structure. Microsponge mainly range from 5 to 300 microns in diameter. The microsponge provide a novel and controlled pharmaceutical product.

Among the other available dosage forms microsponge have shown suitable properties for drug utilization and therapeutic benefits for prolonged drug release characteristics.The microsponges delivers almost perfectly spherical particles exhibiting a very narrow particle size distribution and excellent flow properties. Omeprazole magnesium is a benzimidazole, proton pump inhibitor which is attached to one common distinct site on the alpha subunit of the proton pump and acts by inhibiting the final step in the gastric acid secretion i.e., inhibits the The H^+/K^+ATPase enzyme system. Omeprazole is suited for a sustained release form because of its short elimination half-life in humans and restricted range of effective blood concentration. Omeprazole was utilised as a model drug because of how quickly and thoroughly it is absorbed via the stomach and upper intestine when floating microsponges are made using the quasi emulsion solvent diffusion method. Microsponges offer and efficient drug delivery system for stomach specific delivery with high drug loading capacity. It have the ability to encorporate wide range of active materials with maximum efficiency.

2. MATERIALS AND METHODOLOGY

2.1 Materials

All the materials used in the formulation ,evaluation and other experiments are listed below. The chemicals used were of laboratory reagent grade and distilled water was used in all experiments.Omeprazole magnesium obtained as gift sample from Ang Lifeciences India Ltd. Himachal Pradesh.

Table no.1: List of materials explored in the research work

S. No.	Name	Sources
1	Omeprazole Magnesium	Ang Lifesciences India Ltd, Himachal Pardesh
2	Ethylcellulose	Loba chemise Pvt. Ltd, Mumbai.
3	Eudragit RS 100	Loba chemise Pvt. Ltd, Mumbai.
4	Polyvinyl Alcohol	Loba chemise Pvt. Ltd, Mumbai.
5	Sodium Chloride	E. Merck (India) Ltd, Mumbai.
6	Dichloromethane	Loba chemise Pvt. Ltd, Mumbai.

7	Methanol	Loba chemise Pvt. Ltd, Mumbai.
8	Hydrochloric Acid	Loba chemise Pvt. Ltd, Mumbai.
9	Ethanol	Loba chemise Pvt.Ltd, Mumbai.

2.2 Methods

2.2.1 Formulation of Floating microsponge: Floating microsponge were prepared by quasi-emulsion solvent diffusion technique using sodium chloride as porogen. Solution of ethyl celllulose, Eudragit RS 100 and omeprazole magnesium was prepared in ethanol and dichloromethane (1:1organic phase). 2% (w/v) aqueous solution of the porogen was prepared and sufficient amount of tween 80 was added to it with agitation to obtain 1.5% (v/v) dispersion. The porogen solution was uniformly emulsified in polymeric solution to form w/o emulsion. An aqueous polyvinyl alcohol solution (aqueous phase) was separated and previously prepared w/o emulsion was emulsified in it. This w/o/w emulsion was stirred on homogeniser at 3000 rpm for 1hour. The dispersed droplets were solidified in the aqueous phase by evaporation of the solvent. The microsponges were filtered, and air-dried and stored in dessicator till use.

Table no.2: Composition of Omeprazole magnesium loaded microsponges by quasi emulsion solvent diffusion Method

Formulation Code	Omeprazole Magnesium (mg)	Eudragit RS 100 (mg)	Ethyl Cellulose (mg)	Ethanol/ DCM (ml)	Sodium Chloride (%w/v)	Polyvinyl Alcohol (%w/v)
MS1	200	100	300	10	2	0.5
MS2	200	100	600	10	2	0.5
MS3	200	100	900	10	2	0.5
MS4	200	100	300	10	2	1.0
MS5	200	100	600	10	2	1.0
MS6	200	100	900	10	2	1.0
MS7	200	100	300	10	2	1.0
MS8	200	100	600	10	2	1.5
MS9	200	100	900	10	2	1.5
MS10	200	100	750	10	2	1.5

2.2.2 Physical Appearance- Omeprazole magnesium's physical appearance was evaluated based on a number of organoleptic characteristics, including colour, state, odour, and taste**.**

2.2.3 Melting point determination– The capillary fusion method was used to estimate the melting point of the magnesium component of omeprazole. A little amount of medication

was placed inside a capillary that was sealed at one end, and the capillary was then positioned with the sealed end facing down into the melting point device.

2.2.4 Fourier Transform Infra-red Spectral Analysis (FTIR STUDY)- For the purpose of identifying qualitative compounds, the sample IR spectra was used. FTIR analysis of the material was performed. The infra red spectrum of Omeprazole magnesium was performed on the Fourier Transformed infra-red Spectrophotometer. The sample was scanned at wavelength 4000-400cm^{-1}.

2.2.5 Drug- Polymer Interaction Study- It was crucial to examine the compatibility studies of the medicine and polymers employed within the system when developing floating microsponges. Therefore, it is essential to verify that the medicine does not interact with the polymer while being tested at 40±2°C and 75±5% RH for four weeks. Between 4000cm^{-1} and 600cm^{-1}, the infrared absorption spectra of the drug, polymer, and mixture of polymer and drug were conducted.

2.2.6 Calibration Curve of Omeprazole Magnesium- Calibration curve of omeprazole magnesium was prepared in methanol, distilled water and 0.1N HCL.
2.2.6.1 Preparation of Calibration curve in methanol- 50 mg of the medication were precisely weighed and dissolved in 100 ml of methanol in a 100 ml volumetric flask to create the calibration curve in methanol. From this 50 ml of sample, 100 ml of methanol were added to yield a stock solution with a concentration of 250 µg/ml. Further 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml, and 1.2 ml were taken from this stock solution and transferred to a 10 ml volumetric flask. The volume was then made up to 10 ml with methanol to get various concentrations of 5, 10, 15, 20, and 25µg/ml. Using methanol as the reference solution, the absorbance was measured at 301 nm.
2.2.6.2Preparation of Calibration curve in distilled water-In a 100ml volumetric flask, 50mg of the medication was precisely weighed and dissolved in 100ml of methanol. From this 50 ml of sample, 100 ml of methanol were added to yield a stock solution with a concentration of 250µg/ml. Further 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml, and 1.2 ml were taken from this stock solution and transferred to a 10 ml volumetric flask, where the volume was filled up to 10 ml with distilled water to get various concentrations of 5, 10, 15, 20, and 30 µg/ml. At 300 nm, the absorbance was measured using pure water as the reference solution.
2.2.6.3Preparation of calibration curve in 0.1 N HCL- In a 100ml volumetric flask, 50mg of the medication was precisely weighed and dissolved in 100ml of methanol. From this 50 ml of sample, 100 ml of methanol were added to yield a stock solution with a concentration of 250µ g/ml. Additional 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml, and 1.2 ml were taken from this stock solution and transferred to a 10 ml volumetric flask. The volume was then brought to 10 ml with 0.1 N HCL to achieve various concentrations of 5, 10, 15, 20, 25, and 30µ g/ml. At 300nm, the absorbance was measured using a blank solution of 0.1NHCl.

2.3 Evaluation Parameters
2.3.1Microscopic study- Both an optical and an electron microscope are used to investigate the distribution of particle size. After being mounted on a slide, the sample was

brought down onto the mechanical stage. The size of the microsponges was determined automatically based on their shape and was shown on a computer attachment with a trinocular microscope. By counting the particles on more than 100 microsponges, the mean particle size was determined. A loaded and unloaded microsponge's particle size can be determined using laser light diffractometry or another method.

2.3.2 Determination of percentage yield- Calculating the beginning weight of raw materials and the end weight of microsponges will produce the percentage yield. The following formula can be used to determine percentage yield:

$$\text{Production yield} = \frac{\text{Practical mass of Microsponges}}{\text{Theoretical mass (Polymer+drug)}} \times 100$$

2.3.3 Determination of drug content and encapsulation efficiency: Omeprazole magnesium loaded microsponges that were weighed and placed to a volumetric flask containing methanol in 10 ml were kept in a water bath shaker for 20 min. at 35º C. following proper dilutions, filtered, and spectrophotometric test at 300 nm. Utilizing the following formula, the medication content and encapsulation effectiveness were determined:

$$\textbf{Drug content} = \frac{\text{Practical drug content}}{\text{Theoretical drug content}} \times 100$$

$$\textbf{Loading efficiency} = \frac{\text{Calculated drug content}}{\text{Theoretical drug content}} \times 100$$

2.3.4 Analysis of morphology and surface topography of microsponges: The surface morphology of the improved microsponge formulation was studied using scanning electron microscopy. Using double-sided adhesive tape, the sample was placed directly onto the SEM sample holder, and images were captured using a scanning electron microscope at various magnifications and an acceleration voltage of 10 kV.

2.3.5 In- vitro Release Studies: After adding 900 ml of pH-1.2, 0.1N HCl to the vessel, the USP apparatus type II (Paddle Method) was put together. At a temperature of 37ºC±0.5 ºC, the medium was allowed to equilibrate. The tea bags were filled with prepared microsponges powder, put in the vessel, and spun at 50 rpm for 12 hours. 5 ml of the receptor fluid were taken out, filtered, and then reintroduced at predetermined intervals. Using the dilution media, the samples were diluted appropriately, and they were then examined spectrophotometrically at 300 nm.

2.3.6 In vitro buoyancy study: Spread across the surface of 100ml of 0.1N HCl pH 1.2 with 0.02 percent (w/v) tween 80 was the prepared microsponges. To promote gastric fluid, use tween 80. For 8 hours, the mixture was stirred magnetically at 100 rpm speed and 37ºC±0.5ºC for 8 h . At a predefined time point, every percentage of microsponges that were floating on the surface and those that had settled down were collected. After drying, the collected samples were weighed. The following equation was used to calculate the percent buoyancy.

% Buoyancy = weight of microsponges floating on the surface / initial total weight of microsponges*100

2.3.7 Drug release kinetics- Data from in-vitro drug release experiments were treated to a variety of kinetic models to examine the drug release kinetics-

• Zero order as cumulative amount of drug release Vs time. F = Ko t

Where, 'F' is the drug release at time 't', and 'Ko' is the zero-order release rate constant. The plot of % drug release versus time is linear.

• First order as log % drug remaining Vs time. Log (100-F) = kt

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

• Higuchi model as % CDR Vs square root of time. F = k t1/2

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

2.4 Results and Discussion

2.4.1 Preformulation studies- Organoleptic properties of drug omeprazole magnesium found to be as per I.P. monograph. The Organoleptic properties of omeprazole magnesium were found to the given in table.

Table no.3: Interpretation of organoleptic properties of Omeprazole magnesium

S.No.	Physical parameters	Interpretation
1.	Colour	White
2.	Odour	Odourless
3.	Taste	Bitter
4.	State	Amorphous fine powder

2.4.2 Melting Point:

The temperature at which a substance transitions from its solid to liquid state under a single atmosphere of pressure is known as the melting point of that substance. The drug's purity is implied by the melting point determination. The capillary tube method was used to determine the melting point of omeprazole magnesium, and it was discovered to be remarkably similar to the reported melting point provided in table no.4.

Table no.4: Melting point of omeprazole magnesium

Method employed	Literature value	Experimental value
Capillary Fusion Method	**170°C**	**168°C-170°C**

Discussion: Omeprazole magnesium was discovered to have a melting point between 168 and 170 °C, which is within the range of the pure medication. As a result, the medicine sample was devoid of all contaminants.

2.4.3 Determination of absorption maxima by UV spectroscopy

Chromophoric molecules in solution absorb light of a certain wavelength when exposed to light in the visible/ultraviolet portion of the spectrum, depending on the type of electronic transition involved in the absorption. The primary application of ultraviolet visible spectroscopy is quantitative analysis, and it is a helpful adjunct tool for understanding the structural makeup of many medications. The UV spectrum is typically depicted as a wavelength versus absorbance diagram.

Table no.5: Absorption maxima(λ_{max}) of Omeprazole magnesium

Name of the Solvent	Absorption maxima(λ_{max})
Methanol	301
Distilled Water	300
0.1N HCL	300

Discussion: The maximum wavelength of Omeprazole magnesium was observed lying in the range from 300 to 301 nm in different solvents which is found to be similar with reference standards.

Fig no.1 Absorption maxima of Omeprazole magnesium in methanol

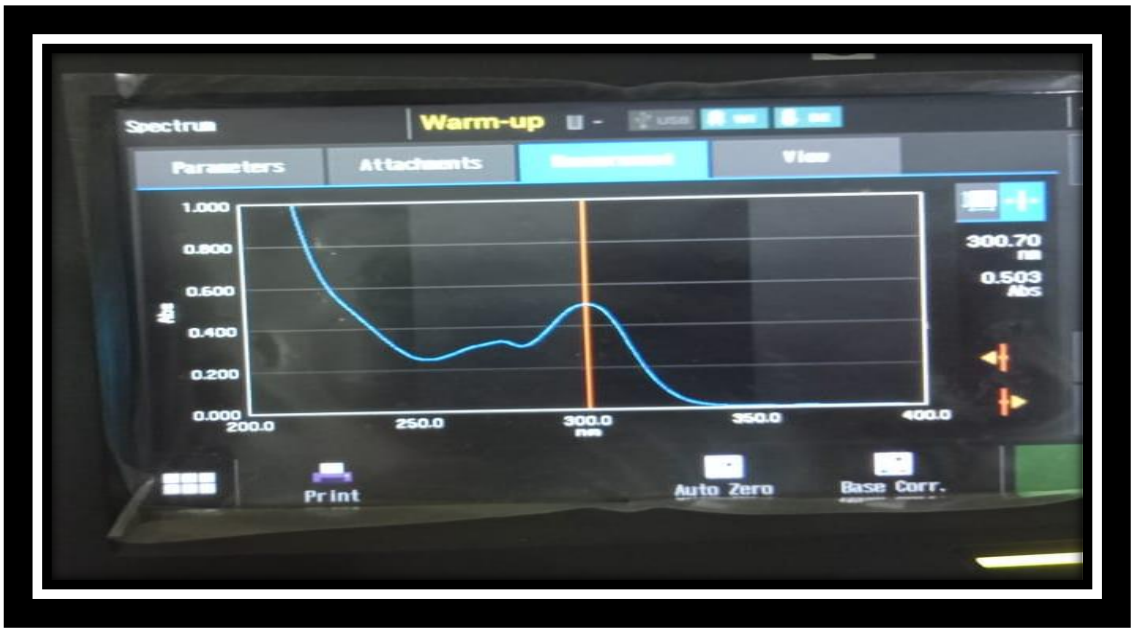


Fig no.2: Absorption maxima of Omeprazole magnesium in distilled water

Fig no. 3: Absorption maxima of Omeprazole magnesium in 0.1 N HCL

2.5 CALIBRATION CURVE OF OMEPRAZOLE MAGNESIUM

2.5.1 Calibration of Omeprazole Magnesium in methanol

Omeprazole magnesium in methanol yield characteristics curve when scanned in the UV range between 200-400 nm. The λ max for Omeprazole magnesium was found at 301 nm. Different concentrations of Omeprazole magnesium in the range 5-25 µg/ml were analyzed spectrophotometrically to obtain their respective absorbance. The data was shown in the below table.

Table no.5: Calibration curve data of Omeprazole magnesium in methanol

Sr. No.	Concentration (µg/ml)	Absorbance
1	5	0.366
2	10	0.505
3	15	0.734
4	20	0.933
5	25	1.136

The calibration curve of the drug in methanol follow Beer's lambert law. The calibration curve was shown in fig no.4.

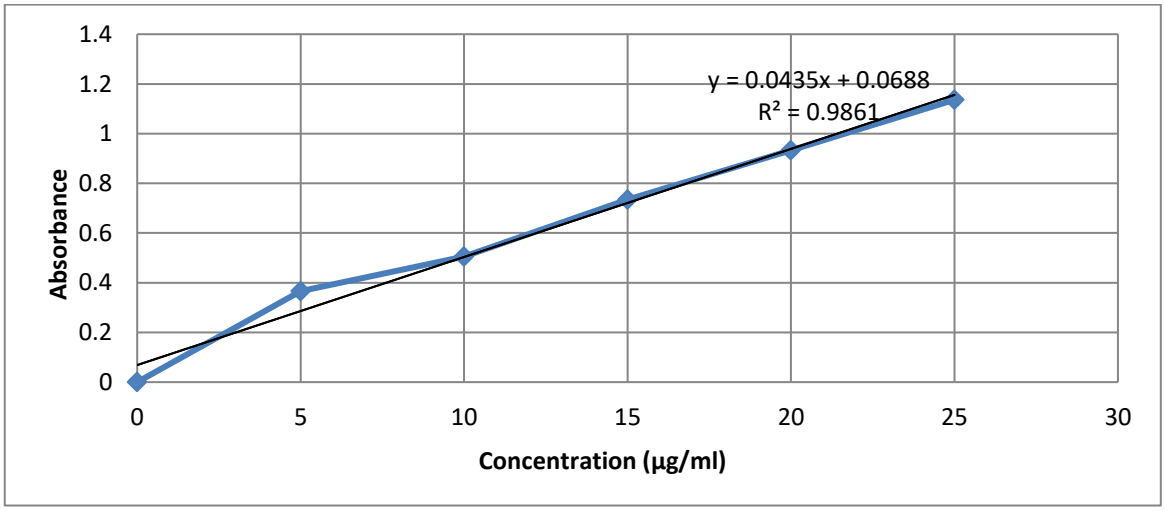


Fig no.4: Calibration curve of Omeprazole magnesium in methanol

Table no. 6: Statistical parameters related to calibration curve

Parameter	Value
Regression coefficient	0.986
Intercept	0.068
Equation of line	Y = 0.043x + 0.068

2.5.2 Calibration of Omeprazole Magnesium in distilled water

Omeprazole magnesium in distilled water yield characteristics curve when scanned in the UV range between 200-400 nm. The λmax for Omeprazole magnesium was found at 300 nm. Different concentrations of Omeprazole magnesium in the range 5-30 µg/ml were analyzed spectrophotometrically to obtain their respective absorbance.

Table no.7: Calibration curve data of omeprazole magnesium in distilled water

Sr. No.	Concentration (µg/ml)	Absorbance
1	5	0.187
2	10	0.343
3	15	0.535
4	20	0.700
5	25	0.806
6	30	1.008

The calibration curve of the drug in distilled water follows Beer's lambert law. The calibration curve was shown in fig no.5.

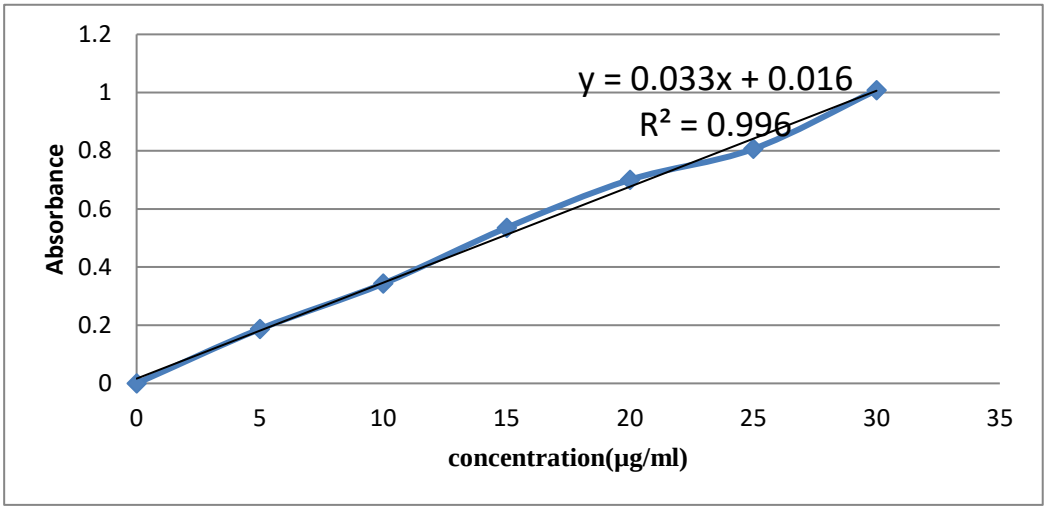


Figure no.5: Calibration curve of Omeprazole magnesium in Distilled Water

Table no.8 : Statistical parameters related to calibration curve

Parameter	Value
Regression coefficient	0.996
Intercept	0.016

Equation of line	Y = 0.033x + 0.016

2.5.3 Calibration curve of Omeprazole magnesium in 0.1 N HCL

Omeprazole magnesium in 0.1N HCL yield characteristics curve when scanned in the UV range between 200-400 nm.The λ max for Omeprazole magnesium was found at 300 nm. Different concentrations of Omeprazole magnesium in the range 5-30 µg/ml were analyzed spectrophotometrically to obtain their respective absorbance. The data was shown in the table no.9.

Table no.9: Calibration curve data of Omeprazole magnesium in 0.1 N HCL

Sr. No.	Concentration (µg/ml)	Absorbance
1	5	0.236
2	10	0.432
3	15	0.602
4	20	0.793
5	25	0.963
6	30	1.156

The Calibration curve of the drug in 0.1 N HCL was follows Beer's lambert law. The calibration curve was shown in fig no.6.

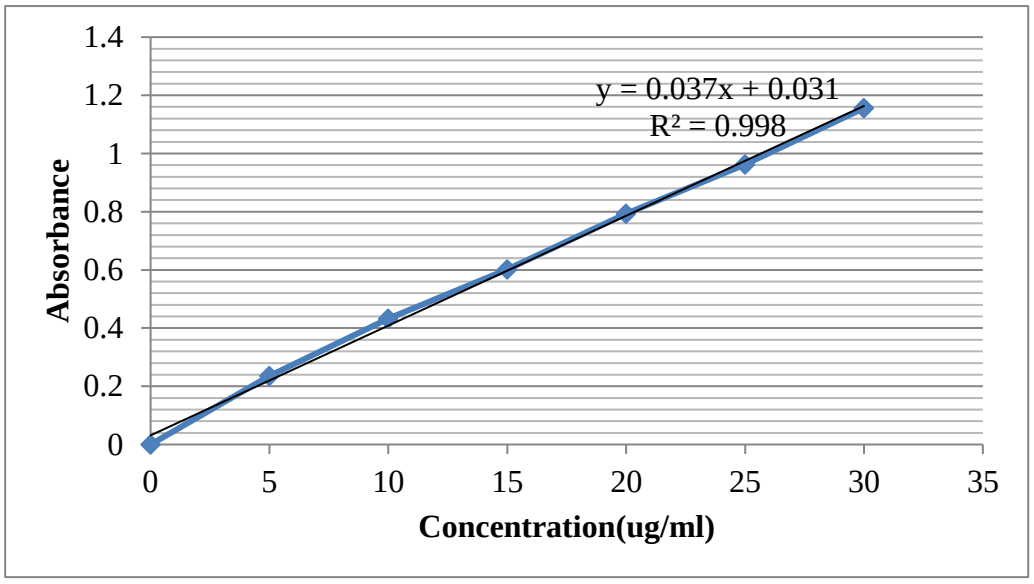


Fig no.6: Calibration curve of Omeprazole magnesium in 0.1 N HCL

Table no.10 : Statistical parameters related to calibration curve

Parameter	Value
Regression coefficient	0.998
Intercept	0.031
Equation of line	Y = 0.037x + 0.031

Discussion: The calibration curve for Omeprazole magnesium was obtained by using different concentration in different solvents. The solvents employed were methanol, distilled water and 0.1N HCL in the concentration range of 0 to 25µg/ml, 0 to 30 µg/ml and 0 to 30 µg/ml respectively. The absorbance was measured in the range from 300-301 nm.

2.6 FOURIER TRANFORM INFRARED ANALYSIS (FTIR)

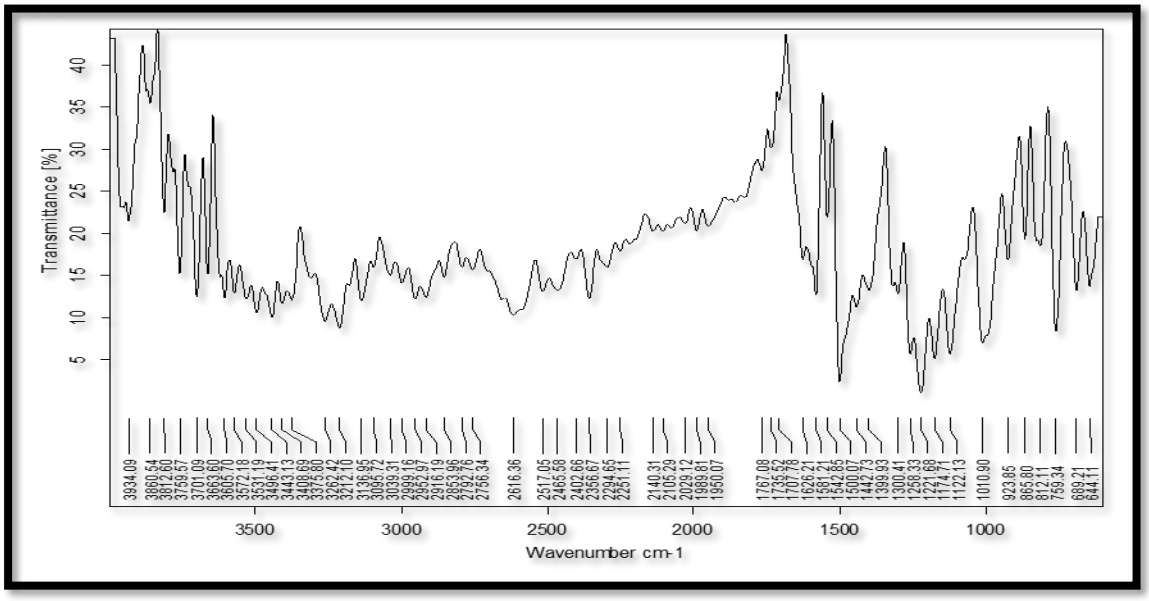


Figure no.7 : FTIR Spectra of drug Omeprazole magnesium

2.6.1 DRUG EXCIPIENT INTERACTION STUDY:

During the drug excipient interaction studied no physical changes was observed in the characteristic peak of the drug in the IR spectrum retained in the mixture. This indicates that no incompatibility has taken place between drug and excipient.

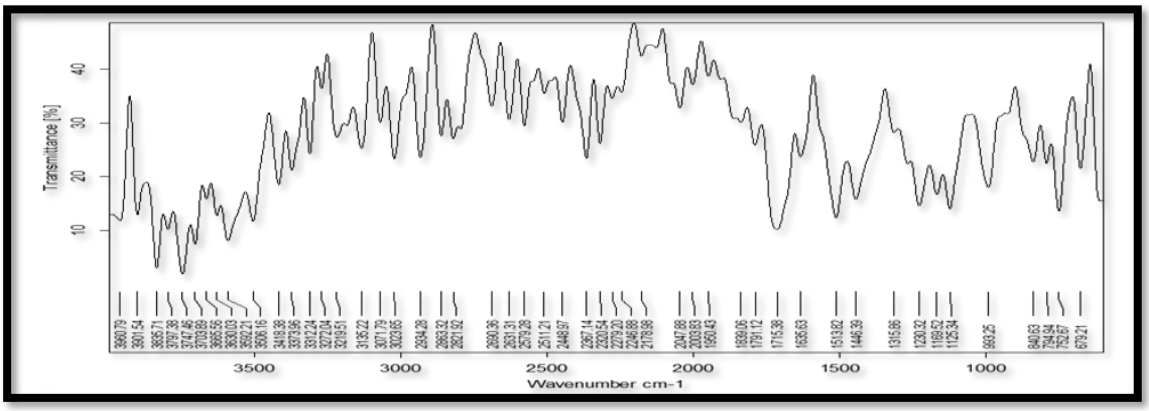


Figure no.8 : IR spectra of Omeprazole magnesium + Eudragit RS 100

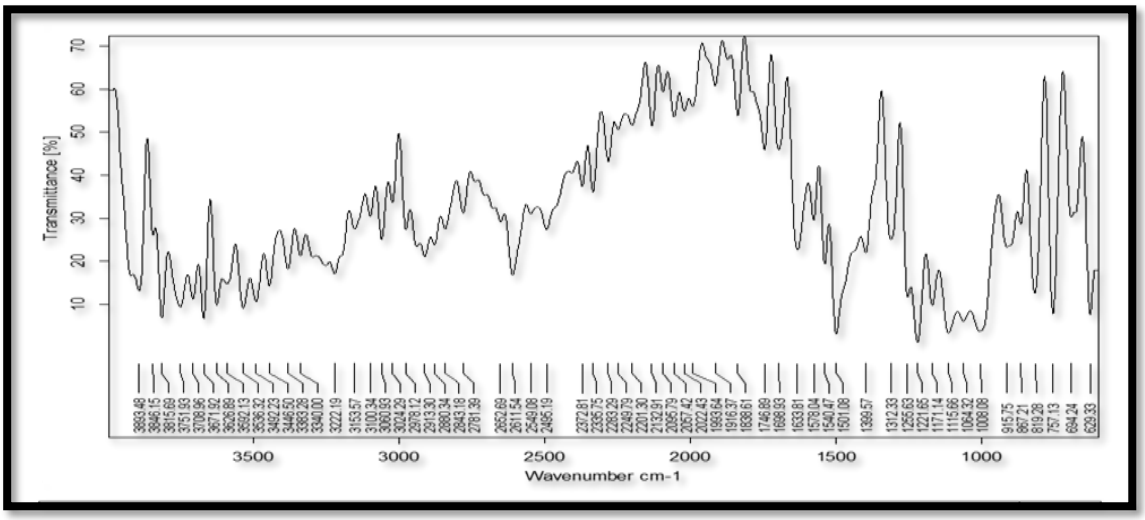


Figure no.9: IR spectra of Omeprazole magnesium + Ethyl Cellulose

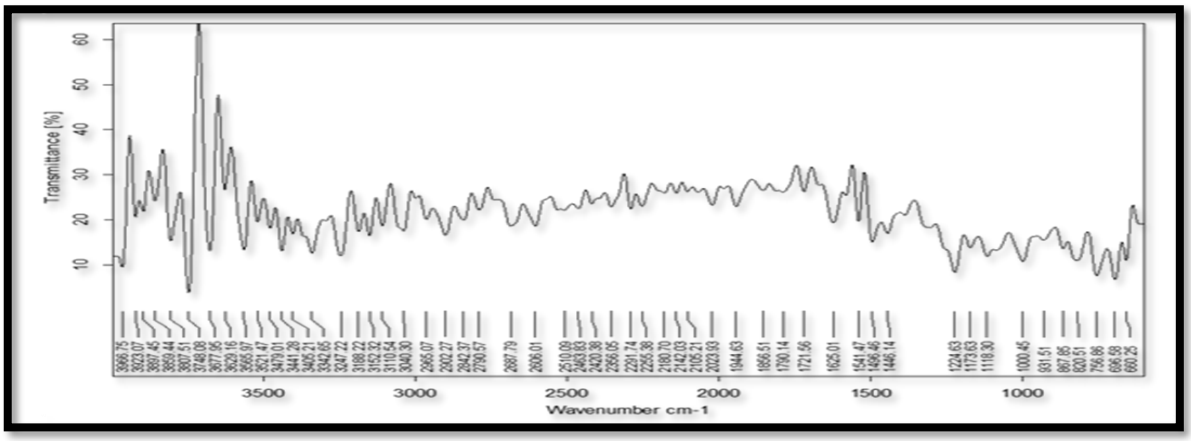


Figure no.10 : IR spectra of Omeprazole magnesium+ Polyvinyl Alcohol

2.7 EVALUATION OF OMEPRAZOLE MAGNESIUM LOADED FLOATING MICROSPONGES

1. Production yield -The production yield of all MS formulations was between 50 to 74 %. It was shown that the production yield rose along with an increase in the medication to polymer ratio.

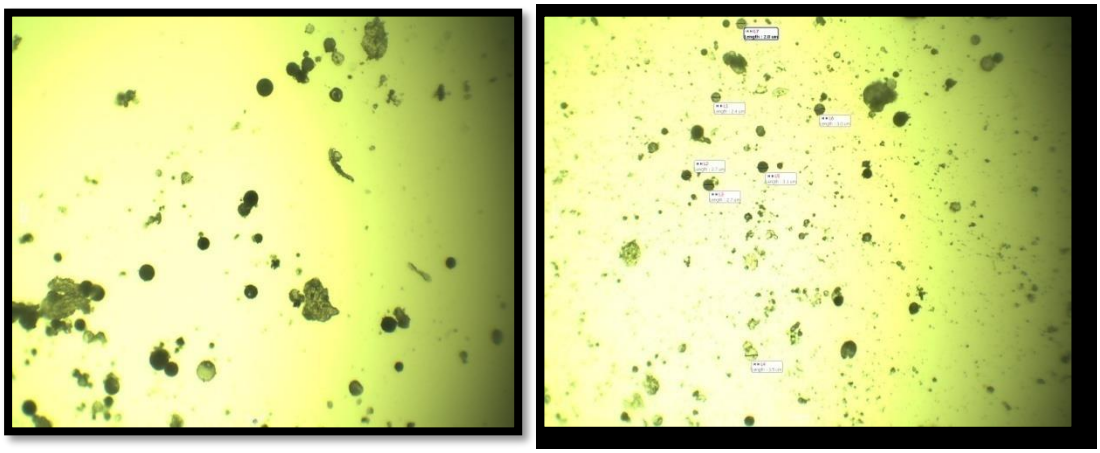
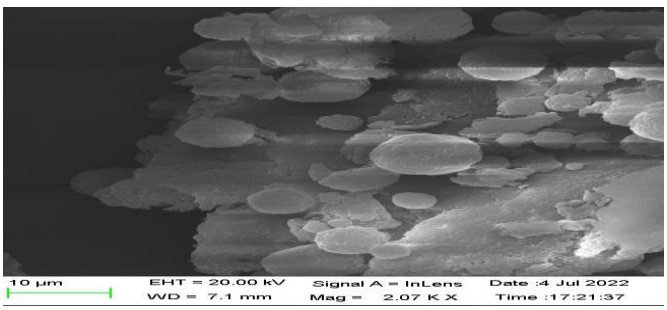


Figure no.10: Optical microscopy images of different formulations of microsponges

2. Particle size Analysis: Optical microscopy was used to analyse the particle size of prepared microsponges. The microsponges particle sizes ranged from 22.09 µm to 50.61µm. When the levels of ethyl cellulose and polyvinyl alcohol were high, the maximum particle size was visible, and when they were low, the opposite was true. The emulsion droplets could not easily be divided into smaller droplets as the PVA concentration increased, which led to the production of bigger microsponges.

3. Actual drug content and encapsulation efficiency: It was discovered that the actual amount of medication entrapped in the manufactured microsponges was less than anticipated. This might be as a result of a medicine dissolving in the solvent and/or employed aqueous phase. The effectiveness of encapsulation was unaffected by the different PVA concentrations (0.5 percent, 1.0 percent, and 1.5 percent) at the same amount of ethyl cellulose. Using the same amount of ethyl cellulose and 0.5, 1.0, and 1.5 percent of PVA, the MS1, MS2, and MS7 formulations demonstrated close entrapment efficiency (64.1, 51.6, 72.5).

4. Scanning electron microscopy: The scanning electron images of the selected formulation MS(9) were examined by SEM analysis operating at 20 kV and photographed at magnification ratio of 500x, 1500x, 2000x and 2500x.



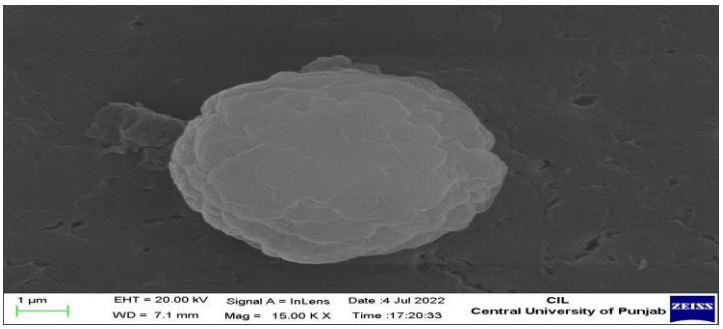


Figure no.11 : SEM study of MS 9 Formulation

Discussion: The choosen formulation MS 9 showed spherical and homogeneous dispersion in scanning electron microscopy pictures. SEM investigation revealed many pores on the microsponge surface. The many pores on the microsponge surface were created by the solvent diffusing from the emulsion droplets when MS 9 was being prepared. **4. Zeta Potential and Zeta size** :The plot displays a peak at -22 mV, indicating that the charge of the microsponge particles was this level. The particles' negative charges demonstrated their lack of interparticle attraction. The distribution was found to be highly concentrated on the negative side, demonstrating the acidic character of the ionized particles. The below-mentioned figure depicts the zeta potential and size.

Results	Mean (mV)		Area(%)	St Dev(mV)
Zeta Potential (mV) -22.5	**Peak1:** -13.7		59.1	9.94
Zeta Deviation (mV) -15.2	**Peak2:** -36.0		40.9	8.80
Conductivity (mS/cm) 4.45	**Peak3:** 0.00		0.0	0.00
Result quality	Good			

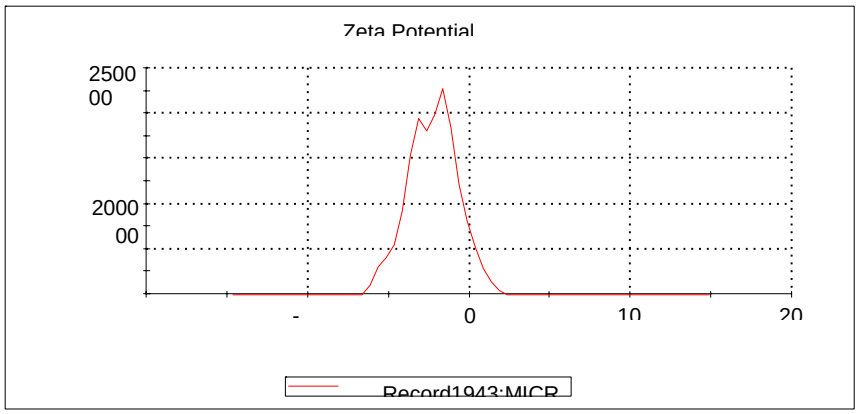


Figure no.12: Zeta Potential (mV)

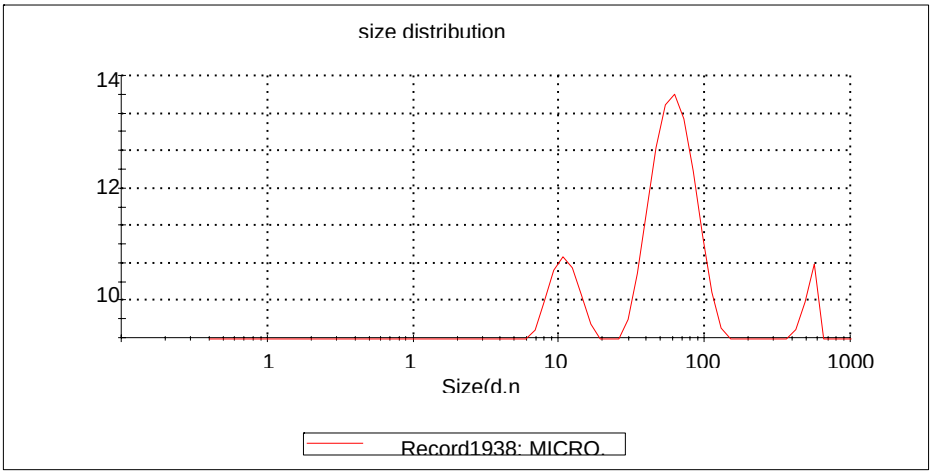


Figure no.13: Size distribution by intensity(nm)

2.8. In vitro drug release study: For in vitro dissolution study of Omeprazole magnesium microsponges, USP type II test apparatus (paddle) was used. Weighed 100 mg of Omeprazole mg microsponges was placed in 900 ml of 0.1 N HCl (dissolution medium) stirred at 25 rpm and the temperature was maintained at 37ºC± 0.5ºC. At predetermined time interval, 5ml samples were withdrawn and substituted with the same volume of fresh buffer to maintain the sink condition.The withdrawn sample was examined spectrophotometrically at 300 nm after filtration. Each sample was implemented in three times and expressed as mean values ± standard deviation

Table no.11: ***In vitro*** **release profile of MS9 microsponge formulation**

S.no.	Time (hrs)	MS9
0	0	0
1	1	6.87±0.2
2	2	13.6±0.2
3	3	18.5±0.3
4	4	35.2±0.4
5	5	45.7±0.2
6	6	51.7±0.3
7	7	57.3±0.1
8	8	62.6±0.1
9	9	64.4±0.2
10	10	67.2±0.2
11	11	72.4±0.1
12	12	75.1±0.2

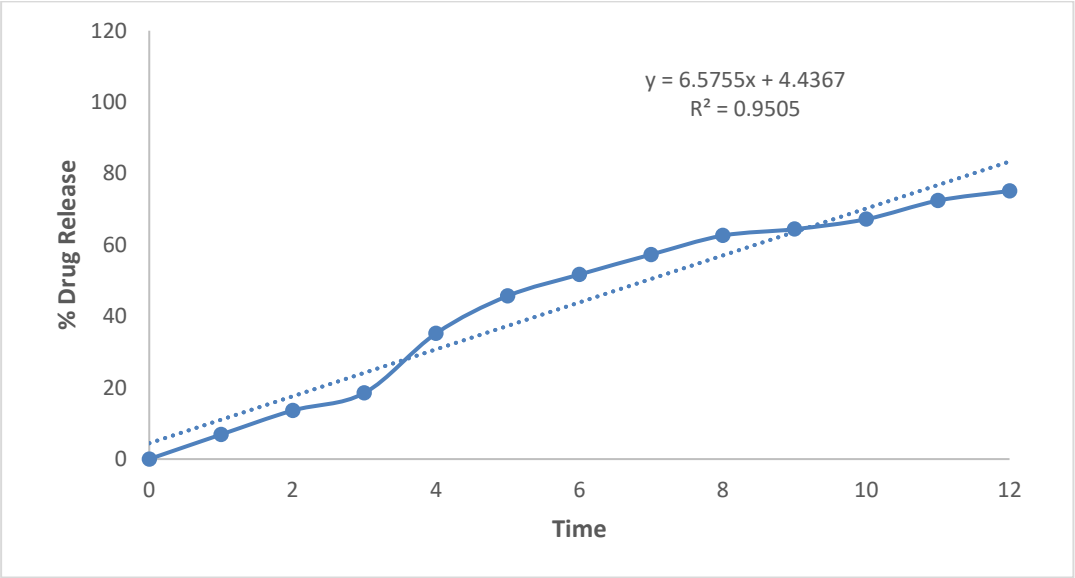


Figure.14: In vitro release profile of MS9 formulation

***2.9 In vitro* buoyancy:** The density and particle size have an impact on the microsponges' buoyancy. Microsponges' in vitro buoyancy is related to the formulations' formulations' low density (0.4 g/cc) of EC. The microsponges made with a high EC concentration floated higher than those made with a low EC concentration. In comparison to those formed with high levels of PVA, the microsponges formed with high concentrations of PVA were less buoyant. Accordingly, when the density of microsponges decreased, so did their buoyancy. Microsponges' buoyant qualities were compromised by their reduced density (1.004 g/cc) compared to SGF. The results are shown in the table below.

Table no.12 : Evaluation data of MS9 Formulation prepared by quasi emulsion solvent diffusion method

Formulation code	Product yield (%)	Particle size (µm)	Drug content (%)	Entrapment efficiency (%)	Buoyancy (%)
MS1	50	22.09	51.8	52.4	63.2±2.3
MS2	56	30.29	66.2	61.2	69±2.0
MS3	64	31.9	64.1	58.4	71±1.0
MS4	58	38.19	69.5	51.6	54.±1.0
MS5	59	27.03	58.6	65.8	72.5±2.0

MS6	73	36.72	55.9	55.1	76±2.0
MS7	49	40.25	56.9	59.2	66.9±2.3
MS8	58	45.03	69.2	63.5	72.5±1.0
MS9	74	50.61	75.2	72.5	78.3±3.0
MS10	65	42.51	74	70.6	69.2±2.0

2.10 RELEASE KINETICS

Table no.13: Showing in vitro drug release profile of MS9 formulation

Time (hrs)	**Log time (hrs)**	**Square root of time (hrs)**	**Cumulative % drug released**	**Log % cumulative drug released**	**Cumulative % drug retained**	**Log cumulative % drug retained**
0	-∞	0	0	0	100	2
1	0	1	6.87±0.2	0.83	93.1	1.96
2	0.3	1.41	13.6±0.2	1.13	86.4	1.93
3	0.4	1.73	18.5±0.3	1.26	81.5	1.91
4	0.6	2	35.2±0.4	1.54	64.8	1.81
5	0.69	2.23	45.7±0.1	1.65	54.3	1.73
6	0.77	2.44	51.7±0.3	1.71	48.3	1.68
7	0.84	2.64	57.3±0.1	1.75	42.7	1.63
8	0.9	2.82	62.6±0.1	1.79	37.4	1.57
9	0.95	3	64.4±0.2	1.8	35.6	1.55
10	1	3.16	67.2±0.2	1.82	32.8	1.51
11	1.04	3.31	72.4±0.1	1.85	27.6	1.43
12	1.07	3.46	75.1±0.2	1.87	24.9	1.39

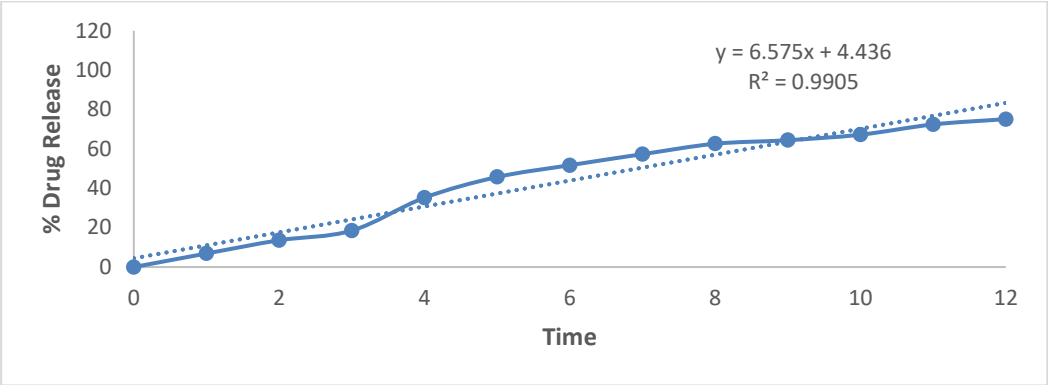


Figure no.15: Zero order release of MS9 formulation

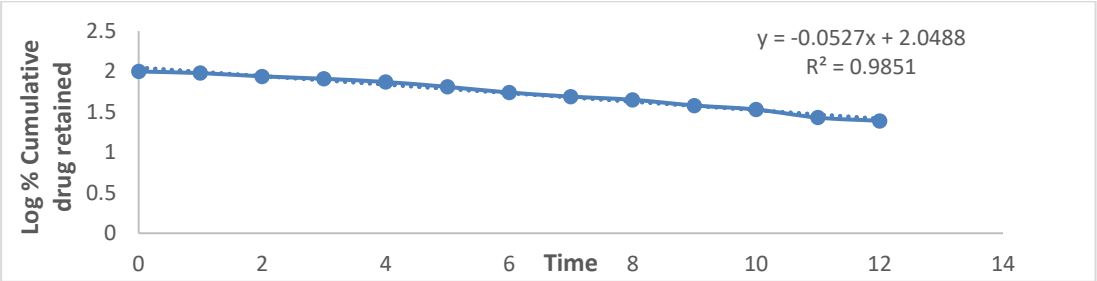


Figure no.16 : First order release of MS9 formulation

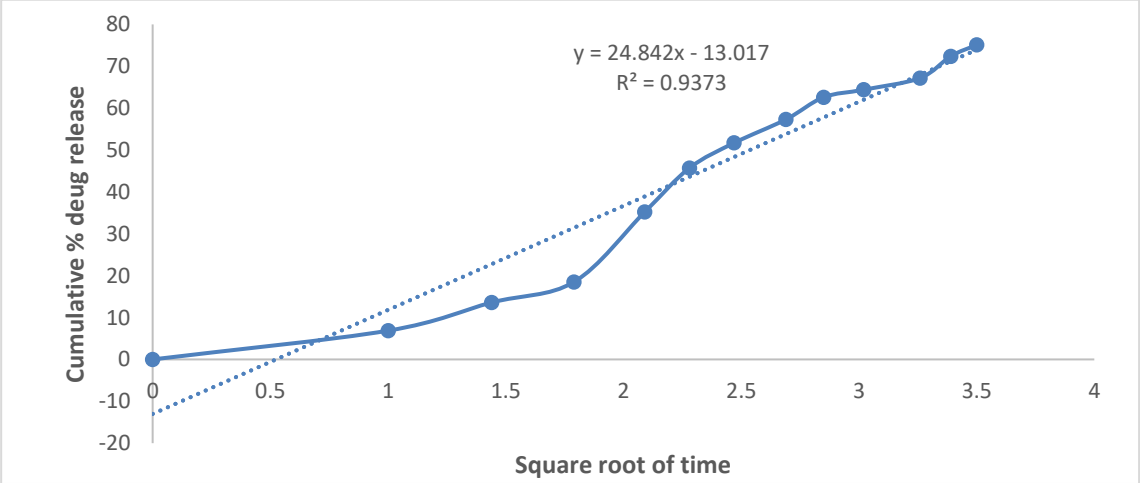


Figure no.17 : Higuchi diffusion of MS9 formulation

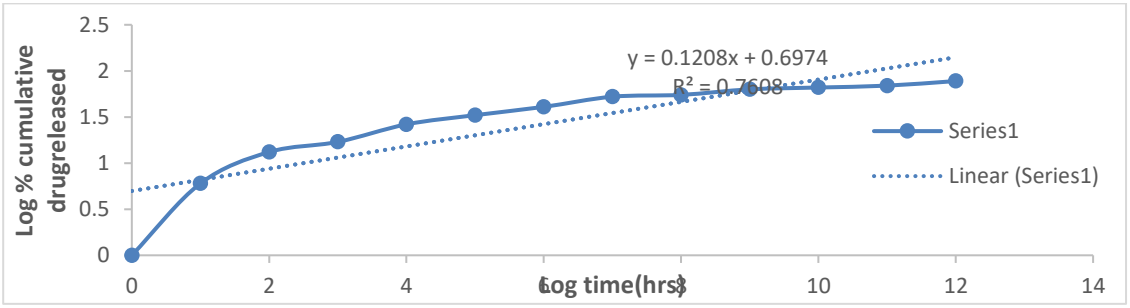


Figure no.18 : Peppas model of MS9 formulation

Kinetics of drug release from floating microsponges MS9 formulation according to different kinetic models

Formulation code	Correlation coefficient (R^2)			
	Zero order	**First order**	**Higuchi diffusion**	**Peppas Plot**
MS9	**0.9905**	**0.9851**	**0.9373**	**0.7608**

Table no.14 : Storage Conditions and sampling intervals for stability studies

Storage conditions	**Sampling intervals**
Accelerated (40°C/75% RH)	0,12,24,36,48,60,72,84 and 90 days

Table no.15 : Physicochemical evaluation of microsponge Capsule of MS9 formulation during stability study at accelerated temperatures

Times in days	**Accelerated (40C/75%RH)**	
	Physical appearance	**Drug content**
0	+	83.03
12	+	83.02
24	+	82.74
36	+	82.62
48	+	82.58
60	+	82.32

72	+	82.21
84	+	82.11
90	+	82.01

+=Good

Table no.16 : Effect of stability conditions on dissolution studies

Time (days)	**Cumulative % drug released**	
	Before storage	**After storage**
0	0	**0**
1	7.3±0.1	5.5±0.15
2	14.5±0.1	13.1±0.10
3	18.1±0.2	17.6±0.17
4	24.1±0.4	22.6±0.34
5	31.2±0.1	30.2±0.12
6	47.4±0.1	45.2±0.001
7	52.4±0.1	50.2±0.08
8	58.2±0.2	56.1±0.23
9	65.5±0.1	63.2±0.15
10	67.8±0.2	65.8±0.12
11	74.2±0.1	73.1±0.04
12	76.5±0.2	75.3±0.01

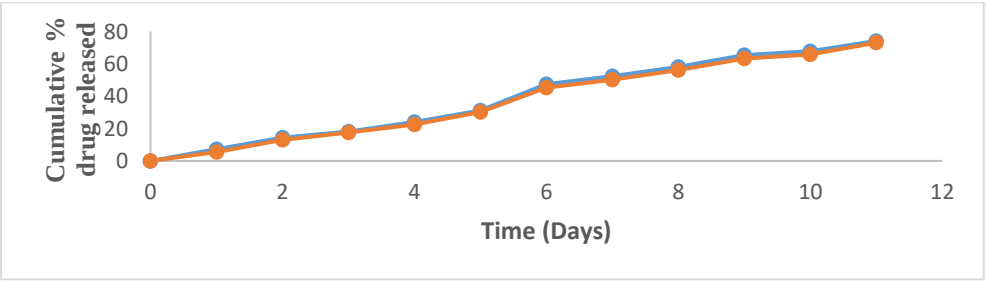


Figure no.19 : Comparison of drug release before and after stability study

The similarity factor between dissolution profiles of the formulation initially and after 3 months was found to be 86.3 which were between 50 and 100. It indicates close similarity between both the dissolution profiles.

CONCLUSION-

Due to its simplicity, patient compliance, and adaptability in formulation, oral drug delivery is one of the preferred delivery methods. Floating systems dramatically lengthen the duration of medicine release, increase patient compliance, and prolong dose intervals. These approaches increase the absorption window, retain in the stomach, and improve oral bioavailability. Omeprazole magnesium is a novel prototype agent of substituted benzimidazoles. Omeprazole magnesium is the drug that is used in the treatment of gastric ulcer, erosive esophagitis, gastroesophageal reflux disease with or without esophageal lesion. It is a highly lipophilic drug and poorly water soluble drug (BCS class II) with bioavailability of 30-40% and half life of 0.5-1 hours. The design and implementation of floating microsponges was done for the current research project. Omeprazole magnesium floating microsponges were created to enhance bioavailability, extend half-life, and prolong stomach residence duration. Microsponges are quickly evolving meadow of a unique novel drug delivery system. From the beginning, these are used for topical delivery of drugs but recently according to many researchers they are also used in oral delivery and biopharmaceutical drug administration. Microsponge technology encompass polymeric microspheres having tiny sponge like porous spherical particles with an active ingredient held in the pores. It is a versatile drug delivery system because this novel technique has many positive characteristics and remarkable advantages. First, the preformulation studies were conducted by its physicochemical properties such as melting point, UV spectrograph, and FTIR studies which were found in concordant as given the literature studies. UV spectrophotometric method was established for quantitative estimation of Omeprazole magnesium in the formulation. The absorption maxima were found to be between 300-302 nm range in different media. The compatibility study of drug and polymer was conducted and found to be compatible to each other.

After preformulation, ten formulations (MS1 to MS10) of floating microsponges of Omeprazole magnesium were prepared by Quasi Emulsion Solvent Diffusion Method. Different ratios of polymers were used for the preparation of microsponges. Eudragit RS 100 and ethyl cellulose were used as polymer. In the formulation ethyl cellulose used as buoyancy increasing agent and on the other hand Eudragit RS 100 made the polymer

permeable and used as floating purpose. Polyvinyl alcohol used as emulsifier in ratio of 0.5% w/v, 1.0% w/v and 1.5% w/v. Temperature maintained at 40℃ and rpm3000 for 1 hour.

The prepared floating microsponges were evaluated for particle size, production yield, % entrapment efficiency, % drug content, morphology and surface topography, in vitro dissolution study, in vitro buoyancy and stability studies. Out of ten batches based on above evaluation parameters, best batch was found to be MS9. The microsponges were found to be smooth and spherical with porous structure. MS9 formulation showed better entrapment efficiency and drug content prepared by using high level of ethyl cellulose (900mg) and PVA (1.5%w/v). Microsponges loaded capsules were evaluated for in vitro drug release which showed better controlled release of drug through microsponges. Stability study of prepared capsules of floating microsponges was carried out for 3 month at 45±2ºC and 75±5% RH. On the bases of this study it was considered that there was no significant change in the formulation parameter and so we can conclude that the prepared capsules are stable after 3 month study at accelerated stress conditions.

It was concluded that quasi emulsion solvent diffusion technique was a useful method for the loading of poorly soluble drugs in microsponges. Hence, floating microsponges provides controlled release of drug and enhance the bioavailability of Omeprazole magnesium. This study presents a new approach based on floating ability of microsponges for treatment of gastric ulcer.

REFERENCES

1. Tiwari A., Tiwari V., Palaria B, et al, Microsponges: a breakthrough tool in pharmaceutical research. Future Journal Pharm Sci 8, (2022).
2. Kumar Neeraj and Semimul Akhtar, Microsponges: A Futuristic approach for oral delivery and current status. Indian Journal of Public Health Research and Development, (2022) 13(2) 101-109.
3. Kumari Nidhi, Verma Shubham, Kumar Sokindra: Microsponge an advanced drug delivery system. J Clin Sci Res (2021); 10: 108-11.
4. Uppuluti Sahiti, Tanniru Lahari Sri, Teddu Raghavi et al, A Review on Microsponge drug delivery system. World Journal of Pharmacy and Pharmaceutical Sciences.(2021): Vol 10, Issue7.
5. Mahmoud A.Y, Marwa R. El-Zahry. Sulpiride gastro-retentive floating microsponges;analytical study, in vitro optimization. Journal of drug targeting.(2020):

Vol 28 issue, 4.

6. Mohammed Jafara Ashfa, Ahmed Mohsina Mohammed Saifuddin Khalid, Ranitidine hydrochloride stomach specific buoyant microsponge: Preparation, invitro characterization, and in-vivo anti-ulcer activity. Journal of Drug Delivery Science and Technology.(2020): vol. 55.
7. Darekar Avinash, Pawar Pooja, Saudagar B. Rabindranath. A Review on microsponges as emerging drug delivery system. JDDT(2019):Vol 9 Issue3 793- 801.
8. Sunil T.G, Killedar S.G, Saboji JK, Imrankhan M.B, Vivek P.K, Nilesh N.G and Bhagwat D.A. Floating Microsponges as Gastro Retentive Drug Delivery System Containing Lafutidine to Treat Gastric Ulcer.Acta Scientific Pharmaceutical Sciences. (2019): 3(2).
9. Buddhabhushan V. Bansod, Roshani B. Khairnar, Kajal L. Sonawane, Microsponge: An Innovative and Novel Strategy for Drug Delivery System. International Journal of ChemTech Research.(2019): 12(5): 299-3.
10. Resmi D S, Preetha Mathew, Asha P. Dev, Elssey Abraham. Formulation and Evaluation of Topical Econazole Nitrate Microsponge Loaded Hydrogel.International Journal of Pharmaceutical Research. (2018): Vol; 12(1).
11. Mowafaq M. Ghareeb, Improvement of Rebamipide Solubility via optimized Microsponge formulation, J. Pharm. Sci. & Res., (2018); 10(6): 1525-1529.
12. S.S. Patel, M.R. Patel, M.J. Patel. Formulation and Evaluation of Microsponge Based Nicorandil Sustained Released Tablet. Journal of Scientific Research.(2017): 9(3), 285-296.
13. Mahmoud H Othman, Gamal M Zayed et al, Preparation and Evaluation of 5-

Fluorouracil Loaded Microsponges for Treatment of Colon Cancer, J Cancer Sci.

Ther (2017), 9:1.

14. Afrasim Moin, Tamal K. Deb, Riyaz Ali M. Osmani et al, Fabricationcharacterization, and evaluation of microsponge delivery system for facilitated fungal therapy, Journal of Basic and Clinical Pharmacy; (2016): 7(2).
15. Dhruvi Patel, Dipti Gohil, Dinal Patel, Harshal Sheth, Snehal Patel , Kartik Pandya, Chainesh Shah. formulation and evaluation of floating microsponges ofallopurinol.an international journal of pharmaceutical sciences. (2016); 7(3).

16. Smita Raghuvanshi and Kamla Pathak. Bioadhesive floating microsponges of cinnarizine as novel gastroretentive delivery: Capmul GMO bioadhesive coating versus acconon MC 8-2 EP/NF with intrinsic bioadhesive property. International Journal of Pharmaceutical Investigation. December 28, (2016), IP: 103.38.70.26.

17. Chaitali R Bhandare and Suvarna A Katti, formulation of microsponges of Risperidone hcl, IJRPC (2016), 6(3), 518-527.

18. JenanM. Mohsinal Mosawi.Formulation& invitro evaluation of clarithromycin floating microsponge capsule.karbala journal of pharmaceutical sciences,(2016); 7(11); 27-35.

19. Riyaz Ali M Osmani, Nagesh Aloor, Bharathi Thaware, Parthasarrathi Kulkarni. Microsponges based novel drug delivery system for augmented Arthritis therapy. Saudi Pharmaceutical Journal.(2015): 1-11.

20. Ramadevi Bhimavarapu, Karuna Priya Chitra, Karunkiran P, Raviteja G, Meharagavendra Y, Sundaramma. S. Itraconazole loaded microsponges- A novel carrier system. International Journal of Inventions in Pharmaceutical sciences. (2015); 3(1): 953-957.

21. Atmaram P Pawar, Aditya P Gholap, Ashwin B Kuchekar, C Bothiraja and Ashwin J Mali. Formulation and Evaluation of Optimized Oxybenzone Microsponge Gel for Topical Delivery.Hindawi Publishing Corporation Journal of Drug Delivery.(2015): 1-9.

22. Ratnaparakhi D.U., Patil S.S., Patil S.V., Formulation and Evaluation of microsponge of benzoyl peroxide by Quasi emulsion solvent diffusion method, International journal of Pharmaceutical Research(2014): Apr-Jun2015;7(2).

23. Hamid Hussain, Archana Dhyani, Divya Juyal, Abhishek Bahuguna.Formulation and evaluation of gel-loaded microsponges of diclofenac sodium for topical delivery. The Pharma Innovation Journal (2014); 3(10): 58-63.

24. Chainesh Shah, Dhiren Shah. Design and optimization of fluconazole microspongescontainingethyl cellulosefortopicaldeliverysystem using Quality by design approach. An International Journal of Pharmaceutical Science (2014); 5(3): 95-133.

25. Roaa Nief and Ahmed Hussein. Preparation and Evaluation of Meloxicam Microsponges as Transdermal Delivery System .Iraqi Journal of Pharmaceutical Sciences.(2014); 23(3):63-74.

26. Ahmed Abbas Hussein. Preparation and Evaluation of Oral Microsponge Drug DeliverySystem ofKetoconazole.American Journal ofPharmaceutical Sciences. (2014); 14(1):1-8.

27. Sha-Sha Li ,Guo-Feng Li ,Li Liu et al. Evaluation of Paeonol Skin-Target Delivery from Its Microsponge Formulation: In Vitro Skin Permeation and In Vivo Microdialysis, PLOS ONE 8(11):e79881doi:10. 1371/journal.pone.0079881.

28. Ravi R, Senthil Kumar SK, Parthiban S. Formulation and evaluation of the microsponges gel for an anti-acne agent for the treatment of acne. Indian Journal of Pharmaceutical Science and Research. (2013); 3(1): 32-38.

29. Mohan Kumar V, Veena N M, Manjula BP. Formulation and evaluation of microsponges for topical drug delivery of Mupirocin. International Journal of Pharm Tech Research. (2013);5(3): 1434-1440.

30. Markand Mehta, Amish Panchal, Viral H Shah, Umesh Upadhyay. Formulation and in-vitro evaluation of controlled release microsponge gel for topical delivery of Clotrimazole.International Journal of Advanced Pharmaceutics. (2012); 2(2): 93-101.

31. Yerram Chandramouli, Shaikh Firoz, B. Rubia Yasmeen et al, microsponges: a novel drug delivery system for controlled delivery of topical drugs, International Journal of Pharmaceutical Research & Analysis, (2012):2(2); 79-86.

32. Swetha A, Gopal Rao M, Venkata Ramana K, Niyaz Basha B and Koti Reddy V. Formulation and in- vitroevaluation ofEtodolacentrapped in microsponge based drug delivery system. International Journal of Pharmacy. (2011); 1(2): 73-90.

33. Saroj Kumar Pradhan, Microsponges as the versatile tool for drug delivery system, IJRPC (2011),1(2).

34. VikasJain and Ranjit Singh.Dicyclomine-loaded Eudragit–based Microsponge with Potential for Colonic Delivery: Preparation and Characterization. Tropical Journal of Pharmaceutical Research.(2010); 9(1):67- 72.

35. Majeti N.V. Ravi Kumar.A review of chitin and chitosan applications. Reactive & Functional Polymers 46 (2000) 1–27.