IJPSR (2017), Vol. 8, Issue 2 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 08 August, 2016; received in revised form, 13 September, 2016; accepted, 17 November, 2016; published 01 February, 2017

DEVELOPMENT AND CHARACTERIZATION OF FLOATING MICROSPHERES OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE BY SOLVENT EVAPORATION METHOD

Maina Chouhan *, A.V. S. Chundawat and C. S. Chauhan

B. N. Institute of Pharmaceutical Sciences, Udaipur, Rajasthan, India.

Keywords:

EMT, HPMC, CA, Carbopol 940, Eudragit L 100, Floating Microspheres

Correspondence to Author:
Maina Chouhan

B. N. Institute of Pharmaceutical Sciences, Udaipur, Rajasthan, India.

Email: chundawat.aditya@gmail.com

ABSTRACT: The objective of this research was to develop and characterize floating microspheres of esomeprazole magnesium trihydrate by solvent evaporation method using various polymers. The esomeprazole magnesium trihydrate floating microspheres was successfully developed by solvent evaporation method using HPMC, CA, Carbopol 940, Eudragit L 100 in various proportions. Further, the prepared floating microspheres were characterized for particle size, morphology, micrometric studies, entrapment efficiency, in vitro drug release, release kinetics, compatibility studies (FTIR), SEM and DSC studies. The EMT microspheres were free-flowing. The mean particle size ranged from 100.08±0.95 to 500.42±1.03µm and the entrapment efficiency ranged from 67.11±3.01 to 96.38±2.34%. SEM revealed a hollow spherical structure of microspheres with a smooth surface morphology and the internal surface was porous due to the evaporation of solvent entrapped within the shell of microspheres. The IR Spectrum obtained from EMT and polymers were identical and there was no change in the functional group absorption of any molecule present in formulated product. Formulation F9 was found to be highest *in-vitro* buoyancy 94.95±1.43. Amongst the formulation, F9 was found to be the best formulation as it release EMT 94.60% in a sustained manner. The results obtained was clearly indicated that prepared floating microspheres of EMT may prove to be potential candidate for safe and effective sustained drug delivery over an extended period of time which can reduce dosing frequency.

INTRODUCTION: Floating drug delivery systems were first described by Davis in 1968. It is possible to prolong the gastric residence time of drugs using these systems [1]. Several techniques are used to design gastro retentive dosage forms. These include floating, swelling, inflation, adhesion, high-density systems and low density systems that increase the gastric residence time. Gastric retention is useful for drugs which (i) act locally; (ii) have a narrow absorption window in the small intestinal region; (iii) unstable in the intestinal environment; (iv) low solubility at high pH environment.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.8(2).686-97

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.8 (2).686-97

Various dosage forms developed for gastric retention include, floating tablets, floating beads, pellets, floating granules, floating microspheres [2].

The synthetic polymers have been used to prepare floating Microsphere of various drugs. These Microspheres exhibited good *in vitro* floatability but showed drastically decreased drug release with increasing polymer concentration. Many researchers reported work on floating microsphere using different polymer [3].

Proton pump inhibitors (PPIs) are the most potent inhibitors of gastric acid secretion and are effective for treating all gastric acid-related disorders. EMT is indicated for the treatment of gastroesophageal reflux disease in adults and children; risk reduction of NSAIDs associated gastric ulcer, *H. pylori* eradication and control of pathological hypersecretory conditions associated with Zollinger-Ellison syndrome.

Peptic ulcers are open sores that occur on the inside lining of human esophagus (esophageal ulcers), stomach (gastric ulcers) and the upper portion of small intestine i.e. Duodenum (duodenal ulcers). A physiologic imbalance between peptic acid secretion and gastro duodenal mucosal defense causes ulcers [4].

In the present study EMT was selected as the payload model drug to treat the peptic ulcer. EMT is a proton pump inhibitor with a bioavailability of 50- 90%. Its metabolism is mainly by liver and excretion by renal and fecal. It acts by irreversibly blocking the (H+K+) ATPase enzyme system of the gastric parietal cell. Its half-life is 1-1.5 hrs with poor absorption may be because of degradation and poor solubility. The solubility and absorption can be improved with an increase in the gastric residence time and also by creating basic pH with incorporation of carbon dioxide [5].

MATERIALS AND METHODS: Esomeprazole magnesium trihydrate was obtained as a gift sample from Torrent Pharmaceutical Ahmadabad (Gujarat). Carbopol 940, CA, Liquid Paraffin, Acetone were obtained from Loba Chemie Pvt. Ltd. Mumbai. Eudragit L 100 was obtained from Chemdyes corporation. HPMC were obtained from hi media laboratories Pvt. Ltd. Mumbai. All other chemicals and reagents were of analytical grade were used without further purification.

Instruments used:

S. No.	Name	Supplier/manufacturer
1.	Digital Balance	ROY Electronics, Varanasi
2.	pH Meter	HANNA Instruments, Mauritius
3.	Magnetic Stirrer	IEC 35 A-Type, Mumbai
4.	Mechanical Stirrer	Remi (RQ-122) Motors Ltd., Mumbai
5.	UV Spectrophotometer	ThermoSpectronic UV1, UK
6.	Objective Micrometer	Erma O-KYO
7.	Scanning Electron Microscopy	Jeol 5400, Japan
8.	FTIR	Bruker Alpha Model, Germany

Preperation Method of Esomeprazole Floating Microspheres:

Solvent Evaporation Technique: In this technique, drug and polymer (CA, HPMC, Carbopol 940, Eudragit L 100) were dissolved in a 20 ml. acetone which placed in small beaker with magnetic bead on magnetic stirrer at room temperature. The drug-polymer mixture was poured into 100 ml. liquid paraffin containing Span 60 maintained at a temperature of 30-40°C and subsequently stirred by mechanical stirrer at ranging agitation speed for 60 minutes to allow the volatile solvent to evaporate. The microspheres formed were filtered, washed with n-hexane and air-dried for 24 hours and stored in dessicator.

TABLE 1: COMPOSITION OF PREPARED FLOATING MICROSPHERES

S.No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	Drug(mg.)	50	50	50	50	50	50	50	50	50
2.	CA(mg.)	500	500	500	500	500	500	500	500	500
3.	EudragitL100(mg.)	250	500	750	_	_	_	_	_	_
4.	Carbopol 940(mg.)	_	_	_	250	500	750	_	_	_
5.	HPMC(mg.)	_	_	_	_	_	_	250	500	750
6.	Acetone(ml.)	20	20	20	20	20	20	20	20	20
7.	Liquid Parrafin(ml.)	100	100	100	100	100	100	100	100	100

Characterization of Microspheres: [19]

1. Particle size analysis: Particle size of floating microspheres is determined by using an optical microscopy and size distribution is carried out by sieving method. This is useful in the determination of mean particle size with the help of calibrated ocular micrometer.

2. Tapped density, compressibility index and hausner's ratio: The tapping method is used to

determine the tapped density and percentage compressibility index as follows:

$$\text{Tapped density} = \frac{\text{Mass of microspheres}}{\text{Volume of microspheres after tapping}}$$

$$\%\ \text{compressibility} = \left[1 - \frac{V}{Vo}\right] \times 100$$

Where *V* and *Vo* are the volumes of the sample after and before the standard tapping, respectively.

Hausner's ratio: Hausner's ratio of floating microspheres is determined by comparing the tapped density to the fluff density using the equation.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Fluff density}}$$

TABLE 2: COMPRESSIBILITY INDEX, FLOW CHARACTERS AND HAUSNER'S RATIO [19]

Compressibility Index (%)	Flow Characters	Hausner's Ratio
≤ 10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
32-38	Very poor	1.46-1.59
≥38	Very-very poor	≥1.60

3. Percentage Yield: Percentage yield of floating microspheres is calculated by dividing actual weight of product to total amount of all nonvolatile components that are used in the preparation of floating microspheres and is represented by following formula:

$$\%\ \text{Yield} = \frac{\text{Weight of hollow microspheres}}{\text{Weight of drug taken} + \text{total polymer weight}} \times 100$$

4. Buoyancy studies: *In vitro* floating tests can be performed in USP type II dissolution test apparatus by spreading the floating microspheres on a simulated gastric fluid (pH 1.2) containing the surfactant. The media is stirred at 100 rpm at 37± 0.5°C. After specific intervals of time, both the fractions of microspheres (floating and settled microspheres) are collected and buoyancy of the floating microspheres is determined by using formula:

$$\text{Buoyancy (\%)} = \frac{Qf}{Qf + Qs} \times 100$$

Where, Qf and Qs are the masses of floating and settled hollow microspheres, respectively.

5. Drug entrapment efficiency: Estimation of drug content in floating microspheres can be carried out by dissolving the weighed amount of crushed microspheres in required quantity of 0.1 N HCl and analyzed spectrophotometrically at a particular wavelength using the calibration curve. Each batch should be examined for drug content in a triplicate manner. The entrapment efficiency of floating microspheres is calculated by dividing the actual drug content by the theoretical drug content of microspheres.

$$\%\ \text{drug entrapment} = \frac{\text{Calculated drug concentration}}{\text{Theoritical drug content}} \times 100$$

6. Surface morphology: Surface characteristics of floating microspheres are analyzed using a scanning electron microscopy. Samples are coated with gold dust under vacuum prior to observation. Cross sections should be made in order to observe the core and internal structure of the microspheres. These studies are useful in the examination of internal and external morphology of floating microspheres.

7. *In-vitro* drug release studies: Release rate of drug from hollow floating microspheres is determined using USP dissolution apparatus type I or type II at 37± 0.5 °C. The dissolution test is carried out using 900 ml. of 0.1 N HCl dissolution medium at 100 rpm for the required period of time. At an appropriate interval, specific volume of aliquots are withdrawn and replaced with an equivalent volume of fresh dissolution medium to maintain the constant volume of dissolution medium. The sample solutions are filtered through Whatman filter paper and solutions are analyzed using UV spectrophotometer.

RESULTS AND DISCUSSION: In the present study floating microspheres of EMT were prepared. The EMT drug was identified and characterized as per requirement of the Indian Pharmacopoeia, 2010. The physical appearance was determined by visual examination.

TABLE 3: ORGANOLEPTIC STUDY

S.No.	Properties	Results
1	Description	Powder
2	Odour	Odourless
3	Colour	Off-white

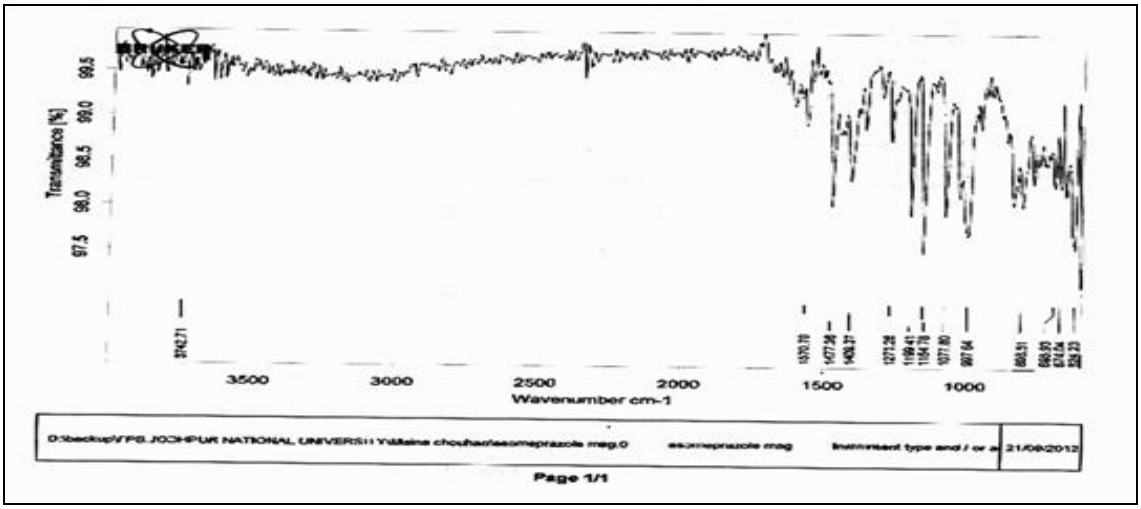


FIG. 1: IR IDENTIFICATION OF DRUG

TABLE 4: IR INTERPRETATION OF DRUG

S.No.	Functional Group	IR Absorbance (cm^{-1}) (Theoritical)	IR Absorbance (cm^{-1}) (Observed)
1	S=O str.	980-1225	1077.80
2	C-N str.	1250-1335	1271.28
3	C-H band.	675-900	808.51

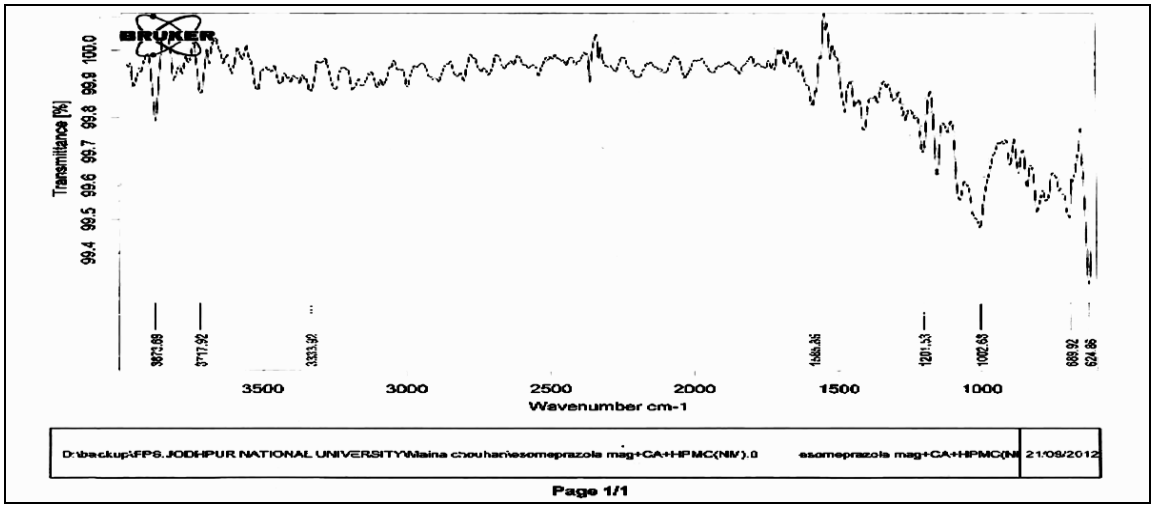


FIG. 2: DRUG-EXCIPIENTS COMPATIBILITY DRUG+HPMC+CA (1:1:1)

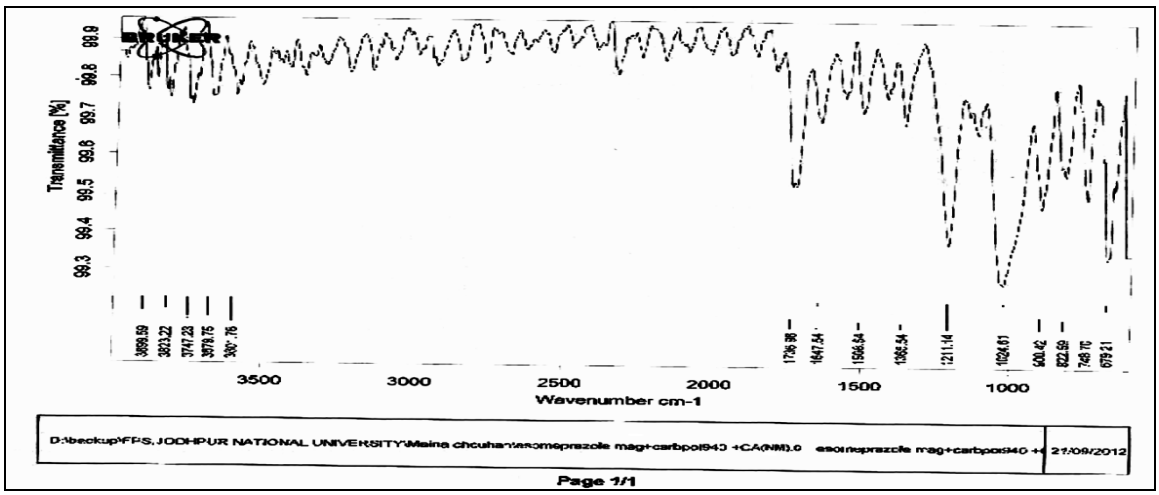


FIG. 3: DRUG-EXCIPIENTS COMPATIBILITY DRUG+ CARBOPOL 940+CA (1:1:1)

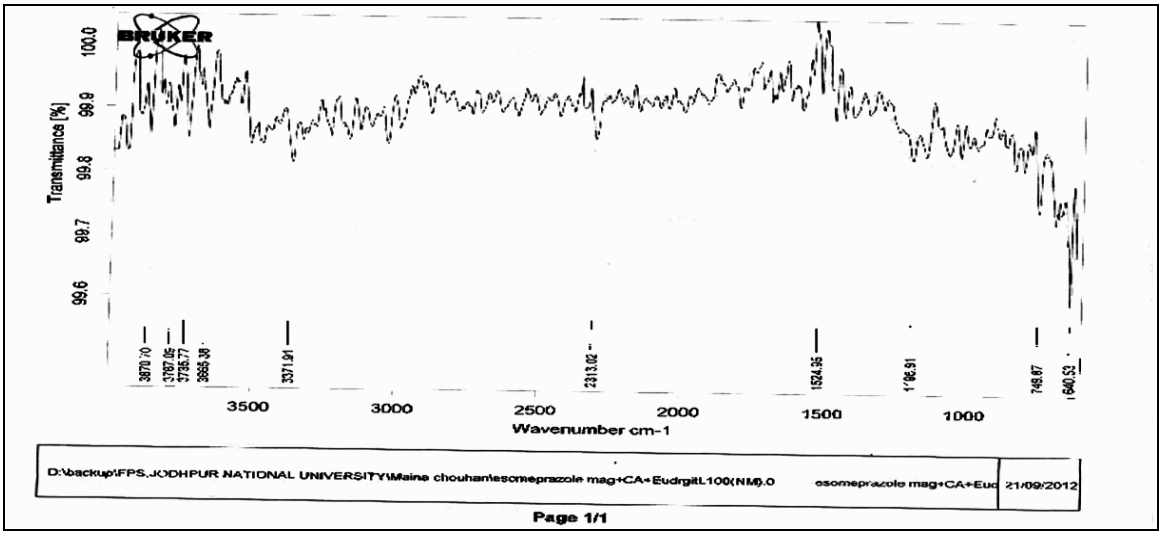


FIG. 4: DRUG-EXCIPIENTS COMPATIBILITY DRUG+EUDRAGIT L100+CA (1:1:1)

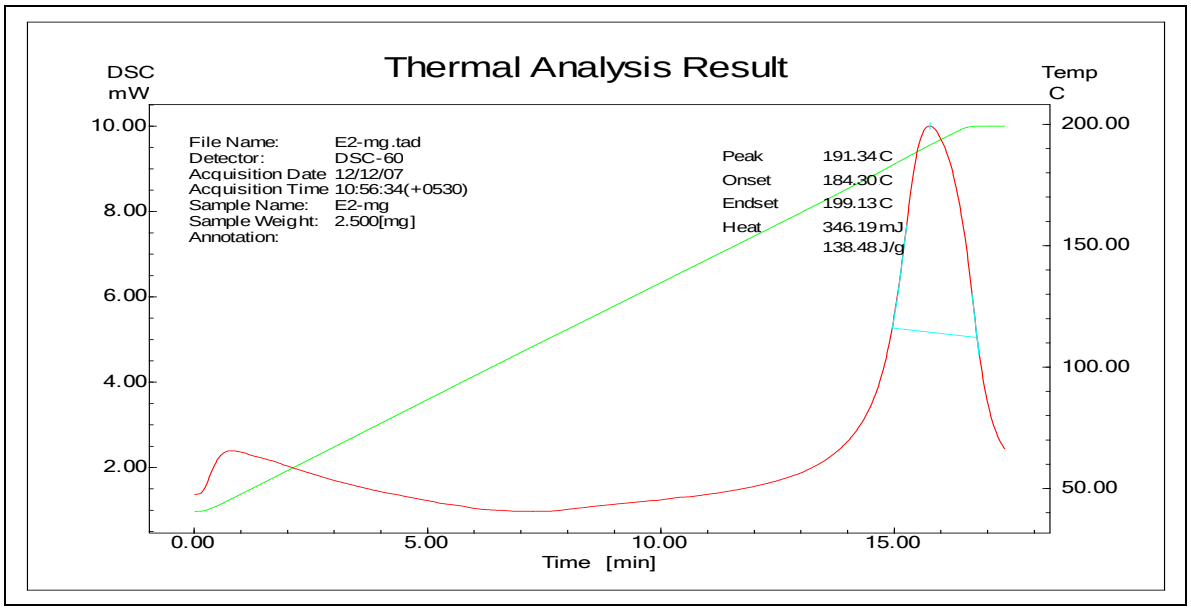


FIG. 5: DSC IDENTIFICATION OF DRUG

TABLE 5: MELTING POINT DETERMINATION

S.No.	Reading in thermometer(°C)
1.	177-179°C

TABLE 6: PARTITION COEFFICIENT VALUES OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE

S.No.	Solvent System	Partition Coefficient
1.	n-Octanol : Distilled water	0.649

TABLE 7: CALIBRATION DATA OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE IN SGF

S.No.	Concentration(µg/ml)	Absorbance(nm)
1.	0	0.000
2.	2	0.124
3.	4	0.225
4.	6	0.351
5.	8	0.485
6.	10	0.612
7.	12	0.722
8.	14	0.825
9.	16	0.955

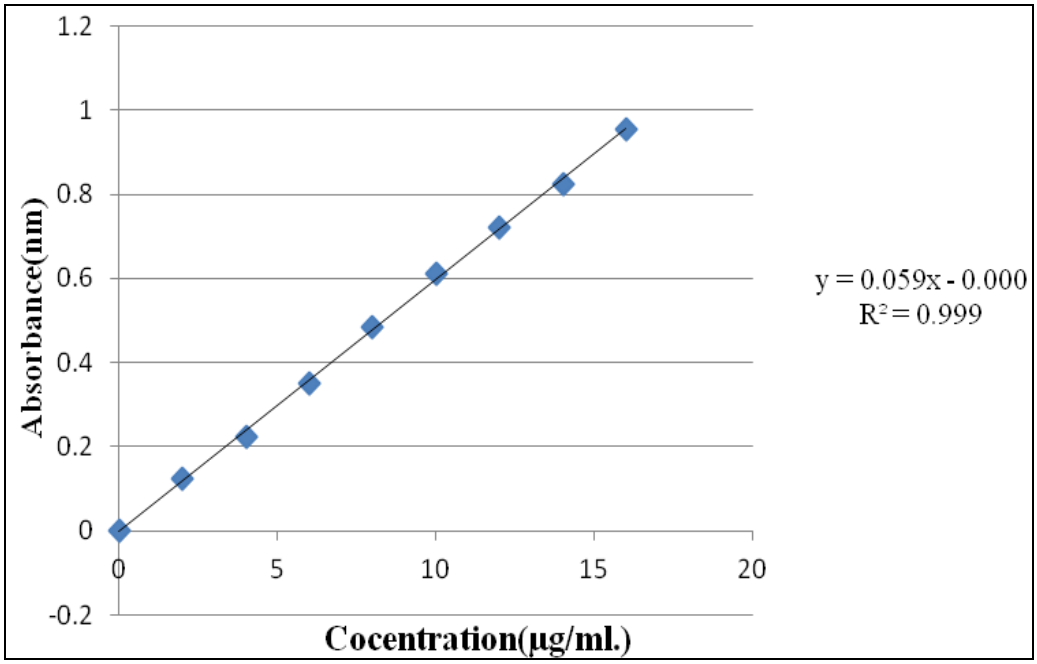


FIG. 6: CALIBRATION CURVE OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE IN SGF

TABLE 8: STATISTICAL PARAMETERS RELATED TO STANDARD CURVE

Parameters	Values
Correlation coefficient	0.999
Equation of line	0.059x-0.000

DISCUSSION: UV spectrum of Esomeprazole Magnesium Trihydrate in Simulated Gastric Fluid showed that the drug has λ xam at 215 nm**.** The calibration curve of EMT was prepared in Simulated Gastric Fluid. The slope of the calibration curve is as follows and the solution follows Beer's law in the range of 2-20µg/ml.

TABLE 9: VALUES OF TOTAL WEIGHT OF FORMULATIONS

S. No.	Formulation Code	Total Weight
1	F1	0.6241 mg.
2	F2	0.8288mg.
3	F3	1.0189 mg.
4	F4	0.5699 mg.
5	F5	0.9214 mg.
6	F6	1.1287 mg.
7	F7	0.5215 mg.
8	F8	1.2026 mg.
9	F9	1.4361 mg.

Table 10: Particle Size of Prepared Microspheres

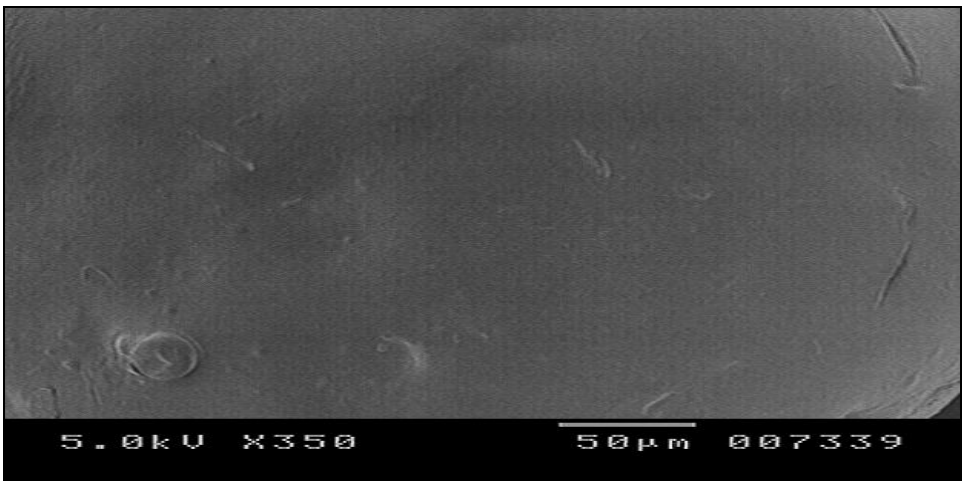
S.No.	Formulation Code	Average Particle Size (µm)
1	F1	100.08±0.95
2	F2	160.24±0.78
3	F3	310.32±0.20
4	F4	200.51±1.23
5	F5	300.08±1.16
6	F6	500.42±1.03
7	F7	180.67±0.36
8	F8	240.33±0.54
9	F9	300.18±0.98

TABLE 11: VALUES OF ANGLE OF REPOSE, CARR'S INDEX AND HAUSNER'S RATIO AS AN INDICATION OF FLOW PROPERTIES OF PREPARED MICROSPHERES

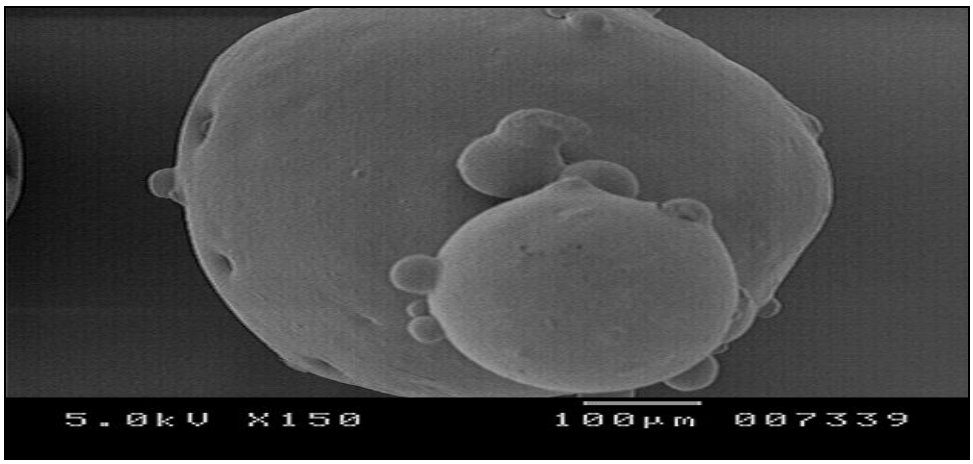
F. Code	Bulk density (g/cm3)	Tapped density (g/cm3)	Angle of Repose (ɵ)	Carr's Index (%)	Hausner's Ratio
F1	0.36±0.03	0.30±0.02	20.60±0.10	14.34±2.11	0.83±0.03
F2	0.38±0.05	0.32±0.05	20.58±0.21	15.92±0.24	0.84±0.01
F3	0.40±0.06	0.34±0.01	20.32±0.42	16.23±0.56	0.85±0.04
F4	0.35±0.01	0.31±0.04	24.54±0.50	14.78±0.86	0.88±0.01
F5	0.37±0.13	0.33±0.03	24.31±0.42	14.96±2.18	0.89±0.02
F6	0.38±0.02	0.34±0.12	24.22±0.63	15.78±0.32	0.89±0.05
F7	0.41±0.11	0.35±0.05	22.34±0.45	13.05±3.36	0.85±0.04
F8	0.42±0.03	0.36±0.01	22.15±0.71	14.26±2.15	0.86±0.03
F9	0.44±0.05	0.36±0.03	22.53±0.64	15.65±1.74	0.81±0.02

TABLE 12: PERCENTAGE YIELD, *IN-VITRO* BUOYANCY AND INCORPORATION EFFICIENCY OF FLOATING MICROSPHERES OF EMT

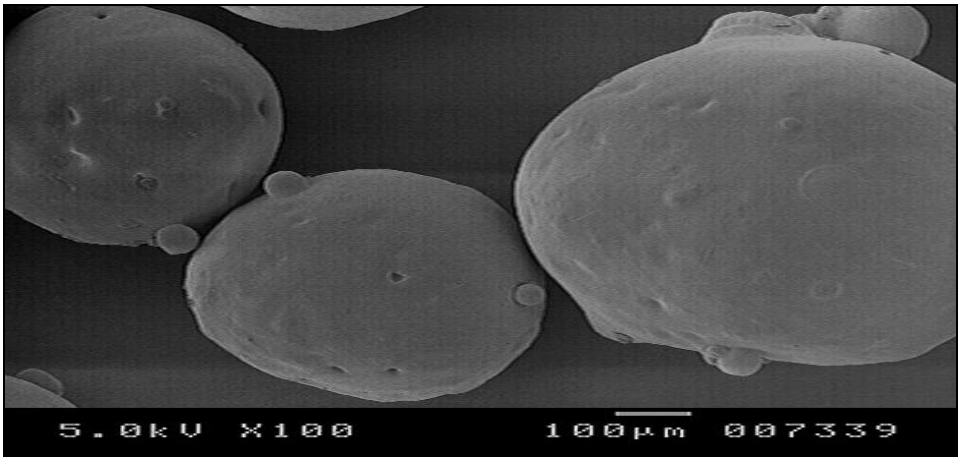
Formulation Code	Percentage Yield (%)	*In-vitro* buoyancy (%)	Incorporation efficiency (%)
F1	67.84±0.64	76.66±1.52	77.43±2.72
F2	85.59±0.69	82.39±2.07	87.34±2.84
F3	92.50±0.51	89.96±1.04	91.94±2.17
F4	70.67±0.66	75.43±2.02	67.11±3.01
F5	82.26±0.43	83.96±1.07	88.11±2.59
F6	89.84±0.72	90.39±2.00	92.30±2.88
F7	88.63±0.65	79.33±1.32	79.76±1.58
F8	92.29±0.74	87.12±1.00	93.91±2.02
F9	93.78±0.55	94.95±1.43	96.38±2.34



(a)



(b)



(c)

FIG. 7: SEM OF FLOATING MICROSPHERES OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE. (a) SURFACE MORPHOLOGY. (b) AND (c) THE PARTICLE SIZE AND SHAPE OF FLOATING MICROSPHERES.

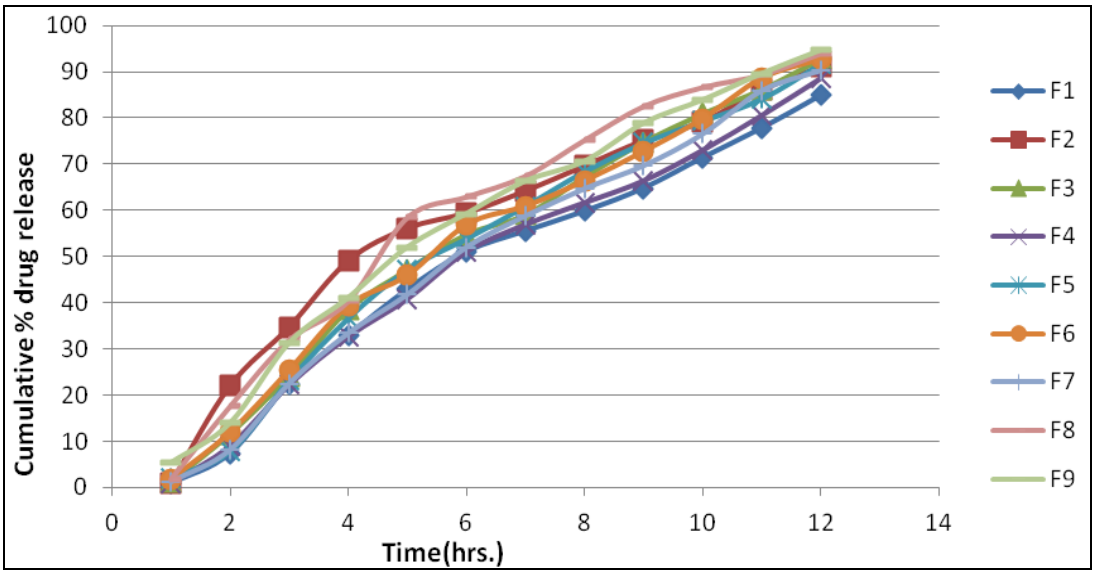


FIG. 8: CUMULATIVE PERCENTAGE DRUG RELEASE OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE FROM FORMULATION F1 TO F9

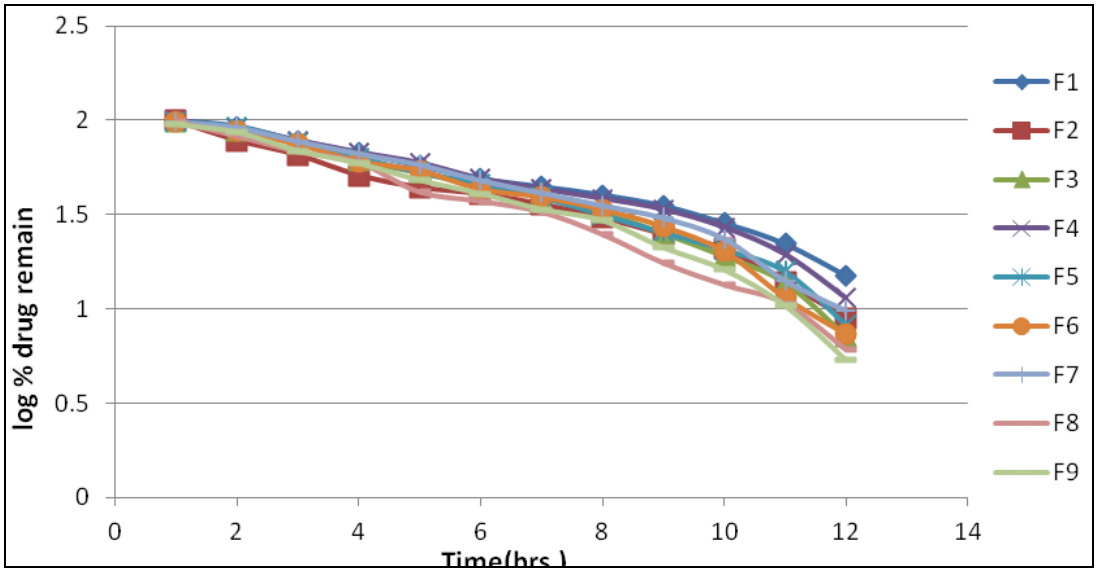


FIG. 9: FIRST ORDER PLOTS OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE FROM FORMULATION F1 TO F9

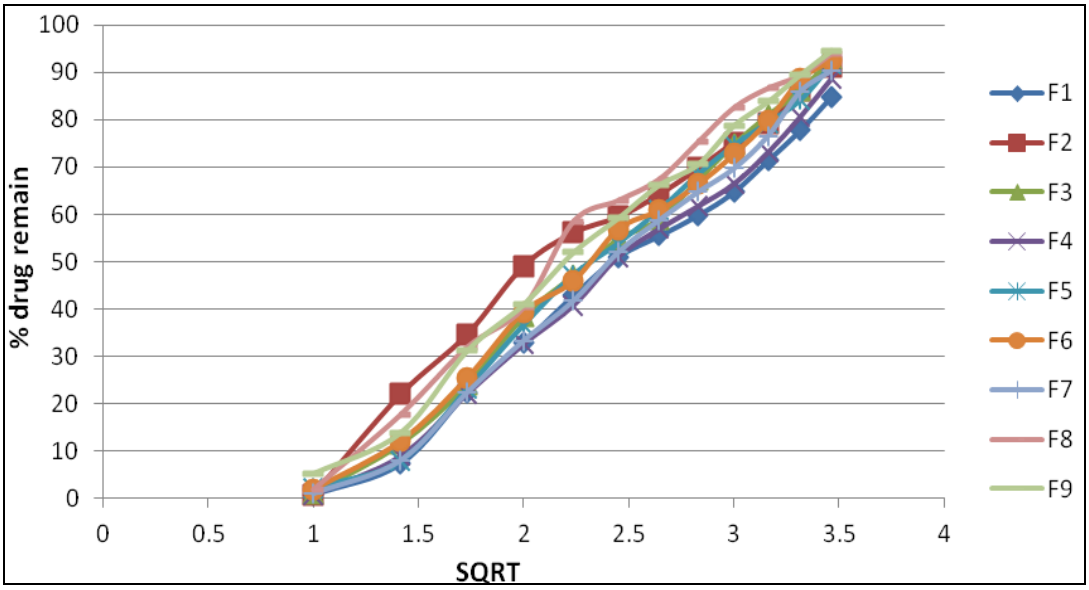


FIG. 10: HIGUCHI ORDER PLOTS OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE FROM FORMULATION F1 TO F9

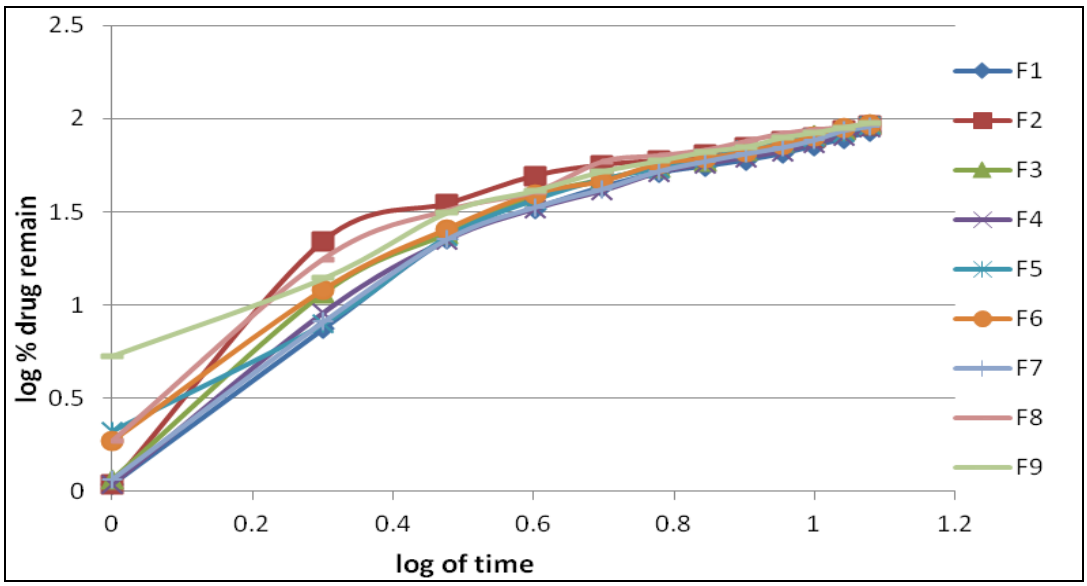


FIG. 11: PEPPAS ORDER PLOTS OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE FROM FORMULATION F1 TO F9

TABLE 13: KINETICS DATA OBTAINED FROM *IN-VITRO* RELEASE PROFILE FOR FLOATING MICROSPHERES OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE

Form. Code	Zero-order kinetic data	First-order kinetic data	Higuchi matrix data	Peppas kinetic data	
	Regression Coefficient (R^2)	Regression Coefficient (R^2)	Regression Coefficient (R^2)	Regression Coefficient (R^2)	n-value
F1	0.9767	0.9707	0.9927	0.8967	0.3349
F2	0.9360	0.9625	0.9811	0.7731	0.5642
F3	0.9816	0.9436	0.9965	0.8915	0.4540
F4	0.9850	0.9471	0.9944	0.8977	0.3542
F5	0.9760	0.9585	0.9929	0.9362	0.5244
F6	0.9981	0.9369	0.9954	0.9135	0.5728
F7	0.9860	0.9487	0.9942	0.9173	0.3849
F8	0.9547	0.9768	0.9887	0.9551	0.8553
F9	0.9738	0.9449	0.9956	0.8687	0.6580

DISCUSSION: Floating microspheres have a bulk density less than gastric fluids and thus it remains buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from stomach. This results in an increased gastric residence time and a better control of the fluctuation in plasma drug concentration. Single unit formulations (floating tablet) are associated with problems such as sticking together or being obstructed in the gastro-intestinal tract, which may have a potential danger of producing irritation. On the other hand a floating system made of multiple unit forms (floating microspheres) has relative merits compared to a single unit preparation. Floating microspheres provide a constant and prolonged therapeutic effect which will reduce dosing frequency.

Calibration curve for estimation of EMT was constructed in Simulated Gastric Fluid at 215 nm. The method obeyed Beer's Lambert law in the range of 0 to 16 mcg/ ml. or µg/ml. Microspheres prepared by emulsion solvent evaporation method and in this method emulsion was stabilized by Span 60 and the volatile solvent (acetone) get evaporated leaving a solidified thin film at the interface between aqueous phase and organic phase, where EMT get encapsulated in the core coat of polymers.

Micromeritic properties: The mean particle size of microsphere formulations F1 to F9 containing different polymers in the range of 100.08±0.95 to 500.42±1.03 respectively. The mean particle size of the floating microspheres was found to increase with increasing polymer concentration. The viscosity of the medium increases at a higher polymer concentration resulting in enhanced interfacial tension. Shearing efficiency is also diminished at higher viscosities. This results in the formation of larger particles. The values of Carr's index and angle of repose indicate excellent flow properties. The percentage yield of the floating microspheres increased with increasing polymer concentration.

***In-vitro* buoyancy:** The buoyancy test was carried out to investigate the floatability of the prepared microspheres. The microspheres were spread over the surface of a SGF and the fraction of microspheres buoyant and settled down as a function of time was quantitated. The *in-vitro* buoyancy of formulation F1 to F9 was in range of 75.43±2.02 to 94.95±1.43 respectively. Among all formulations F9 was found to be highest in-vitro buoyancy 94.95±1.43. The results also showed a tendency that the larger the particle size, the longer floating time.

Incorporation efficiency: The incorporation efficiency of formulation F1 to F9 was in range of 67.11±3.01 to 96.38±2.34 respectively. Results demonstrated that increase in concentration of polymer increased the entrapment of the drug. The drug entrapment efficiency was found to be good in all the formulations.

***In-vitro* drug release:** *In-vitro* drug release studies of EMT from floating microspheres were performed in pH 1.2 for 12 hours in dissolution test apparatus. Amongst the formulation, F9 was found to be the best formulation as it release EMT 94.60% in a sustained manner with constant fashion over extended period of time (after 12 hours).

It was observed as the concentration of polymer was increased percent release of EMT decreases. The increase in polymer concentration leads to the increased density of polymer matrix into the microspheres which results in an increased diffusional path length. This may increase the overall drug release from polymer matrix. Furthermore, smaller microspheres are formed at lower polymer concentration and have larger surface area exposed to dissolution medium.

The R2-values of zero order of the above 9 formulations were in the range of 0.9360 to 0.9981. Similarly the R2-value of first order was in between 0.9369 to 0.9768. Among the 9 formulations some formulations F9, F3, F4, F6 and F7 release the drug by zero-order kinetics and some are F1, F2, F5, F8 release by first-order kinetics. The results suggest that, the drug was released by mixed order kinetics. To ascertain, the drug release mechanism the in-vitro release data were also subjected to Higuchi's diffusion equation ($Q = k.t_{1/2}$) the R2-values of all the formulations of Higuchi's equation were 0.9800 and above.

It suggests that the Higuchi diffusion plots of all the formulations were fairly linear and we can conclude that the drug released by Higuchi's diffusion mechanism. The formulations are also treated to Peppa's plots by taking log percent versus log time.

The plots are found to be fairly linear and regression values (n value) of all formulations ranges from lowest 0.3349 to highest 0.8553 which in the range of $0.45 < n < 0.89$. This suggests that the drug was released by non-Fickian control (Anomalous diffusion) with swelling. Four types of graphs i.e. cumulative percent drug release, first order, Higuchi diffusion and Peppa's exponential plots of all formulations.

Infrared Spectroscopy (FTIR): The prepared microspheres were characterized by FTIR Spectroscopy to find out any chemical interaction between EMT and polymers used. The IR Spectrum obtained of EMT and polymers like HPMC, CA, Eudragit L 100 and Carbopol 940 were identical and there was no change in the functional group absorption of any molecule present in formulated product.

Scanning Electron Microscopy (SEM): Morphology of microspheres was examined by SEM. The view of the microspheres showed a hollow spherical structure with a smooth surface morphology. Some of the microspheres showed a dented surface structure but they showed good floating ability on the surface of the medium, indicating intact surface. The internal surface was porous it may be caused by the evaporation of solvent entrapped within the shell of microspheres after forming a smooth and dense layer.

SUMMARY AND CONCLUSION: Floating microspheres of EMT can be successfully prepared using HPMC, CA, Carbopol 940 and Eudragit L 100 as polymers by solvent evaporation method. The percentage yield of all floating microsphere formulations was more than 60% suggesting the method used for encapsulation was effective. The percent yield was significantly increased as the amount of polymer was increased in each formulation. The entrapment efficiency was good in all the cases. This suggested that optimized parameters were used in the method of preparation. The *in-vitro* buoyancy was more than 70% after 12 hours indicated satisfactory performance of proposed formulations. The percent buoyancy increased significantly as the amount of polymer was increased in each preparation method. The mean particle size of microspheres was in range of 100.08 ± 0.95 - 500.42 ± 1.03 µm depending upon the type of polymer used. The particle size increased significantly as the amount of polymer increased. Among all formulations, F9 was found to be the best formulation as it release EMT 94.60% in a sustained manner with constant fashion over extended period of time (after 12 hours).

Hence, finally it was concluded that prepared floating microspheres of EMT may prove to be potential candidate for safe and effective sustained drug delivery over an extended period of time which can reduce dosing frequency.

REFERENCES:

1. Iannuccelli V, Coppi G, Bernabei MT, Cameroni R. Int J Pharm 1998; 174: 47–54.
2. Gouda MM, Shyale S, Kumar PJ and Shanta Kumar SM. J Chem Pharm Res 2010; 2:187.
3. Soppimath KS, Kulkarni AR, Aminabhavi TM. Drug Develop Ind Pharm 2001; 27: 507.
4. Sarkar Biresh K, Tanwar Sandeep Singh *et al.* formulation characterisation *in vitro* evaluation of floating microspheres of esomeprazole, ijbio research article 2012 ; 7: 11-12.
5. Manivannan R, Senthil Kumar B, Parthiban KG and Jijin C. Once daily intestinal mucoadhesive esomeprazole magnesium tablet: formulation and *in vitro* evaluation, J Global Pharm Technology. 2010; 2(8): 10-18.
6. http://www.mayoclinic.com/health/peptic-ulcer/DS00242. Online accessed on 11/07/2015.
7. Hirtz J. The git absorption of drugs in man: a review of current concepts and methods of investigation. *Br* J Clin Pharmacol 1985; 19: 77-83.
8. Singh BN, Kim KH. Floating drug delivery systems an approach to oral controlled drug delivery via gastric retention, J Control Rel 2000; 63: 235-59.
9. Stanley SD. Formulation strategies for absorption windows. 2005; 10: p. 249-257.
10. Chueh SR, Zia H, Rhodes CT. Drug Develop Ind Pharm 1995; 21: 1725–1747.
11. Lin VLS, Daggy BP, Mirchandani HL, Chien YW. Int J Pharm 2003; 253: 13.
12. Muthusamy K, Govindarazan G, Ravit K. Indian J Pharm Sci 2005; 67: 75-79.
13. Cremer K. Pharm. J 1997; 19(108): 259-262.
14. Tanwar YS, Naruka PS, Ojha GR. Development and evaluation of floating microspheres of verapamil hydrochloride, Brazilian J Pharm Sci 2007; 43: 432.
15. Senthilkumar SK, Jaykar B, Kavimani S. Formulation Characterization and *In vitro* Evaluation of Floating Microsphere Containing Rabeprazole Sodium. JITPS 2010; 1 (6): 274-276.

16. Schmidt W, Roessling G. Novel manufacturing process of hollow polymer microsphere. Chem Eng Sci 2006; 61: p. 4983.
17. Sarkar Biresh K, Tanwar Sandeep Singh *et al.* formulation characterization *in vitro* evaluation of floating microspheres of esomeprazole, ijbio research article 2012 ; 7: 11-12.
18. Kumar PJ, Shyale S, Gouda MM and Kumar SMS. Physico-chemical characterization, UV spectrophotometric method development and validation studies of Esomeprazole Magnesium Trihydrate. J Chem Pharm Res 2010; 2(3): 484-490.
19. Putta Rajesh Kumar *et al*. Physico-chemical characterization, UV Spectrophotometric method development and validation studies of Esomeprazole Magnesium Trihydrate. J Chem Pharm Res 2010; 2(3): 484-490.
20. Ghosh Amitava *et al.* Development of oral drug delivery system using floating microspheres. J Microencapsul 2009; 16: 715-29.
21. Bornare PN, Avachat AM, Avachat MK, Patel KB, Jain KS. Development and characterization of sustained release microspheres of ropinirole HCl: study of various process parameter In; AAPS annual meeting and exposition, Los Angeles; 2009. *Proceedings.* Los Angeles; AAPS 2009: 3219.
22. Shrivastava A, Ridhurkur DN, Wadhwa S. Floating microspheres of cimetidine: Formulation, characterization and *In vitro* evaluation. Acta Pharm 2005; 55.
23. Sato Y, Kawashima Y, Takeuchi H, Yamamoto H. *In vitro* evaluation of floating and drug releasing behaviors of hollow microspheres (Microballoon) prepared by emulsion solvent diffusion method. European J Pharma Biopharm 2004; 57: 235- 243.
24. Baykara T, Kilicarslan M. The effect of the drug/polymer ratio on the properties of the verapamil HCl loaded microspheres. Int J Pharm 2003; 52: 99-109.
25. Mitsutoshi N, Kikuchi Y, Sano Y, Nabetani H, Kawakatsu T, Kobayashi I, Takao H. Continuous manufacturing method for microspheres and apparatus, January 25, 2001; US patent 6, 177, 479.
26. Verma VK. Modeling of drug release from delivery systems based on hydroxy propyl methyl cellulose (HPMC). Adv Drug Deli Rev 2001; 48: 139-47.
27. Navya AG, Sandeep. Formulation Characterization and *In vitro* evaluation of gastroretentive floating microspheres containing Esomeprazole Magnesium Trihydrate. IRJP 1998; 112.
28. Spickett RGW, Vidal JLF, Escoi JC. Antacid preparation having prolonged gastric residence. February 22, 1993; US patent 5, 288, 506.
29. Esomeprazole Drug Profile, Wikipedia, a free encyclopedia, "en.Wikipedia.Org/wiki/ Esomeprazole**".**
30. Illum L, Furraj N, Critcheley H, Davis SS. Polymers in Controlled delivery system . Int J Pharm 1998; 46: 261-265.
31. Sweetman SC. Martindale. The complete drug reference. 33rd ed. Pharm press; 2002. p. 605.
32. Indian Pharmacopoeia. Vol. II. New Delhi: The Controller of Publications; 2015. p. 1295-96.
33. Merck Index. Kenilworth, NJ: Merck and Co Inc; 2012. p. 6565.

How to cite this article:
Chouhan M, Chundawat AVS and Chauhan CS: Development and characterization of floating microspheres of esomeprazole magnesium trihydrate by solvent evaporation method. Int J Pharm Sci Res 2017; 8(2): 686-97.doi: 10.13040/IJPSR.0975-8232.8(2).686-97.