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FORMULATION AND EVALUATION OF METOPROLOL SUCCINATE FLOATING MICROSPHERES

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Abstract:

The present study an attempt has been made to formulate metoprolol succinate into microspheers floating dosage form which can be expected to prolong the gastric residence time of active compounds and reduce the variability of transit. They are supposedly capable of increasing the bioavailability of drugs that are mainly absorbed in the upper gastrointestinal tract. For that purpose, drug release has to be sustained. It would be faster and more economical to alter beneficially the properties of the existing drugs than developing new drug entities. Metoprolol succinate is ß2 selective blocking agent which is used in management of hypertension. Metoprolol succinate floating drug delivery system was prepared using natural and gas forming agent Sodium bicarbonate. prepared microspheres were evaluated for buoyancy test, swelling study, drug content and In Vitro release profile. The prepared microspheres showed acceptable physicochemical characteristics. All the prepared batches showed fine In Vitro buoyancy. The release data were subjected to different models zero order, first order Higuchi and Pappas in order to evaluate their release kinetics and mechanisms. Floating microspheres of Metoprolol succinate can be prepared well with combination of Xanthan gum and guar gum that shows controlled drug release up to 12 hours.

Keywords: *Floating drug delivery, Metoprolol succinate, microspheres.*

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INTRODUCTION:

Oral controlled release drug delivery is a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either local or systemic action[1,2].

All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage form (solid dispersion or liquid), must be developed within the intrinsic characteristics of GI physiology [3]. Therefore the scientific framework required for the successful development of oral drug delivery systems consists of basic understanding of (i) Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug (ii) the anatomic and physiologic characteristics of the gastrointestinal tract and (iii) physicochemical characteristics and the drug delivery mode of the dosage form to be designed [4,5].

Conventional oral controlled dosage forms suffer from mainly two adversities. The short gastric retention time (GRT) and unpredictable gastric emptying time (GET). A relatively brief GI transit time of most drug products impedes the formulation of single daily dosage forms. Altering the gastric emptying can overwhelm these problems. Therefore it is desirable, to formulate a controlled release dosage form that gives an extended GI residence time [6,7].

Floating drug delivery systems either float due to their low density than stomach contents or due to the gaseous phase formed inside the system after they come in contact with the gastric environment. Based on the mechanism of buoyancy, two distinctly different technologies i.e. non-effervescent and effervescent systems have been utilized in the development of FDDS [8,9]:

1. Non-Effervescent FDDS.
2. Effervescent FDDS.

Metoprolol succinate, an anti-hypertensive drug has been chosen as a model drug in the formulation of floating drug delivery systems for the present work. It is a drug of choice in treatment of hypertension. However it has been reported that absolute bioavailability of metoprolol succinate when given orally is (12%) and half life of 3-7 hours. A floating drug delivery system was planned for metoprolol succinate as such a system when administered would remain buoyant on the gastric fluids for a prolonged period of time and drug would be available in the dissolved form. This would lead to improvement in the bioavailability of the drug. In this way it stands an advantage over conventional dosage form.

The present study an attempt has been made to formulate metoprolol succinate into microspheers floating dosage form which can be expected to prolong the gastric residence time of active compounds and reduce the variability of transit. They are supposedly capable of increasing the bioavailability of drugs that are mainly absorbed in the upper gastrointestinal tract. For that purpose, drug release has to be sustained. It would be faster and more economical to alter beneficially the properties of the existing drugs than developing new drug entities.

MATERIALS AND METHOD:

Metoprolol Succinate Succinate gift sample from Aurobindo Pharma, Hyderabad. Xanthan Gum, Guargum, Xanthan Gum and Sodium Bicarbonate from SD Fine Chemicals Ltd., Mumbai. All othr reagents are analytical grade.

Calibration curve of Metoprolol succinate in water:

The standard solutions were prepared by proper dilutions of the primary stock solution with absolute water to obtain working standards in the concentration range of 5-25µg/ml of pure sample of Metoprolol succinate. The concentration of Metoprolol succinate present in the microspheres was obtained from the calibration curve.

Drug-Excipients Compatibility study:

Niacin was mixed with all excipients, used in the formulation in different ratios and subjected to Physical observation/FTIR.

Drug-Excipient Compatibility study (FTIR):

The IR absorption spectra of the pure drug and with different excipients were taken in the range of 4000-400 cm^{-1} using KBr disc method, 1-2 mg of the substance to be examined was triturated with 300-400 mg, specified quantity, of finely powered and dried potassium bromide .These quantities are usually sufficient to give a disc of 10-15mm diameter and pellet of suitable intensity by a hydraulic press.

Preparation of Floating Microspheres of Metoprolol Succinate

Table 1: Formulation of Metoprolol succinate Floating Microspheres

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Metoprolol succinate	1	1	1	1	1	1	1	1	1
Sodium alginate	1	2	3	0.75	1.5	2.25	0.75	1.5	2.25
Guargum	-	-	-	0.25	0.5	0.75	-	-	-
Xanthum	-	-	-	-	-	-	0.25	0.5	0.75
$NaHco_3$	1	2	3	1	2	3	1	2	3
water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Evaluation of Floating Microspheres:

Percentage Yield:

The prepared microspheres of all batches were accurately weighed. The measured weight of prepared microspheres was divided by the total amount of all the excipients and drug used in the preparation of the microspheres, which give the total percentage yield of floating microspheres. It was calculated by using following equation,

$$\% \text{ Yield} = \frac{\text{Actual weight of product}}{\text{Total weight of Excipients and drug}} \times 100$$

Micromeritic Studies:

The prepared microspheres are characterized by their micromeritic properties, such as microsphere size, tapped density, Carr's compressibility index, Hausner's ratio and angle of repose.

Bulk Density

Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. Bulk density is determined by pouring pre sieved granules into a graduated cylinder via a large funnel and measure the volume and weight.

$$\text{Bulk density} = \frac{\text{Weight of granules}}{\text{Bulk volume of granules}}$$

Bulk density was expressed in g/cc.

Tapped Density:

Tapped density is determined by placing a graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. using the weight of the drug in the cylinder and this minimum volume, the taped density may be computed.

$$\text{Tapped density} = \frac{\text{Weight of granules}}{\text{Tapped volume of granules}}$$

Carr's Index (CI):

Carr's index is measured using the values of bulk density and tapped density. The following equation is used to find the Carr's index.

$$CI = \frac{(TD-BD)}{TD} \times 100$$

Where TD = Tapped density

BD = Bulk density

Hausner's Ratio:

It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder or granules.

Hausner's Ratio = Tapped density / Bulk density

Angle of Repose:

The manner in which stresses are transmitted through a bead and the beads response to applied stress are reflected in the various angles of friction and response. The method used to find the angle of repose is to pour the powder ion a conical heat on a level, flat surface and measure the included angle with the horizontal.

$$\text{Tan}\theta = h/r$$

Where, h= height of the heap

r= Radius of the heap

Evaluation of Microspheres:

Scanning Electron Microscopy (SEM)

The morphology of the microspheres was studied using scanning electron microscopy (SEM).The samples for SEM were prepared by lightly sprinkling on a double adhesive tape stuck to an aluminum stub. The stubs were then coated with gold film under reduced pressure. The stub containing the coated samples was placed in the scanning electron microscope (Hitachi S3400N) chamber. The samples were then randomly scanned, and photomicrographs were taken at the acceleration voltage of 5 kV. Microphotographs were taken on different magnification and higher magnification was used for surface morphology.

Drug Content:

20 microspheress of each formulation were weighed and powdered. The quantity of powder equivalent to 100 mg of Ofloxacinwas transferred in to a 100 ml volumetric flask and the volume adjusted to 100ml

with 0.1N HCl. Further 1ml of the above solution was diluted to 100 ml with 0.1N HCl and the absorbance of the resulting solution was observed at 221 nm.

***In Vitro* Buoyancy Studies:**

The in vitro buoyancy was determined by floating lag time, and total floating time. (As per the method described by Rosa et al[39]) The microspheress were placed in a 100ml beaker containing 0.1N HCl. The time required for the microspheres to rise to the surface and float was determined as floating lag time (FLT) and the duration of the time the microspheres constantly floats on the dissolution medium was noted as the Total Floating Time respectively (TFT).

$$\% \text{ Buoyance} = Q_f / (Q_f + Q_s) \times 100$$

Where Q_f and Q_s are the weight of the floating and settled microspheres respectively.

Swelling Index Studies:

The swelling behavior of a dosage unit was measured by studying its weight gain. The swelling index of microspheres was determined by placing the microspheress in the basket of dissolution apparatus using dissolution medium as 0.1N HCl at 37±0.5°C. After 0.5, 1, 2, 3, 4, 5, and 6h, each dissolution basket containing microspheres was withdrawn, blotted with tissue paper to remove the excess water and weighed on the analytical balance (Schimdzu, AX 120). The experiment was performed in triplicate for each time point. Swelling index was calculated by using the following formula

Swelling index = (Wet weight of microspheres – Dry weight of microspheres)/Dry weight of microspheres.

Drug Loading and Drug Entrapment:

Microspheres equivalent to 50 mg of the drug were taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres and extracting with aliquots of 0.1N HCl (pH-1.2) repeatedly. The extract was transferred to a 100ml volumetric flask and the volume was made up using 0.1N HCl (pH-1.2). The solution was filtered and the absorbance was measured after suitable dilution spectrophotometrically (UV 1700, Shimadzu, Japan) at 275 nm against appropriate blank. The amount of drug loaded and entrapped in the microspheres was calculated by the following formulas: **Drug loading = weight of drug in microspheres/ microspheres sample weight × 100**

(**Drug entrapment efficiency (%) = Amount of drug actually present/ Theoretical drug load expected × 100**

Determination of Percentage Yield

The dried microspheres were weighed and percentage yield of the prepared microspheres was calculated by using the following formula.

$$\text{Percentage yield} = \frac{\text{Practical yield (mg)} \times 100}{\text{Theoretical yield}}$$

***In-vitro* Release Study:**

The drug release study was performed for microsphere containing quantity equivalent to 15mg of Metoprolol succinate by using USP dissolution apparatus Type I in 900 ml of 0.1N HCl dissolution media (pH-1.2) at 100 rpm and 37^{0}C temperature. 10 ml of sample was withdrawn at predetermined time interval for 12 hours and same volume of fresh medium was replaced to maintained sink condition. Withdrawn samples were assayed spectrophotometrically at 275 nm. Drug release was also performed for pure drug.

The cumulative % drug release was calculated using standard calibration curve.

Release Kinetics:

The matrix systems were reported to follow the Peppas release rate and the diffusion mechanism for the release of the drug. To analyse the mechanism for the release and release rate kinetics of the dosage form, the data obtained was fitted in to,Zero order, First order, Higuchi matrix, Peppas and Hixson Crowell model. In this by comparing the r-values obtained, the best-fit model was selected.

***In vivo* Floating Behavior:**

Healthy rabbits weighing approximately 2-2.5 kg was used to assess *in vivo* floating behaviour. Ethical clearance was obtained from Institutional Animal Ethics Committee (IAEC Reg. No.: 627/02/a/CPCSEA) J.N.M.C., Belgaum, before conducting the experiment. The animals were fasted for 12 h and the first X-ray photographed to ensure absence of radio opaque material in the stomach. The rabbits were made to swallow barium sulphate loaded microspheres with 100ml of water.

During the experiment rabbits were not allowed to eat but water was provided. At predetermined time intervals the radiograph of the abdomen was taken using an X-ray machine.

Stability Studies:

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications.

RESULTS AND DISCUSSION:

Calibration curve of Metoprolol succinate in simulated gastric fluid pH 1.2

Table2 shows the calibration curve data of Metoprolo l succinatein simulated gastric fluid pH 1.2 at 275nm. Fig. 5.2 shows the standard calibration curve with a regression value of 0.993, slope of 0.0292 and intercept of 0.0097 in simulated gastric fluid pH 1.2. The curve was found to be linear in the concentration range of 5-25 µg/ml.

Table 2: Calibration Curve Data for Metoprolol Succinate In Simulated Gastric Fluid pH 1.2

Concentration (µg /ml)	Absorbance
0	0
5	0.16
10	0.3
15	0.454
20	0.605
25	0.739

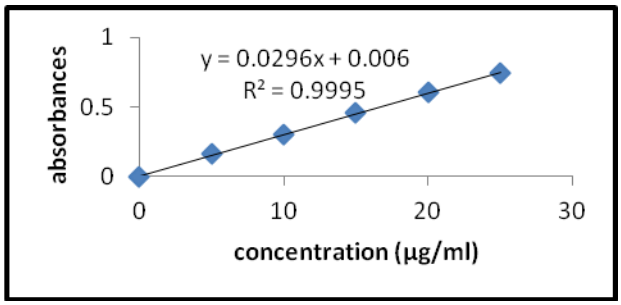

Fig 1: Standard graph Of Metoprolol succinate in Simulated Gastric Fluid pH 1.2

Compatibility Studies

Drug polymer compatibility studies were carried out using FT-IR to establish any possible interaction of Metoprolol succinatewith the polymers used in the formulation.

The FT-IR spectra of the formulations were compared with the FTIR spectra of the pure drug. The results indicated that the characteristic absorption peaks due to pure Metoprolol succinatehave appeared in the formulated microspheres, without any significant change in their position after successful encapsulation, indicating no chemical interaction between Metoprolol succinateand Polymers shown in figures 2&3.

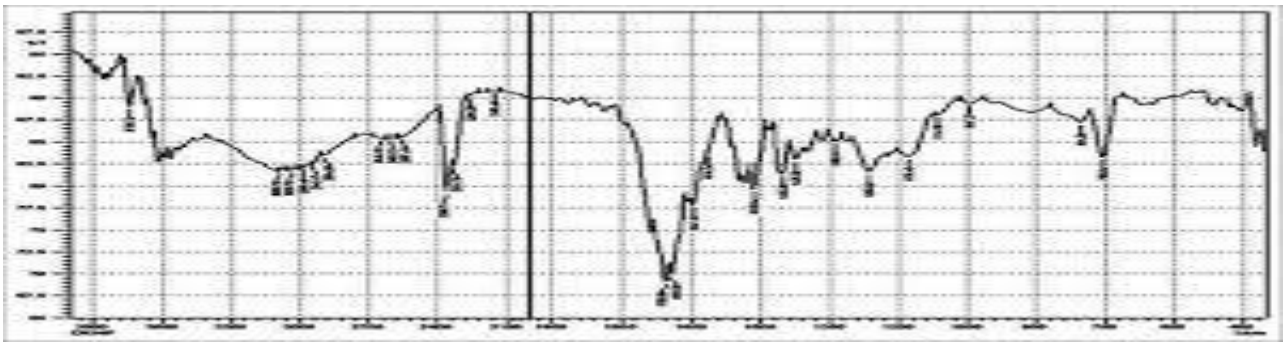

Fig 2: FTIR spectra of pure drug

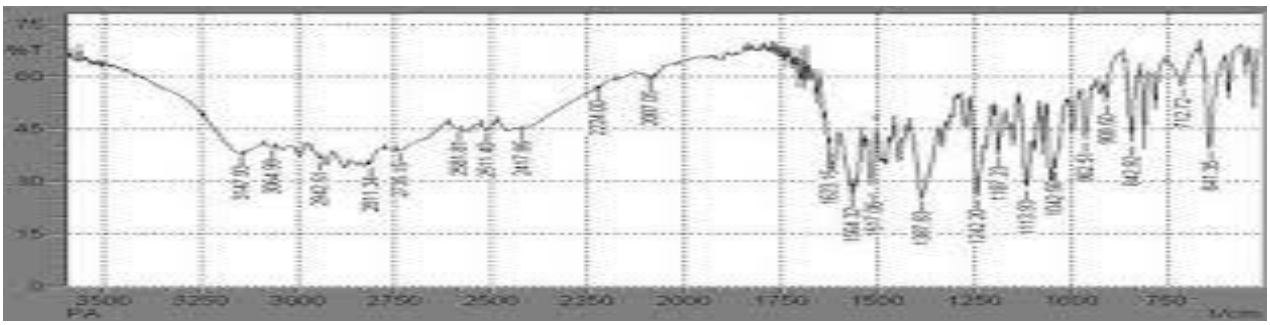

Fig 3: FTIR spectra of physical mixture

Preformulation Parameters

Table 3-Microparticulate Analysis

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Carr's Index	Hausner Ratio	Angle of repose(θ)
F1	0.45±0.045	0.52 ± 0.09	15.60±0.2	1.15±0.02	28.06± 0.31
F2	0.45±0.045	0.50 ± 0.07	12.23±0.6	1.11±0.04	27.58± 0.15
F3	0.44±0.044	0.50 ± 0.09	12.58±0.8	1.13±0.08	28.44± 0.11
F4	0.45±0.045	0.52 ± 0.04	15.19±0.1	1.15±0.06	28.36± 0.13
F5	0.44±0.044	0.52± 0.01	15.48±0.6	1.18±0.08	28.52± 0.19
F6	0.45±0.045	0.51 ± 0.04	13.48±0.8	1.13±0.09	29.32± 0.19
F7	0.51±0.045	0.59 ± 0.04	14.48±0.8	1.15±0.09	29.69± 0.19
F8	0.44±0.044	0.52± 0.01	15.48±0.6	1.18±0.08	28.52± 0.19
F9	0.45±0.045	0.50 ± 0.07	12.23±0.6	1.11±0.04	27.58± 0.15

All the formulations were evaluated for bulk density, tapped density, % compressibility, hausner's ratio and angle of repose. The results of % compressibility, hausner's ratio and angle of repose were found to be <16, <1.25 and <30 respectively. These results show that the formulations have very good flow properties shown in table 3.

Evaluation and Characterisation of Microspheres

Percentage Yield

It was observed that as the polymer ratio in the formulation increases, the product yield also increases. The low percentage yield in some formulations may be due to blocking of needle and wastage of the drug- polymer solution, adhesion of polymer solution to the magnetic bead and microspheres lost during the washing process. The percentage yield was found to be in the range of 80 to 86% for microspheres containing sodium alginate along with Guargum as copolymer, 80 to 88% for microspheres containing sodium alginate along with Xanthum as copolymer. The percentage yield of the prepared microspheres is recorded in Table 4 and displayed in Figures 4 to 8.

Drug Entrapment Efficiency

Percentage Drug entrapment efficiency of Metoprolol succinate aranged from 56 to 72% for microspheres containing sodium alginate along with guargum as copolymer, 80 to 92% for microspheres containing sodium alginate along with xanthum as copolymer and . The drug entrapment efficiency of the prepared microspheres increased progressively with an increase in proportion of the respective polymers. Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. The higher viscosity of the polymer solution at the highest polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in higher entrapment efficiency. The % drug entrapment efficiency of the prepared microspheres is displayed in Table 4, and displayed in Figure 4 to 8.

Table 4: Percentage Yield and Percentage Drug Entrapment Efficiency of the Prepared Microspheres

S.No.	Formulation code	% Yield	Drug Content (mg)	% Buoyancy	% Drug entrapment efficiency	%Swelling Index
1	F1	80	59.40	63	62.66	33.32
2	F2	83.33	58.66	67	72	35.66
3	F3	85	58.70	75	89	30.91
4	F4	86	59.5	79	56	32.33
5	F5	82.22	61.07	85	67	35.11
6	F6	80	62.25	89	72	38.18
7	F7	88	65.29	70	80	36.55
8	F8	87	63.5	76	82	37.32
9	F9	80	63.01	84	92	35.66

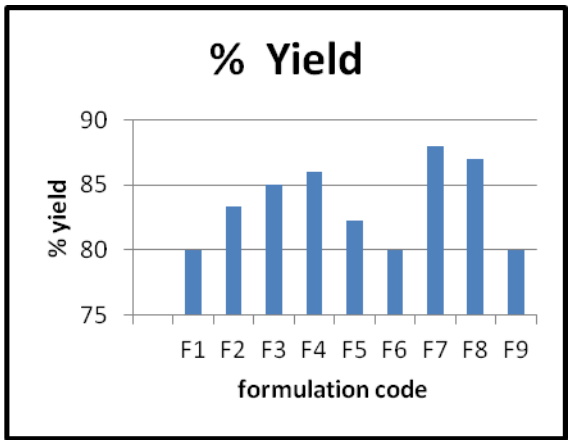

Fig 4: Graph for % Yield vs Formulation Code

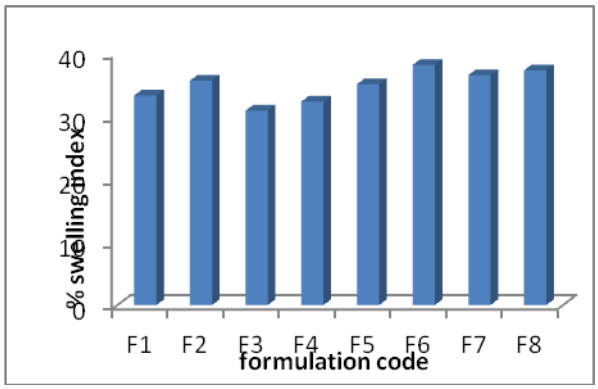

Fig 6: Graph for % Swelling Index vs Formulation Code

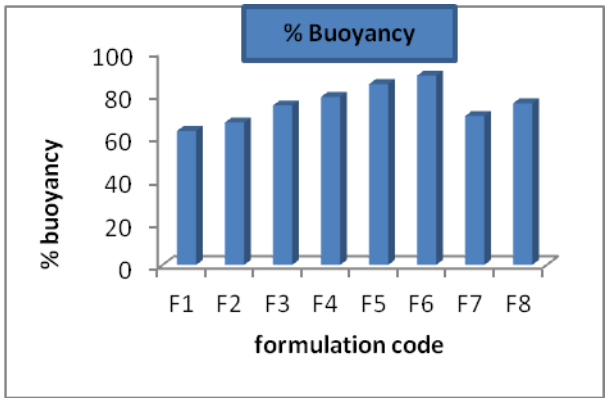

Fig 5: Graph for % Buoyancy vs Formulation Code

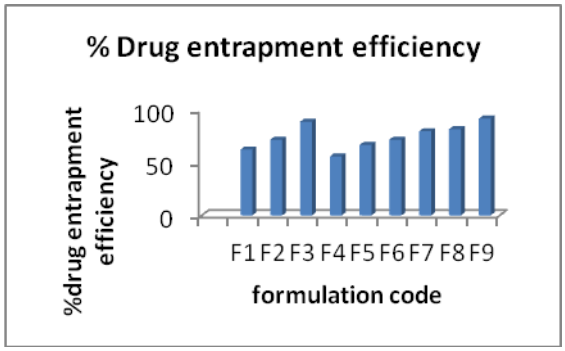

Fig 7: Graph for % Drug Entrapment Efficiency vs Formulation Code

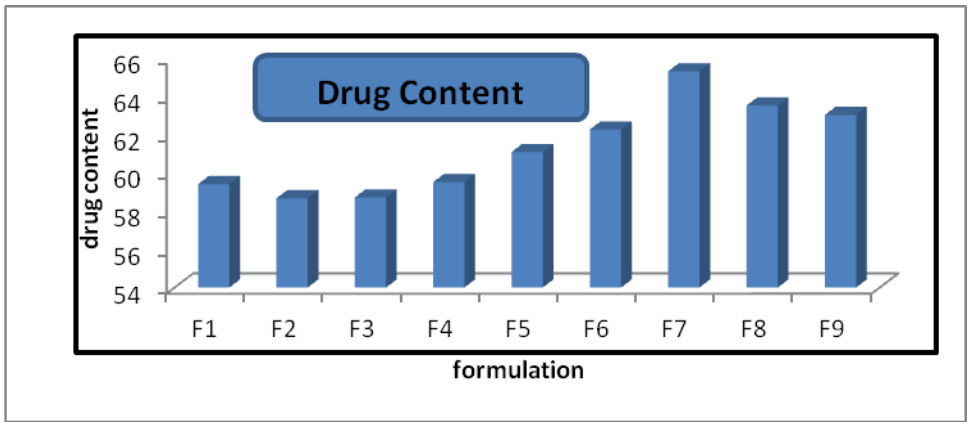

Fig 8: Graph for % Drug Content vs Formulation Code

***In-Vitro* Drug Release Studies**

Dissolution studies of all the formulations were carried out using dissolution apparatus USP type I. The dissolution studies were conducted by using dissolution media, pH 1.2. The results of the in-vitro dissolution studies of formulations F1- F9 are shown in table 5 . The plots of Cumulative percentage drug release Vs Time. Figures 9-11 .

The formulations F_4, F_5, F_6 containing Sodium alginate along with Guargum as copolymer showed a maximum release of 86.9% after 9 hours, 83% after 10 hours, 76% after 11 hours respectively.

The formulations F7, F8, and F9 containing Sodium alginate along with Xanthum as copolymer showed a maximum release of 85.2% after 9 hours, 86.2 % after 10 hours, 71.2% after 11 hours urs respectively.

That shows that more sustained release was observed with the increase in the percentage of polymers. As the polymer to drug ratio was increased the extent of drug release decreased. A significant decrease in the rate and extent of drug release is attributed to the increase in density of polymer matrix that results in increased diffusion path length which the drug molecules have to traverse. The release of the drug has been controlled by swelling control release mechanism. Additionally, the larger particle size at higher polymer concentration also restricted the total surface area resulting in slower release.

Table 5: Percentage Cummulative Drug Release For All Formulations

TIME	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	23	18	16	28.4	23	14	25.3	**16.25**	11.30
2	32	27.2	24	40.3	38	20	37.2	**21.3**	19.6
3	41.5	36	31	49.7	45	26	44.3	**28.6**	25.4
4	57.6	45	42	55.3	50	28	52.4	**30.4**	28.2
5	68.2	53	49	62.4	54	38	57.8	**38.2**	36.3
6	79.7	67	54	68.3	63	42	65.2	**44.3**	40.4
7	86.4	72	58.7	76.9	69	48	70.8	**51.6**	46.8
8	-	84	70.4	83.2	78	54	79.2	**57.2**	59.3
10	-	-	-	86.9	83	63	85.2	**78.3**	62.4
12	-	-	-	-	-	76	-	**86.2**	71.2

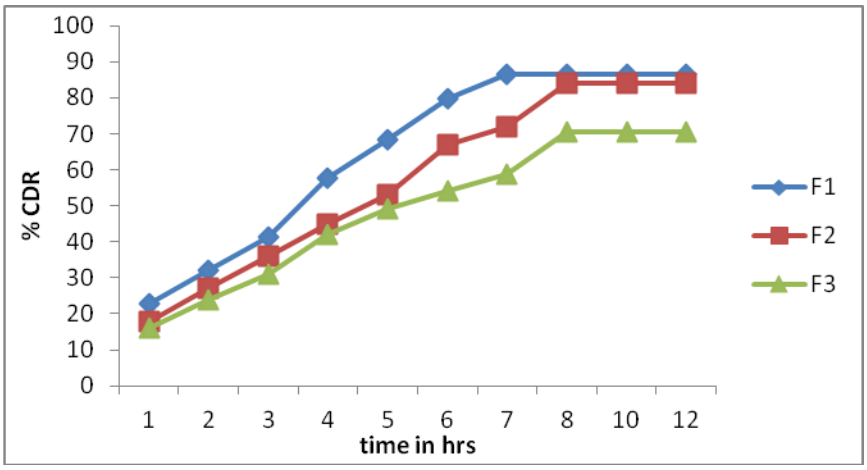

Fig 9: Dissolution Graph for Formulation F1-F3 (Drug: Sodium alginate)

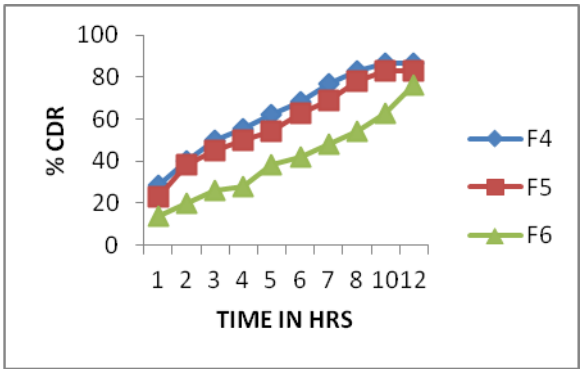

Fig 10: Dissolution graph for formulation F4 –F6 (Drug: Sodium alginate + Guargum)

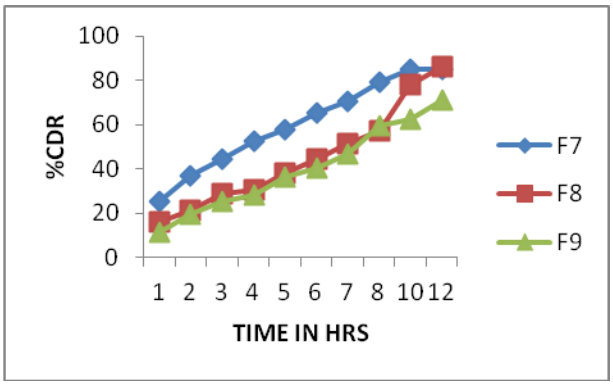

Fig 11: Dissolution Graph for Formulation F7 –F9 (Drug: Sodium alginate + Xanthum)

In-Vitro Drug Release Kinetics

For understanding the mechanism of drug release and release rate kinetics of the drug from dosage form, the in-vitro drug dissolution data obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix, and Krosmeyer-Peppas model. The values are compiled in Table 6. The coefficient of determination (R^2) was used as an indicator of the best fitting for each of the models considered. The kinetic data analysis of all the formulations reached higher coefficient of determination with the Korsmeyer-Peppas model (R^2 = 0.9595) whereas release exponent value (n) ranged from 0.498 to 0.743. From the coefficient of determination and release exponent values, it can be suggested that the mechanism of drug release follows Korsmeyer-Peppas model along with non-Fickian diffusion mechanism which leading to the conclusion that a release mechanism of drug followed combination of diffusion and spheres erosion.

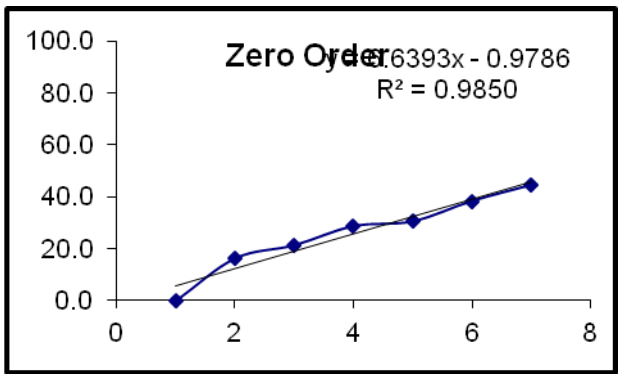

Fig 12: Zero Order Kinetic Graphs for F8 Batch

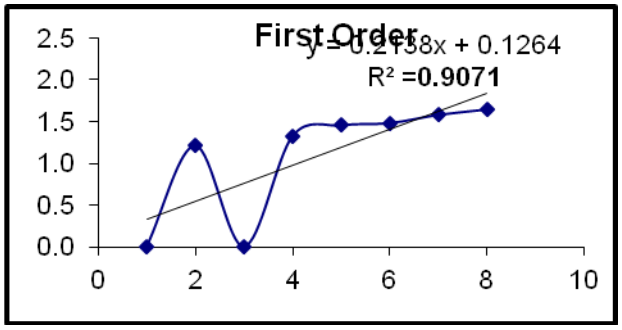

Fig 13: First Order Kinetic Graph for F8 Batch

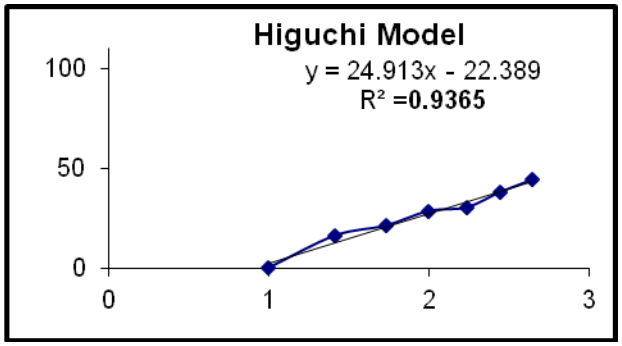

Fig 14: Higuchis Model Kinetic Graph for F8 Batch

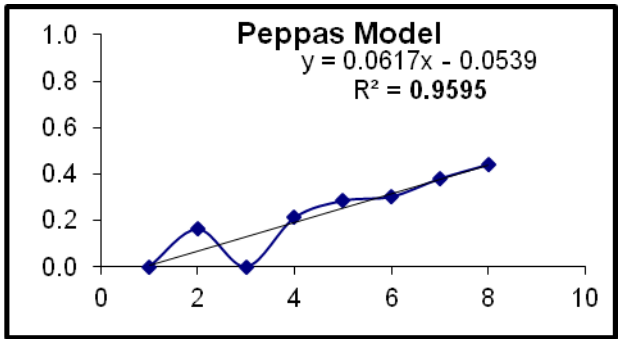

Fig 15: Peppas Model Kinetic Graph for F8 Batch

Table 6: R^2 Values for Release Kinetics

RELEASE KINEITCS				
	ZERO	**HIGUCHI**	**PEPPAS**	**FIRST**
	1	**2**	**3**	**4**
	Q Vs T	**Q Vs √T**	**Log C Vs Log T**	**Log % Remain Vs T**
Slope	**6.8513**	**29.1672**	**0.6913**	**-0.0107**
Intercept	**4.9976**	**-21.6524**	**1.1385**	**2.1666**
Correlation	**0.9925**	**0.9677**	**0.9796**	**-0.9524**
R 2	**0.9850**	**0.9365**	**0.9595**	**0.9071**

Stability Studies of Metoprolol Succinate Complexes:

Table 7: Stability Studies of Metoprolol Succinate Complex at Room Temperature

Time	**Colour**	**Percent drug content ± St.D. at Room Temperature**	**Cumulative % drug release ± St.D. at 60min**
First day	White	86.20± 0.91	86.20±0.55
30 days	White	86.14 ± 0.23	86.01±0.72
60 days	White	86. 06 ± 0.62	85.62±0.65
90 days	White	85. 92 ± 0.31	85.20±0.98

The inclusion complexes of Metoprolol succinate (F8) were subjected to short-term stability testing by storing the complexes at room temperature.

Results from stability studies indicate that the formulated microspheres are stable for a period of 3 months under room temperature i.e., 30˚C temp and 65±5% RH. There were no remarkable changes were observed during the period of storage.

CONCLUSION:

The present study has been a satisfactory attempt to formulate a floating Microspheres of metoprolol succinate with a view of improving its oral bioavailability and giving a controlled release of the drug. From the experimental results it can be concluded that, FT-IR study shows no significant shifting of the peaks therefore it confirms the short term stability of the drug in the microspheres. Biocompatible polymers like sodium alginate,guargum and xanthum can be used to formulate a floating Microspheres . Good percentage drug entrapment and practical yields were obtained with both the polymers. The flow properties of all formulations were within the acceptable range and therefore they could be easily filled into capsules. The floating microspheres of drug with guargum were less buoyant while those with xanthum showed greater buoyancy. Cumulative percentage drug release significantly decreased with increase in polymer concentration. The overall curve fitting into various mathematical models was found to be on an average. The formulations F 8 best fitted into zero order kinetic model and peppas model. Formulated microspheres were stable and compatible at the selected temperature and humidity in storage for 45 days. From the stability studies it was found that there was no significant change in the drug entrapment, release characteristics and floating behavior of the microspheres.

Thus, the formulated floating microspheres seem to be a potential candidate as an oral gastroretentive controlled drug delivery system in prolonging the drug retention in stomach and increasing the bioavailability of drug.

REFERENCES:

1.Hong SI, Oh SY. Dissolution kinetics and physical characterization of three-layered tablet with poly(ethylene oxide) core matrix capped by Carbopol. Int J Pharm2008;356:121-9.

2. McGinity JW, Koleng JJ, Repka MA, Zhang F. Hot melt extrusion technology. In: Swarbrik J, editor.

Encylopedia of Pharmaceutical Techonology. 3 rd ed. New York: Informa Healthcare USA, Inc; 2005. p. 2004-20.
3. Trotta M, Gasco MR, Morel S. Release of drugs from oil-water microemulsions. J Control Release 1989;10:237-43.
4. C. Narendra, M. S. Srinath and G. Babu, Optimization of bilayer floating tablet containing metoprolol tartrate as a model drug for gastric retention,AAPS PharmSciTech. 7 (2006) 23-29; DOI: 10.1208/pt070234.
5. H. Ravishankar, P. Patil, A. Samel, H-U. Petereit, R. Lizio and J. Iyer-Chavan, Modulated release metoprolol succinate formulation based on ionic interactions: in-vivo proof of concept, J. Control. Rel. 111 (2006) 65-72.
6. Narendra C, Srinath M, Ganesh B, Optimization of bilayer floating tablets containing Metoprolol tartrate as a model drug for gastric retention, AAPS Pharm Sci.Tech 2006; 7;E1-E7.
7. S. Arora, J. Ali, A. Ahuja, R. K. Khar and S. Baboota, Floating drug delivery systems: a review, AAPS PharmSciTech 6 (2005) 372–390.
8. Health and Family Welfare, Govt. of India. Thecontroller of publications, New Delhi.1996, A-54.Ajit Kulkarni and Manish Bhatia Development and evaluation of regioselective bilayer floating tablets of Atenolol and Lovastatin for biphasic release profile Iranian Journal of Pharmaceutical Research (2009), 8 (1): 15-25.
9. Bhise SD, Aloorkar NH: Formulation and Invitro evaluation of floating capsules of Theophylline. Ind J Pharm Sci. 2008; 70(2): 88-93.