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GASTRORETENTIVE FLOATING MICROSPHERES FOR THE MANAGEMENT HYPERTENSION BASED ON DRUG COMBINATION OF AMLODIPINE /LOSARTAN

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ABSTRACT

Background: Hypertension is one of the serious global health issues that affect millions of people and leads to cardiovascular damage if remain untreated. Various antihypertensive drugs have been developed but it is difficult to achieve better control of blood pressure by using mono-therapy so in this research work, combination therapy having sustained effect for the treatment of hypertension was developed. **Method:** Gastroretentive floating microspheres of amlodipine besylate and losartan potassium were formulated for the purpose of increasing the time of retention of drugs in the upper gastrointestinal tract and ultimately extend drug release. Eudragit RS100 was used as release controlling agent. The method adopted to prepare microspheres was solvent extraction. Formulated microspheres after that tested for assessing flow properties, buoyancy (%), percentage yield, drug release, surface morphology, by FTIR drug and polymer compatibility, size analysis and entrapment efficiency. Release kinetics on cumulative release data were applied. **Results:** It was observed from the findings that all the formulation remained buoyant in 1.2 pH buffer up to 12 hrs. It was also found that release of drug from formulation was prolonged which indicates sustained effect of dosage form. All the other results were satisfactory and it was also found that entrapment efficiency of formulation increased when concentration of polymer increased. On the basis of results, formulation 1 with 1:1 drug polymer ratio was selected as optimum formulation. **Conclusion:** It was concluded from the study that gastroretentive floating microspheres could be a one of best approach to extend the release of drug delivery system.

Keywords: Gastroretentive drug delivery system, Floating microspheres, Amlodipine besylate, Losartan potassium, Sustained release drug delivery

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INTRODUCTION

Oral dosage forms is deliberately the auspicious and widely used approach of drug delivery because of several advantages of oral administration which includes; easy to administer drug, patient conformity and plausibility in dosage form design.Unfortunately, conventional dosage form have some drawbacks due to unpredictable gastrointestinal tract (GIT) atmosphere i.e. short half life , no control over drug delivery and limited absorption which leads to poor management in constant plasma drug concentration or fluctuations in plasma drug level. This fluctuation in plasma drug level is overcome by frequent administration of drug but frequent administration of drugs leads to toxic effects of the drugs and poor patient compliance. Rational approach to control release of drug in precise way resolve this undesired features of conventional dosage. So to achieve this goal, Controlled Drug Delivery System (SDDS) have been established [**1**]. The CDDS is improved now. CDDS releases the drug in ordered manner and provide the steady state plasma concentration of administered for long period of time. Thus increasing the safety, efficacy, bioavailability and improved patient compliance [**2**]. There are many difficulties associated while crafting controlled system for enhanced bioavailability and improved immersion. The major problem is to keep the drug in a preferred place of GI tract. As the drug absorption from GIT directly related to the time for which drug stayed in interaction with intestinal mucosa so the stomach emptying is a important factor for the complete absorption of drug. Several methodologies has developed to enhance the gastric residence time

(GRT) of drug given orally in the stomach. By enhancing GRT of dosage form, drug will get more time to absorb in gastro intestinal tract and ultimately bioavailability of the drug will be increased [**3**]. One of the main approach is Floating Drug Delivery System (FDDS) or gastro retentive system which can be defines as the systems that has density less than stomach contentwhich permits the dosage form to glide on gastric stomach for longer time and ultimately increasing the residence time of dug. It is also referred as hydro dynamicallybalance system [**4, 5**].

Hypertension is one of the serious global health issues that affects millions of people that leads to cardiovascular damage if remain untreated. Various antihypertensive drugs have been developed but it is difficult to achieve better control of blood pressure by using mono- therapy so the main purpose is to develop combination therapy for hypertension. One of the most appropriate routes for delivery of drug is oral route but conventional oral delivery system provides poor management of plasma drug concentration and no targeted effects. This significant fluctuation results in decreased efficacy of drug. One of the techniques to overcome this challenge is the development of floating microsphere which releases the drug in controlled rate. So in this study, floating microspheres of combination drugs wereprepared for better control of hypertension.

This study aimed to develop the gastro retentive floating microsphere of antihypertensive drugs of two different class i.e. Amlodipine (Calcium channel blocker) and Losartan (Angiotensin receptor Blockers); To evaluate in vitro buoyancy of the prepared floating microsphere; To evaluate the effective release of drug molecules from the microsphere; and To determine acute toxicity in animal models. There are several techniques which can be used to achieve the gastric retention in stomach.

MATERIALS & METHODS

Materials

Amlodipine besylate and Losartan Potassium were obtained by Saffron Pharmaceutical Pvt. Ltd. Faisalabad, Pakistan. Eudragit RS100 was obtained by Surge Laboratories Pvt Ltd Pakistan. Magnesium stearate was obtained from Govt. College University Faisalabad Pharmaceutics Laboratory. Hydrochloric acid, Sodium Lauryl Sulphate, Methanol, Dichloromethane, Ethanol, Tween 80 were obtained from Govt. College University Faisalabad Pharmaceutics. All the chemicals used in this research work are manufactured by Sigma Aldrich, USA.

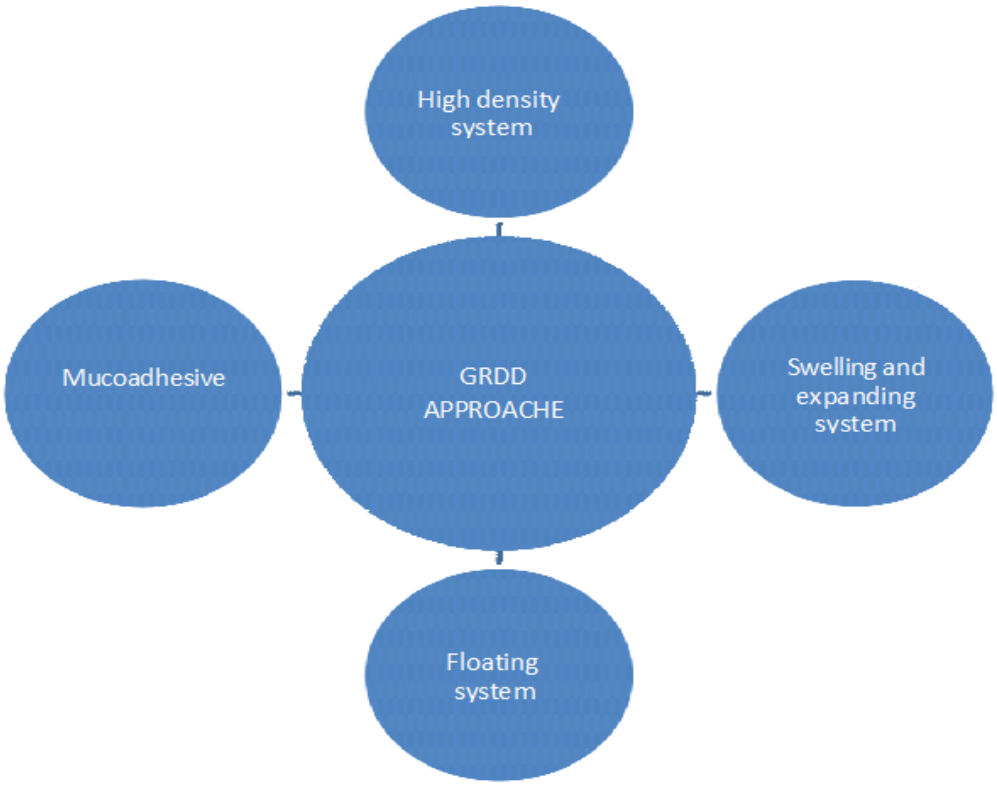

Figure 1: Approaches to gastro-retentive drug delivery system.

Preparation of Amlodipine Besylate Floating Microsphere

ALB microspheres were synthesized by using solvent evaporation. To prepare microspheres, the specified amount of Eudragit RS100 (1:1, 1:2, 1:3 and 1:4) and Mg-stearate were dissolved in organic solvents with continuous magnetic stirring at 300rpm at room temperature. Then weighed quantity of drug was dissolved in polymeric solution under same condition. This polymer dispersion was poured drop wise into 100ml distilled water containing 0.2%SLS. The resultant emulsion was stirred continuously by using overhead stirrer at 800rpm for 1.5 hour until all the solvent will be evaporated. The formed microsphere was filtered through filtration. Then obtained microspheres werewater washed followed by overnight drying at 25-30ºC (**Fig. 2**). Dried microspheres were stored in air tight glass vials and stored in desiccator. Similarly, preparation of losartan potassium floating microsphere was done.

Evaluation of Microsphere

Physical Appearance of Microspheres

The polymeric microspheres were evaluated with naked eye to check the appearance.

Micromeritics Properties of Microspheres

The prepared floating microsphere were evaluated for micromeritics properties like compressibility index, Hausner's ratio and angle of repose. The micromeritics studies performed for evaluation of flow properties of prepared microsphere [**6**].

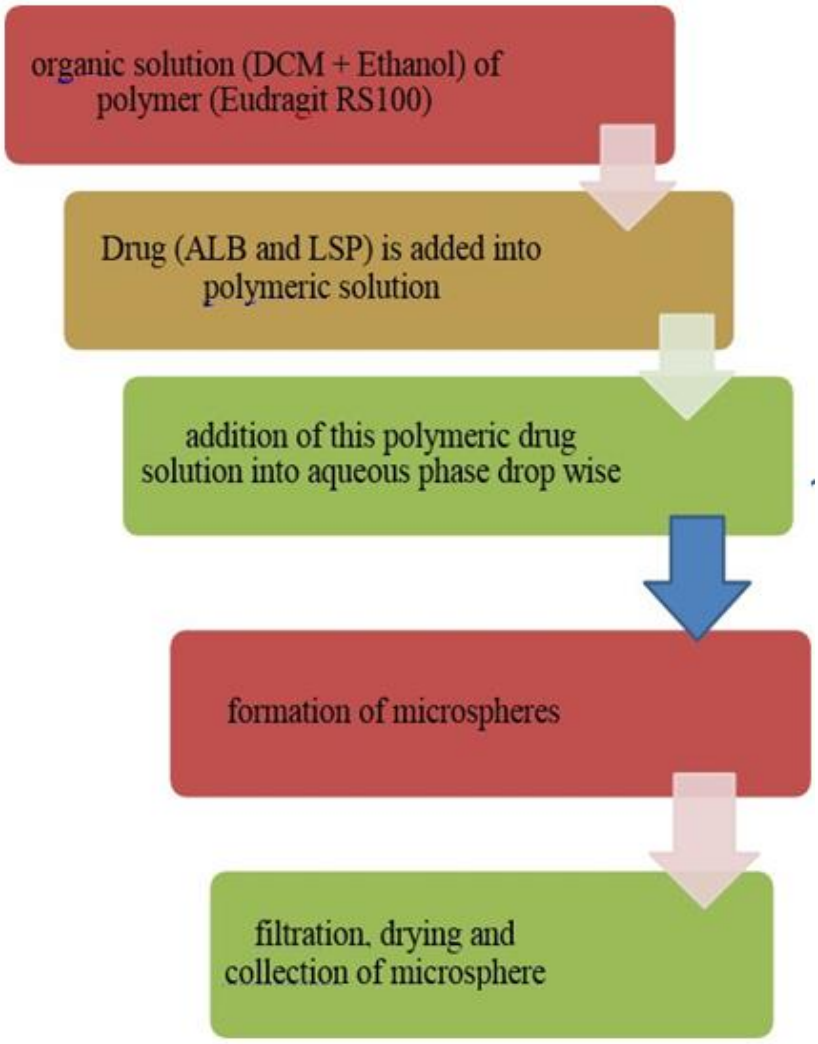

Figure 2: Representation of solvent evaporation method.

Determination of Entrapment Efficiency (%)

For % entrapment efficiency of drug, specific quantity of the prepared microsphere equivalent to 10mg of drugs were obtained and crushed to fine powder. The powdered microspheres were transferred to 100ml volumetric flask and then making up the volume upto 100ml with methanol. The solution was 50 vortexed, filtered and the suitable dilution were made by using methanol. The absorbance of the dilution was obtained through UV-visible spectrophotometer against appropriate blank. The absorbance value was putt in calibration curve to determine the drug content [**7**].

In vitro Buoyancy or Floating Behavior

USP dissolution apparatus type II was used to determine the in vitro buoyancy of microspheres. Fill the dissolution basket with 900ml of 1.2 pH buffer possessing 0.02% w/v tween 80. 50mg of the microsphere were taken being spreaded on simulated gastric fluid (0.1N HCl of pH 1.2) surface. The mixture was agitated at 100 rpm for 12 h at 37 ºC. After 12 h, the layer of the floating microsphere was pipetted and filter it to collect floating microsphere. Similarly, particles that were sinked down separated by filtration to collect sinked microsphere. Both the portion of microsphere were dried in dessicator and weighed [**8, 9**]

Percentage Yield Determination

To determine the %age yield, collect the prepared microsphere and weigh them accurately on digital weighing balance. Then this weight is divided by the total weight of all non- volatile components that were used for preparation of microsphere [**10**]. The formula is given as;

In vitro Release

In vitro studies done using paddle apparatus. The dissolution media that were used to perform drug release was 1.2 pH buffer. Firstly, 900ml of buffer were placed in baskets of dissolution apparatus. Microsphere equivalent to 50mg of losartan potassium and 10mg of amlodipine besylate were added together to the dissolution medium at 37ºC at 100 rpm. 1ml of sample was withdrawn after specific time up to 24 hrs. Then absorbance of aliquots was determined by using ultra visible spectrophotometer at respective λmax after suitable dilution compared to appropriate blank. The volume that was withdrawn were replaced by equal volume of fresh 1.2 pH buffer and constant volume of dissolution medium was maintained [**11**].

Compatibility of Drug and Polymer by FTIR

The interaction between drug and polymer was studied by FTIR. Infrared spectra of Eudragit RS100, pure drugs i.e. losartan potassium and amlodipine besylate and of prepared floating microsphere were carried out by KBR pellet technique. IR spectra were recorded on FTIR spectrometer [**12, 13**].

Microsphere Image Analysis

To study the surface of prepared microspheres, scanning electron microscopy (SEM) was performed. Before examination, gold coated microspheres coated with gold film under reduced pressure were placed directly on sample stub. This conducting gold films allow flowing of electron stream. The photographs of surface of microspheres were taken with SEM [**14, 15**].

Particle Size Analysis

Particle size of prepared microsphere was analyzed by using Zeta sizer (Malvern Instruments, UK). To prevent agglomeration, particles (to be analyzed) was suspended by using water and this suspension was filtered through a filter of 0.45 micrometer. Then this suspension was placed in clear disposable zeta cell. Evaluation of particle size were measured by dynamic light scattering method and recorded [**16**]

Release Kinetics Model

Release kinetics model i.e. zero order, first order, higuchi model and Korsmeyer-Peppas model equation were applied on cumulative drug release data of amlodipine besylate and losartan potassium [**17**].

Differential Scanning Calorimetry (DSC)

10mg of samples was placed in standard aluminium pans. The heating rate was 10ºC per minute and DSC curves was scanned between 40 °C to 300 °C by using differential scanning calorimetry, DSC60, (Shimadzu, Japan). DSC of pure drugs, polymer and prepared microsphere were done to get information about melting point of drug and glass transition temperature (Tg) of polymer and to find the changes in endotherm peaks of prepared microsphere.

In vivo Acute Toxicity Studies

Rats were selected to perform acute toxicity studies. For this purpose, rats were divided in two groups. Each group was comprised of 3 rats (n=3). Group I was named as control group and group II was named as treatment group.

Group 1 rats were only given normal saline orally (2ml/kg). Similarly, group II rats were treated with combination of ALB & LSP microspheres equivalent to 10mg & 100mg of drugs respectively and observed specially for the first 4hrs for the appearance of any sign and symptoms. All the rats were kept under observation for 7 days for any sign of toxicity.

After completion of 7 days, all the animals were sacrificed to obtain blood samples of all rats. Complete blood count and liver function tests of all samples were done to determine any changes [**18**].

RESULTS & DISCUSSION

Floating microsphere is one the most promising approach to prolong the drug release. Main objective of research was to synthesize the floating microsphere of amlodipine besylate and losartan potassium. The prepared microspheres were evaluated for different parameters mentioned previously.

Physical Appearance of Polymeric Microspheres

Fabricated polymeric microspheres were physically evaluated with naked eye. They were small granular particle being white in color.

Micromeritics Properties of Microspheres

Compressibility Index

The compressibility index of formulations ALP1 to ALP4 ranged from 9.78-11.53% and compressibility index of formulation LSP1 to LSP 4 ranged from 8.32- 11.12% (**Fig. 3**). The order of compressibility index of all ALB formulation was ALB1>ALB2>ALB3>ALB4 and the order of compressibility index of all LSP formulation was LSP1>LSP2>LSP3>LSP4. Compressibility index is inversely proportional to flowability of formulation so the formulation having low compressibility index will have greater flowability. As the value of Carr's index high, the flow properties decreases. Here in case of all formulations, the value of Carr's index indicated that all the formulation had excellent to good flow properties [**19**].

Hausner's Ratio

The Hausner's ratio of formulations ALP1 to ALP4 ranged from 1.09-1.15 and Hausner'r ratio of formulation LSP1 to LSP 4 ranged from 1.08-1.13. The order of Hausner ratio of all ALB formulation was ALB1>ALB2>ALB3>ALB4. Similarly, the order of Hausner ratio of all LSP formulation was LSP1>LSP2>LSP3>LSP4.

Hausner's ratio is inversely proportional to flow ability of formulation so the formulation having low H.R will have better flowability. As the value of Hausner ratio increases, the flow properties decreases. Here in case of all formulations, the value of Hausner ratio indicated that all the formulation had excellent to good flow properties.

Angle of Repose

Angle of repose of formulations ALP1 to ALP4 ranged from 23.41-26.78 and angle of repose of formulation LSP1 to LSP 4 ranged from 22.94-25.53. The order of angle of repose of ALB formulation was ALB1>ALB2>ALB3>ALB4. Similarly, the order of angle of repose of LSP formulation was LSP1>LSP2>LSP3>LSP4. As the angle of repose is inverse to flow properties so when value of angle of repose increases, the flow properties decreases. Here in case of all formulations, the value of angle of repose indicated that all formulation had excellent flow properties.

Determination of Entrapment Efficiency (%)

The entrapment efficiency of ALB formulations was ranged from 64.77 to 73.40. The entrapment efficiency of LSP formulations were ranged from 62.54 to 76.15. It was found that when the concentration of polymer was increased, the entrapment efficiency was increased. The reason behind increasing of encapsulation efficiency with increase in polymer concentration can be described by two ways. First, when the concentration of polymer increased, it got precipitated fastly on the surface of drug particle or dispersed phase. This action prevents the diffusion of drug across boundary and ultimately increase in entrapment efficiency. Secondly, when the concentration of polymer increased, the viscosity of the solution also increased followed by delay in drug diffusion and enhancement in encapsulation efficiency [**20**].

In vitro Buoyancy or Floating Behavior

The in vitro buoyancy of ALB formulations were ranged from 71.20 to 76.42 and the in vitro buoyancy of LSP formulations were ranged from 65.76 to 70.86 (**Fig. 4**). It was found that all the formulation remained buoyant for 12 hours [**21**].

Percentage Yield Determination

Percentage yield of ALB microsphere were ranged from 76.14-79.65% and of LSP microsphere ranged from 69.70-72.35%. In case of formulation ALB3 and LSP3, the percentage yield was decreased from 79.30 to 77.52 and 70.92 to 70.15. This may be due to loss of some microsphere while washing the microsphere or may be due to sticking of some microsphere to the mixer of overhead stirrer.

In vitro Drug Release Study

All the batches formulations of ALB microsphere and LSP microsphere were evaluated for 24hrs to determine the drug release of each formulation and then polymer effect on release was calculated. The cumulative release of amlodipine besylate were ranged from 17.20 to 82.673 and the cumulative release of losartan potassium were ranged from 19.85 to 83.95. The order of release of all ALB formulation was ALB1<ALB2<ALB3<ALB4. The order of release of all LSP formulation was LSP1<LSP2<LSP3<LSP4. It was also found that increasing the concentration of polymer decrease the release of drug. This is due to the reason that when the concentration of polymer increased, the density and viscosity of the polymer matrix increased and this delays the diffusion of entrapped drug or increase in diffusional path length resulting in slow release of drug at higher concentration.

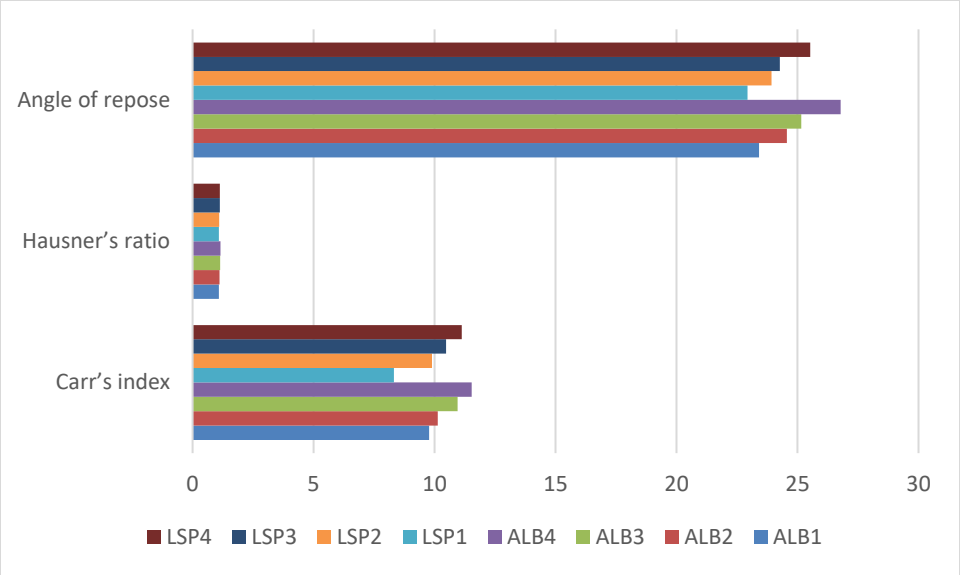

Figure 3: Micromeritics properties of microsphere.

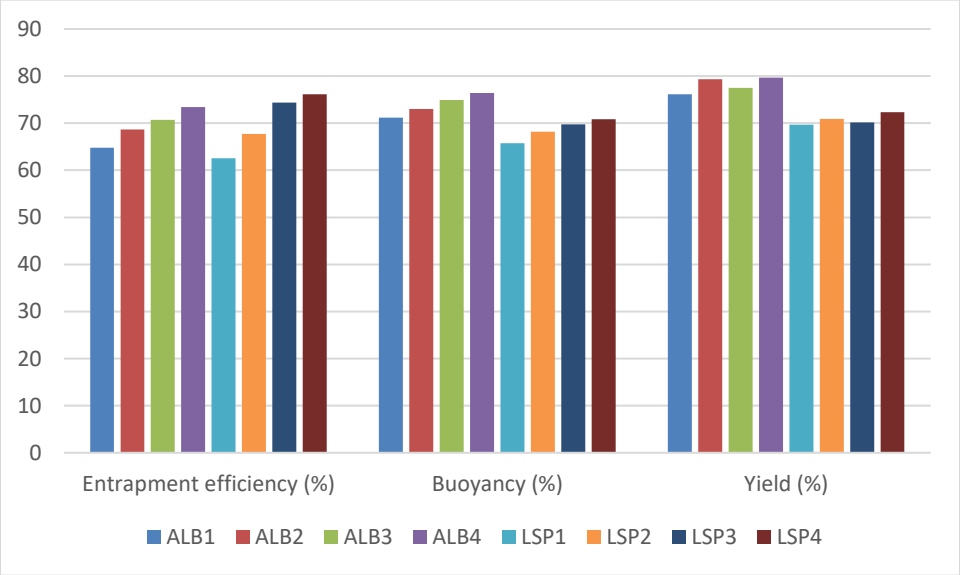

Figure 4: Entrapment, buoyancy and yield of microspheres.

FTIR

Fourier Transformer Infrared Spectroscopy of polymer (Eudragit RS100), active drugs (amlodipine besylate and losartan potassium), microsphere formulation of ALB and LSP were done by scanning them in range of 4000 to 650cm^{-1} to obtain their respective spectra.

FTIR spectra of eudragit RS100 showed the absorption peaks at 2985.6cm^{-1} is due to the stretching vibrations of C-H group. A band in the spectrum of eudragit RS100 at 1382.8 cm^{-1} are due to C-N groups vibration. FTIR spectral peak at 1140.6 cm^{-1} is because of stretching of C-O group. At 1722.0 cm^{-1}, peak is because of C=O stretching vibrations. All the characteristics peaks confirm the structures of eudragit RS100.

In FTIR spectra of ALB, the absorption peaks at 3291.2 cm^{-1} shows the stretching vibrations of N-H group. A band in the spectrum of ALB at 2981.9 cm^{-1}are due to aliphatic C-H groups. FTIR spectral peak

at 1669.8 cm^{-1} is because of stretching of carbonyl (C=O) parts. Spectral peak at 1200.2 cm^{-1} is because of C-N bending vibrations. Spectral band at 1613.9 cm^{-1} and 706.8 cm^{-1} are due to the presence of aromatic parts stretching vibration because of C=C and C-H vibrations. At 1722.0 cm^{-1}, band shows C-S group showing presence of sulfur group in structure of amlodipine besylate. All the characteristics peaks confirm the structures of amlodipine besylate.

Fig. 6 represents the FTIR spectra of ALB microsphere. In the FTIR spectrum of ALB microsphere, characteristic spectral peak indicative of alkyl C-H stretching vibrations is shifted a little from 2981.9 cm^{-1} to 2922.2 cm^{-1}. The absorption peaks of drug at 3291.2 cm^{-1} that showed the stretching vibrations of N-H group was shifted to 3321.1 cm^{-1} due to the linkage formed between drug and polymer. Carbonyl (C=O) group stretching vibration of drug molecule at 1669.8 cm^{-1} is shifted to 1662.4 cm^{-1} in case of fabricated microsphere. Peak at 1200.2 cm^{-1} due to C-N group bending vibrations is shifted to 1595.3 cm^{-1} in spectrum of ALB microsphere. Spectral peaks at 1613.9 cm^{-1} due to the presence of aromatic parts stretching vibration is shifted to 1662.4 cm^{-1}. At 752.9 cm^{-1} peak is due to C-S group and is shifted to 756.6 cm^{-1} in the spectrum of ALB prepared microsphere.

Fig. 6 represents the FTIR spectra of LSP. The absorption peaks at 3567.1 cm^{-1} represents the stretching vibrations of N-H group. A band at 3175.7 cm^{-1} shows stretching of aromatic OH functional group. The absorption peaks 2955.8 cm^{-1} represents C–H Stretching vibrations. FTIR spectral peaks at 1580.4 cm^{-1} shows stretching of C=N vibration and the peaks at 1461.1 cm^{-1} represents C=C Stretching vibrations and 790.2 cm^{-1} shows C-Cl Stretching vibrations. At 1751.8 cm^{-1}, peak is due to C-O bending vibrations and peak is due at 1358.8 cm^{-1} which shows the presence C-N stretching vibrations [**22**].

The FTIR spectra of LSP microsphere presented absorption band of N-H group vibrations at 3567.1 cm^{-1} shifted to 3436.6 cm^{-1}. A band at 3175.7 cm^{-1} due to stretching of aromatic OH group is shifted to 2985.6 cm^{-1}. FTIR spectral peak at 2955.8 cm^{-1} which was due to valence vibration of C- H is little bit shifted to 2952.1 cm^{-1}. FTIR spectral peaks at 1580.4 cm^{-1} which showed stretching of C=N vibration shifted to 1561.8 cm^{-1} and the peaks at 1461.1 cm^{-1} that showed C=C Stretching vibrations shifted to 1446.2 cm^{-1}. C-Cl Stretching vibration absorption peak at 790.2 cm^{-1} shifted to 752.9 cm^{-1}. C-O bending vibrations representative spectral peak is displayed at 1751.8 cm^{-1} and shifted to 1561.8 cm^{-1}. The absorption peaks at 1358.8 cm^{-1} showed the presence C-N stretching vibrations and this shifted to 1382.8 cm^{-1} in case of fabricated microsphere. These results indicates that eudragit RS100 successfully formed the microsphere that entrapped the drug without interfering with drug molecule. It was found that all the characteristics peaks of drug were present in spectra of prepared microsphere which shows that there was no compatibility issue between drug and polymer.

Table 1: Release kinetics and model fitting of ALB and LSP formulations.

Sr.	Formulation code	Kinetic models				
		Zero order model	First order model	Higuchi model	Korsmeyer- Peppas model	
		Parameters	Parameters	Parameters	Parameters	
		R^2	R^2	R^2	n	R^2
1	ALB1	0.8009	0.9567	0.9811	0.578	0.9897
2	ALB2	0.7301	0.9218	0.9937	0.525	0.9947
3	ALB3	0.6946	0.9066	0.9919	0.508	0.9920
4	ALB4	0.7097	0.8917	0.9896	0.517	0.9901
5	LSP1	0.7547	0.9419	0.9923	0.539	0.9946
6	LSP2	0.5718	0.8592	0.9912	0.448	0.9963
7	LSP3	0.5800	0.8551	0.9912	0.452	0.9956
8	LSP4	0.5553	0.8234	0.9885	0.441	0.9951

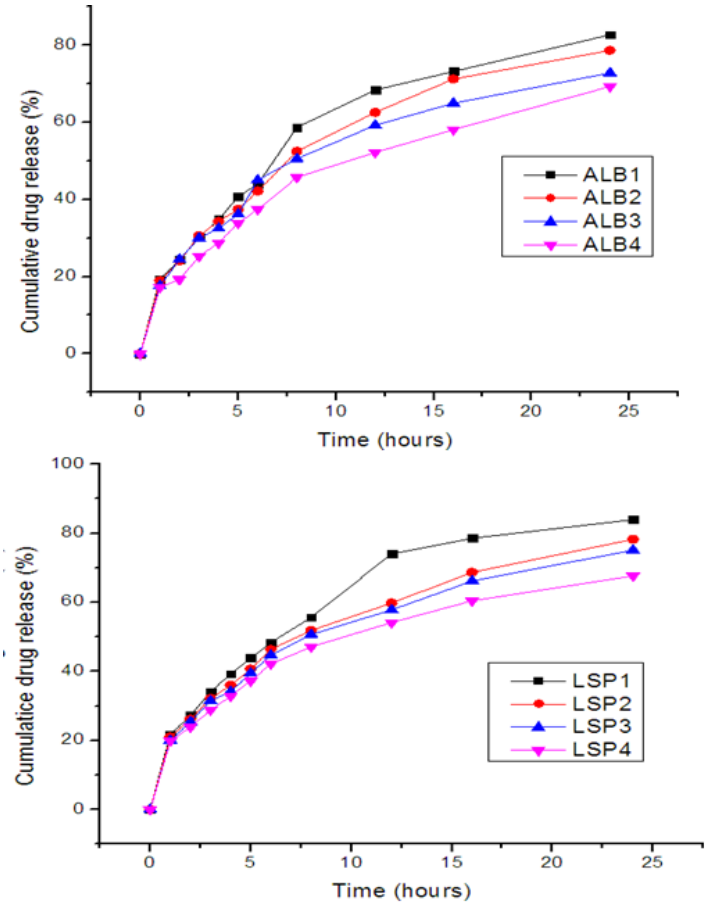

Figure 5: Release profile of losartan from floating microspheres.

Microsphere Image Analysis

Surface morphology of optimum floating microsphere formulation were evaluated by scanning electron microscope. Pictures were captured at high resolution of magnifications of 2.00kx, 500x, 111x and 80x as shown in **Fig. 7**. Photographs of SEM showed particles with porous structure. Some particles were of round shape with rough surface and some of irregular shape were seen. Porous structure increases the uptake of water causing swelling followed by release of entrapped drug molecules. White colored spots indicate effective drug loading within polymeric network.

Particle Size Analysis

Average hydrodynamic diameter of microsphere formulation was evaluated using Zetasizer (Malvern Instruments, UK) and size found to be 0.5-0.6 µm that is within the range of microsphere size (0.5-1000 µm). This result is in good compliance with the findings by Saharan *et al* [**23**].

Release Kinetics Modeling

Release kinetics model i.e. zero order, first order, Higuchi model and Korsmeyer-Peppas model equation were applied on cumulative drug release data of amlodipine besylate and losartan potassium. Coefficient of regression (R^2) of zero order were ranged from 0.5 to 0.8 and for first order model, R^2 value ranged from 0.8 to 0.9567. R^2 value of Higuchi modelwere ranged from 0.9885 to 0.9937. The highest coefficient of correlation was observed by Korsmeyer-Peppas model as R^2 values ranged from 0.9897 to 0.9963. This model also provides the value of 'n' i.e. diffusion exponent that shows the release mechanism followed by drug to be released. The n value was less than 0.5 which shows that the predominant mechanism followed by drug to release was Fickian diffusion.

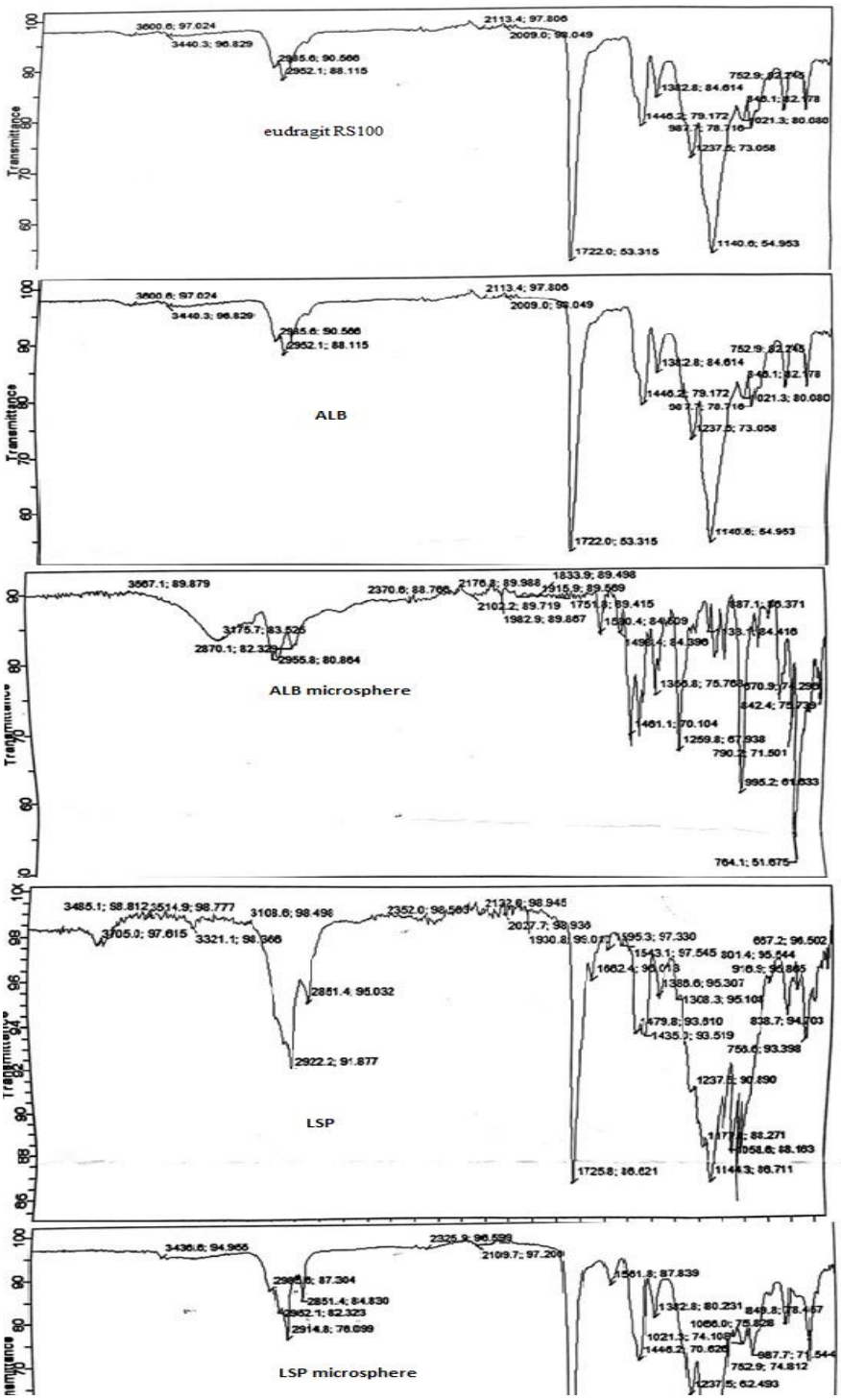

Figure 6: FTIR specra of microsphers and their components.

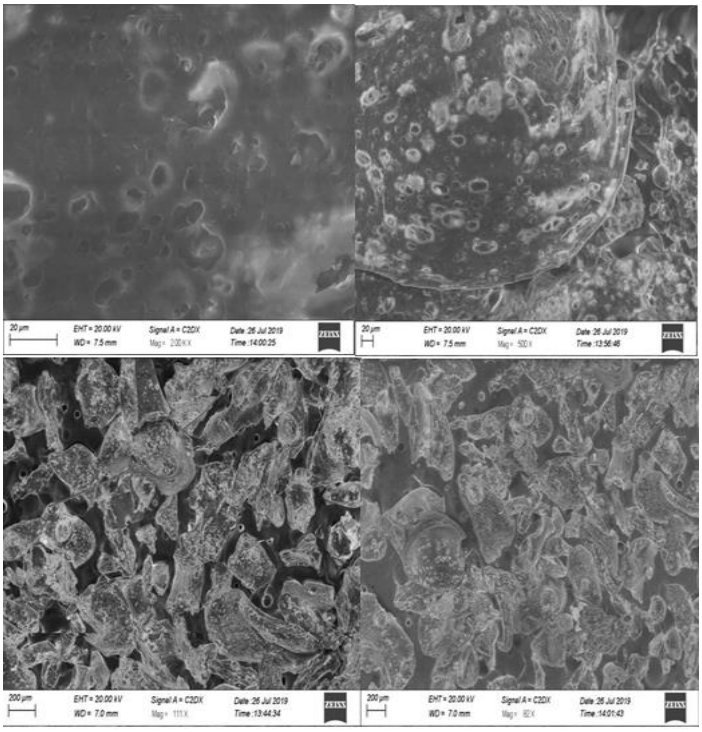

Figure 7: Scanning electron microscopy photographs of optimum microsphere.

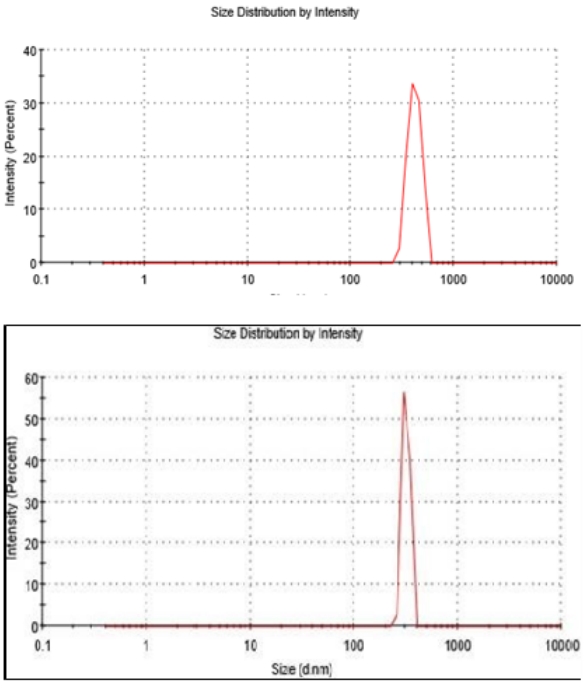

Figure 8: Particle size of microsphere optimum formulation.

Differential Scanning Calorimetry (DSC)

The DSC curves of pure drug ALB and its microsphere, pure drug LSP and its microsphere and Eudragit RS 100 are shown below. Differential scanning calorimetry was used to determine the thermal stability and physical state of the drug. The DSC thermographic peak for amlodipine besylate was observed at 213.83 ºC which showed that drug was thermally stable up to 213.83 ºC. In case of DSC curves of ALB microspheres, thermographic peak for ALB was found at 211.20 °C, so this results showed that there were no major interactions between the drug and the polymer. The DSC endothermic peaks for ALB and of formulation were shown in **Fig. 9**.

The DSC curve of pure losartan potassium showed endothermic peak at 279.08 °C which correspond to its melting point. In case of DSC curves of LSP microspheres, thermographicpeak for LSP was shifted to 288.13 °C as small peak and showed amorphous nature which might be due to dissolution of losartan potassium.

The DSC curve of eudragit showed exothermic peak at 422˚C which showed that melting points of eudragit RS 100 was much beyond the melting point of the drugs alone or in formulation. From this study, it was concluded that polymer does not affect the melting points of drugs [**24**].

In vivo Acute Toxicity Studies

The result of CBC and liver enzymes were shown in **Table 2**. It was observed from the results that there was no significant change in the lab values of control and treated group. No sign & symptoms of toxicity were appeared during seven days of toxicity study so it was concluded that the prepared microspheres were safe [**25**].

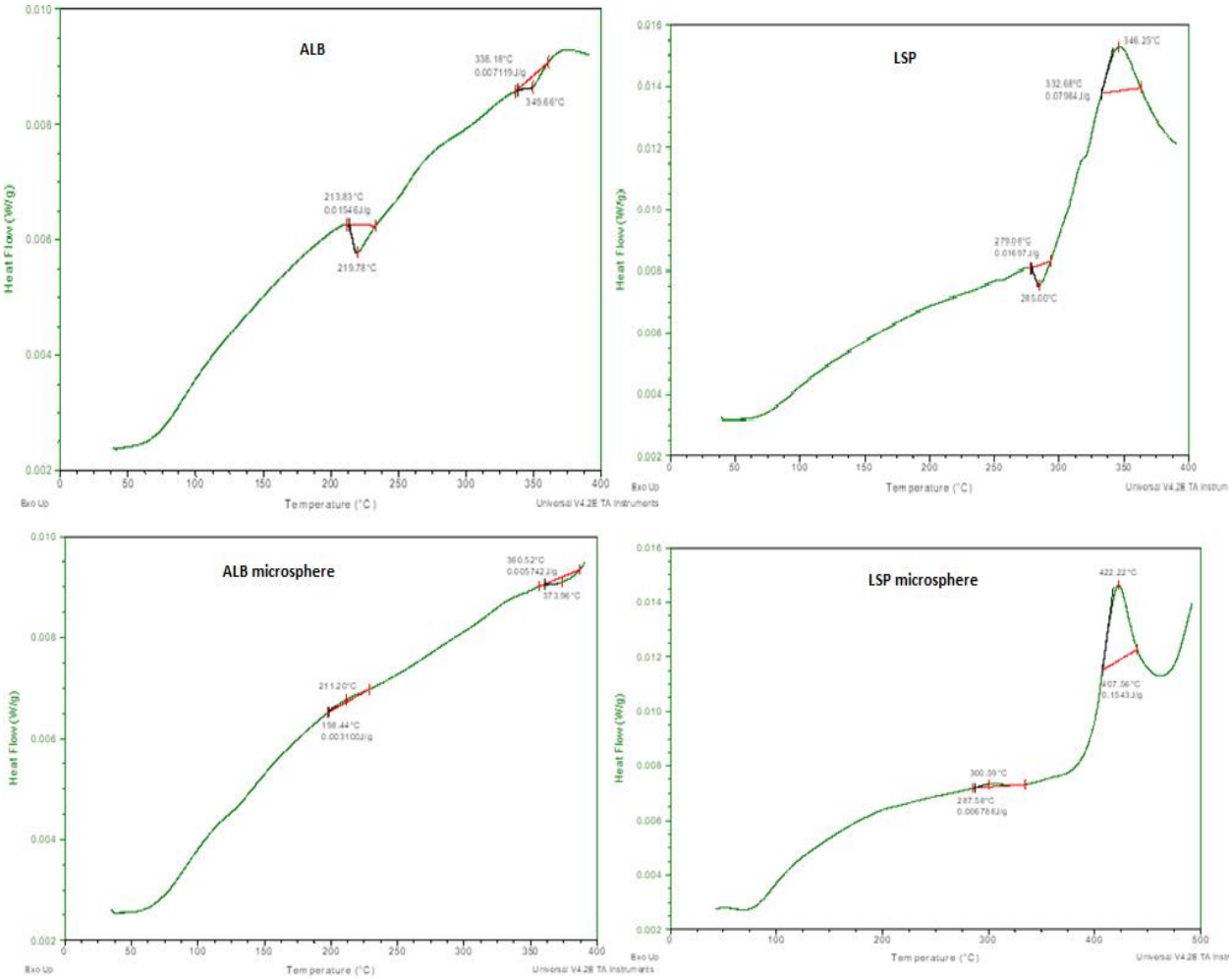

Figure 9: DSC curve of drugs and microspheres.

Table 2: Lab values of CBC & LFT tests

Test	Control	Treated				Units	NormalValues
		1st	2nd	3rd	Avg.		
Heamoglobin	14.6	15.2	14.4	14.8	14.8	g/dl	M:(14-18) F:(12-15)
RBC	5.54	5.84	5.63	5.7	5.72	x1012/L	M:(4.6-6) F:(4-5.4)
Platelets	608	450	475	389	438	x109/L	150 – 400
AST	34	43	30	31	34.67	u/l	10.0 - 35.0
ALT	31	31	26	27	28	u/l	9.0 - 43.0
ASP	189	181	176	180	179	u/l	65 – 306
Total Bilirubin	0.34	0.37	0.29	0.33	0.33	mg/dl	0.2 - 1.2

CONCLUSION

Gastroretentive floating microsphere is the most promising approach to extend the release of drug by increasing the gastric retention of drug in stomach. The objective of this research work was to formulate the floating microsphere by solvent evaporation technique. Two drugs i.e. amlodipine besylate and losartan potassium were used for this research work. Amlodipine besylate is a calcium channel blocker used for hypertension treatment. Losartan potassium belongs to class named as angiotensin receptor blocker and it is also used for the treatment of hypertension. The prepared microspheres were checked for different parameters such as micromeritics, particle size, FTIR, SEM, DSC, entrapment efficiency, percentage yield, in vitro buoyancy and in vitro release. It was observed that prepared microspheres were remain buoyant for more than 12 hrs. Furthermore, it was also checked and confirmed that prepared microspheres were safe in animal models and showed no signs & symptoms of toxicity. Results of all parameters were satisfactory and confirmed that prepared formulation releases the drug in a sustained manner up to 24 hours. Sustained release gastroretentive floating microsphere containing combination of two different antihypertensive drug were prepared successfully. Further studies are required to evaluate the in vivo efficacy of the formulation in animal models.

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