Research Article

A Study on Some Variables Affecting the Preparation of Ethyl Cellulose Based Floating Microspheres of Lafutidine

Karrar Talib Khudhair[*1], Eman B.H.Al-Khedairy[2]
[1.] Department of Pharmaceutics, College of pharmacy, University of Kufa, Al-Najaf, Iraq.
[2.] Department of Pharmaceutics, College of pharmacy, University of Baghdad, Baghdad, Iraq.
***Corresponding author's E-mail:** karpharm84@yahoo.com

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ABSTRACT

Lafutidine (LAF) a newly developed histamine H2-receptor antagonist with absorption window makes it a good candidate to be prepared as floating drug delivery system. The current study involves formulation and in- Vitro evaluation of lafutidine as floating microspheres. Different formulation variables that affect the physicochemical properties of the prepared microspheres besides to the drug release behavior were investigated. Fourteen formulas were prepared by emulsion (o/w) solvent evaporation method using Ethyl cellulose (EC) as the polymeric matrix and tween 80 (TW80) as an emulsifying agent. The prepared formulas were evaluated for their percentage buoyancy (%), Percentage yield (%) and Entrapment efficiency (EE %). The results obtained by formulations were in the range of 64.5±1.885% to 96.8±1.22%, 70.4% to 86, 8% and 27±1.39% to 91.2±1.21% respectively. Formulas (FLF10 and FLF10A) which prepared using 3:1 of EC : lafutidine ratio but with different stirring speed show desirable physicochemical properties and optimum, prolonged in vitro drug release profile and about 92.62% and 95.31% of drug dose release within 14 hrs respectively. It can be concluded that the floating microspheres of lafutidine can be made by emulsion solvent evaporation technique with good gastro retention ability and with expected better drug bioavailability.

Keywords: Lafutidine, floating microspheres, ethyl cellulose, emulsifying agent, percentage buoyancy, entrapment drug efficiency.

INTRODUCTION

Oral dosage form capable of having prolonged retention in the stomach to extend drug delivery to a longer time has been receiving much attention nowadays. Gastric residence time (GRT) is one of the important factors affecting the bioavailability of the drug in pharmaceutical dosage forms**.** Drug bioavailability can be sufficiently increased by prolonging GRT through gastro retentive dosage form, so the gastrointestinal tract targeting dosage forms are prepared which have the ability to hold a drug delivery system above the absorption zone or window (stomach and upper part of small intestine), and for the drug to be released at an appropriate rate at such gastrointestinal sites[1].

Floating, hollow microspheres or micro-balloons are gastro-retentive drug delivery systems based on non-effervescent approach. They are in a strict sense, small and approximately spherical, empty particles without core with a bulk density of less than those of gastric fluid, so they have a sufficient buoyancy to float over gastric contents and remain in the stomach for prolonged time[2]. They are characteristically free flowing powders made of proteins, natural or synthetic biodegradable, biocompatible polymers and other protective modified natural material shaving a size range of (1 to 1000 µm). Once these polymeric materials come in contact with gastric fluid, these gel-forming materials are hydrated to form a colloidal barrier that controls the penetration rate of fluid into the device and consequent drug release resulting in releasing the drug at desired rate and minimizing the fluctuations of drug concentration in plasma ,thereby decreasing in dose frequency[3].

Lafutidine is a new histamine H2- receptor antagonist having a biological half-life of 1.92 h. it is selectively absorbed from an upper part of small intestine (absorption window)[4]. It reaches gastric cells via the systemic circulation, and then directly and rapidly binds to gastric cell histamine H2 receptors, resulting in immediate inhibition of gastric acid secretion. It is used in the treatment of gastric ulcers, duodenal ulcers, and gastric mucosal lesions associated with acute gastritis and acute exacerbation of chronic gastritis [5].

The main objective of the present study was to prepare and evaluate floating microspheres of lafutidine using ethyl cellulose as a low-density polymer for prolongation of gastric residence time and thereby increasing the bioavailability. The effect of various formulation variables was also studied

MATERIALS AND METHODS

Materials

Lafutidine was purchased fromHangzhou hyper chemicals limited, Zhejiang, China. Ethyl cellulose, ethanol, methanol and dichloromethane,(BDH chemicals, Ltd., Liverpool, England). Polyoxyethylene sorbitan mono oleate (tween 80) and polyoxyethylene sorbitan laurate (tween 20), (Sinopharm chemical reagent Co., Ltd). Hydrochloric acid, (Gainland chemical company, UK).All chemicals used were of analytical grade and were used

without further purification. Distilled water was used throughout the study.

METHODS

Preparationof lafutidine floating microspheres

Microspheres were prepared by emulsion (Oil-in-water emulsion) solvent evaporation method. Lafutidine and ethyl cellulose (EC) were dissolved in an organic solvent(s), dichloromethane (DCM) or a mixture of DCM and ethanol (ETOL) at room temperature. This solution was poured into 200 ml water containing emulsifying agent of tween80maintained at a temperature of 30-40˚C and subsequently stirred at different stirring speed using mechanical stirrer for specified time to allow the volatile organic solvent to evaporate. The microspheres formed were filtered, washed with water and dried overnight at room temperature[6].

Variables Affecting Preparation of Micro Spheres

Effect of concentration of emulsifying agent

In order to observe the effect of concentration of emulsifying agent on the properties of the formulated lafutidine floating microspheres formulas (FLF1-FLF3) were prepared by using tween80 as an emulsifying agent in different concentrations as shown in table 1.

Effects of volume and type of dispersed phase

To evaluate the effect of volume of organic solvent system on the properties of prepared lafutidine floating microspheres, formulas (FLF4-FLF8) were prepared using different volumes of DCM as shown in table 1

Effect of polymer: drug ratio

The Effect of polymer :drug ratio on the properties of the prepared floating microspheres, formulas (FLF9-FLF12) were prepared in ratios of 2:1, 3:1, 4:1, 5:1 (EC:LAF) respectively showed in table 1.

Effect of stirring speed and stirring time

The effect of stirring speed (FLF10A) and stirring time (FLF10B) on the properties of the formulated lafutidine floating microspheres was also studied to be compared with FLF10 as shown in table 1.

Table 1: Composition of lafutidine floating microspheres formulas

Formula Code	Polymer : drug	Emulsifying agent concentration	Volume of [d] ETOL	Volume of [c] DCM	Stirring speed and stirring time
FLF1	0.5 : 0.5	[e]TW80 0.2%(v/v)	5ml.	5ml.	500 rpm for 1hr.
FLF2	0.5 : 0.5	TW80 0.5%(v/v)	5ml.	5ml.	500 rpm for 1hr.
FLF3	0.5 : 0.5	TW80 1%(v/v)	5ml.	5ml.	500 rpm for 1hr.
FLF4	0.5 : 0.5	TW80 0.2%(v/v)	------	5ml.	500 rpm for 1hr
FLF5	0.5 : 0.5	TW80 0.2%(v/v)	------	10ml.	500 rpm for 1hr
FLF6	0.5 : 0.5	TW80 0.2%(v/v)	------	20ml.	500 rpm for 1hr
FLF7	0.5 : 0.5	TW80 0.2%(v/v)	------	50ml.	500 rpm for 1hr
FLF8	0.5 : 0.5	TW80 0.2%(v/v)	------	100ml.	500 rpm for 1hr
FLF9	1.0 : 0.5	TW80 0.2%(v/v)	------	20ml.	500 rpm for 1hr
FLF10	1.5 : 0.5	TW80 0.2%(v/v)	------	20ml.	500 rpm for 1hr
FLF11	2.0 : 0.5	TW80 0.2%(v/v)	------	20ml.	500 rpm for 1hr
FLF12	2.5 : 0.5	TW80 0.2%(v/v)	------	20ml.	500 rpm for 1hr
FLF10A	1.5 : 0.5	TW80 0.2%(v/v)	------	20ml.	1000 rpm for 1hr
FLF10B	1.5 : 0.5	TW80 0.2%(v/v)	------	20ml.	500 rpm for 2.5 hrs

[a]Ethyl cellulose, [b]Lafutidine, [c]dichloromethane, [d]Ethanol alcohol, [e]Tween80

Characterization of Lafutidine Microspheres

Percentage yield of microspheres and drug entrapment efficiency

The production yield of micro spheres was calculated using the weight of the final product after drying with respect to the initial total weight of the drug and polymers used for the preparation of microspheres [7,8], and the percentage production yield was calculated as given by equation No1.

Yield% = practical mass of microspheres/ Theoretical weight of (drug/polymer)……(1)

Whereas the drug encapsulation efficiency was determined by accurately weighed an amount of floating microspheres powder equivalent to 20mg of lafutidine and then crushed in a glass mortar. The powdered microspheres were placed in 30 ml of methanol and sonicated for 30 minutes .The solution was then filtered through Whatman filter paper . The solution was diluted with fresh solvent and analyzed

spectrophotometrically at 273 nm for lafutidine content using UV spectrophotometer (Shimadzu 1800) [7,8].

The solution of methanol and an equivalent weight of polymer(s) was used as blank and the percent drug entrapped was calculated as given by equation No 2.

%EE= mass of drug present in microspheres/theoretical mass of drug…… (2)

Determination of the buoyancy percentage

Floating microspheres (100mg) were added to 100ml. 0.1 N HCl (pH 1.2) solution containing tween 20 (0.02 w/v %) and stirred at 100 rpm by using a magnetic stirrer. After12 h, the layer of buoyant microspheres was pipetted and separated from the settled microspheres by filtration. Particles of both layers were dried and weighed[7, 8]. The buoyancy of microspheres was calculated by using the following formula given as by equation No 3.

$$\% \text{ Buoyancy} = \frac{Wf}{Wf + Ws} \times 100 \quad \text{..... (3)}$$

Where, Wf and Ws are the weight of the floating and settled microspheres respectively.

Determination of the particle size

By using an optical microscope, the mean particle size will be calculated by measuring randomly selected 100-200 particles with the help of a calibrated ocular micrometer [9].

In-vitro drug releases studies

The drug release rate from floating microspheres was determined using (paddle) type II dissolution test apparatus. A weighed amount of floating microspheres equivalent to 20 mg drug was added to 900ml of 0.1 N HCl (1.2 pH) solution containing Tween 20 (0.02 w/v %) maintained at 37± 0.5 °C at a rotation speed of 100 rpm. Sink condition was maintained during the study. 10 ml sample was withdrawn at a 1hr time interval and replaced by equal volume of fresh, previously heated to 37°C medium then passed through the 0.45µm membrane filter and analyzed spectro photometrically at 286.6 nm. All experiments were performed in triplicate[7, 8].

Surface morphology study

Surface topography, particle size, and morphology of the floating microspheres were investigated with a scanning electron microscope SEM [9].

Drug-polymer compatibility study

Fourier-transform Infrared Spectroscopy (FTIR)

Drug-polymer interactions were studied by FTIR spectroscopy. The spectra were recorded for pure a drug, pure polymers, drug-loaded floating microspheres and physical mixtures of drug and polymer. Samples were prepared in KBr discs. The scanning range was (400- 4000 cm-1) [10].

Differential scanning calorimetry (DSC) analysis

The DSC analysis of pure drug, drug- polymer physical mixture and drug-loaded floating microspheres was carried out to evaluate the internal structure of the floating microspheres after drug incorporation, and any possible drug polymer interaction [11].

Statistical analysis

Using Microsoft excel 2010, analysis of variance (ANOVA) was used for the comparison of multiple characterization results values and figures, for all analyzed results:

P value of more than 0.05 was considered to be non significant. P value of less than 0.05 was considered to be significant.

RESULTS AND DISCUSSION

Effects of concentration of emulsifying agent

The results indicated that TW80 can be used successfully in preparation of lafutidine floating microspheres and it was found that 0.2% (v/v) TW80 is the best concentration among the other used concentrations, based on the best physical characteristics (percentage of yield, entrapment drug efficiency percentage buoyancy and particle size,) that provided by the prepared microspheres of formula FLF1 as shown in table 2.

In addition, it was found that as the concentration of the emulsifying agent increase, as given by formulas FLF2 and FLF3,the percentage of yield, entrapment drug efficiency , percentage buoyancy and particle size of prepared micro spheres decreased significantly ($p<0.05$). The reason behind this is that the low emulsifying agent concentration was insufficient for full reduction of the surface charge so that, the polymer droplets were aggregated during the emulsion phase and resulted in an increase in particle size. So, the entrapment efficiency was high which might be due to increasing in particle size resulting increase in entrapment efficiency of the drug into the increased matrix mass. Whereas high concentration of emulsifying agent resulted in reduction in drug loading due to the decrease in surface charge by the surfactant and better stabilization of internal droplets thus, preventing coalescence dispersion of microcapsules in the microencapsulation system [12].which results in smaller particles and so, insufficient matrix mass was available to get entrap the drug molecules [13,14]. Also when the concentration of emulsifying agent within the aqueous phase was increased it may facilitate, together with ethanol (act as co-solvent), the diffusion or solubilization of drug in the aqueous phase resulting in low encapsulation efficiency.

In addition, the buoyant ability was also decreased along with increasing the concentration of tween80. The formulas (FLF2 and FLF3) showed lower percentage buoyancy. This is may be attributed to a smaller particles size associated with floating microspheres of such formulas [15]as shown in table 2.

Effects of volume and type of dispersed phase

For this purpose, five formulas (FLF4-FLF8) were prepared in which dichloromethane (DCM) alone was used as an organic solvent within the dispersed phase to compare its effect with the solvent system mixture of ETOL/DCM that was previously used in preparation formulas (FLF1-FLF3). DCM was used because of its high volatility, low boiling point (39.7°C) and high water immiscibility. It's high saturated vapor pressure compared to other solvents (at least two times higher) promises a high solvent evaporation rate, which shortens the duration of fabrication of floating microspheres [16, 17].The rapid removal of solvent from the embryonic microspheres leads to polymer precipitation at the o/w interface which leads to the formation of a cavity in microspheres, thus making them hollow to impart the floating properties [18]. In addition, DCM was used as it is considered as a good solvent for both lafutidine and EC.

In this sense most of formulas were succeed to produce a floating microspheres except for FLF4 and FLF5 were failed, because of a small volume of DCM (5ml and 10ml respectively), which was inadequate to produce a stable emulsion due to the rapid evaporation rate of DCM at procedure temperature of 40 °C resulted in sudden aggregation and solidification of EC in an irregular and large size fibers like structures.

The optimum volume of dispersed phase was found to be 20ml DCM based on the characterization features of the obtained floating microspheres, as in formula (FLF6) in which the highest percentages of yield (80.46%), entrapment drug efficiency (62.3±1.36) and percentage buoyancy of 88±1.87 were obtained as illustrated in table 2.

On the other hand, the results indicated that the increase in volume of DCM had a crucial impact on the characteristics of microspheres, as volume of DCM increased from 20ml to 50ml and 100ml (FLF7 and FLF8) the percentage yield, encapsulation efficiency, percentage buoyancy and particles size were significantly ($p<0.05$) decreased [19,20] as illustrated in table 2. This may be due to that at a very high volume of internal phase resulted in an increase diffusion of some entrapped drug molecules from polymer matrix along with DCM into the aqueous external phase which will then precipitated later at the bottom of the vessel as un encapsulated drug particles after the evaporation of DCM. In additional decreasing in the viscosity of dispersed phase along with increasing the volume of organic solvent at a constant amount of polymer and drug resulted in the formation of smaller droplets within the o/w emulsion giving rise to smaller particles size and, so a lower entrapment drug efficiency and percentage buoyancy. Generally, the EC-loaded floating microspheres obtained by using DCM alone were found to be more regular in shape and spherical, with better physical properties than those prepared by using a mixture solvent system of ETOl/DCM as in formula FLF1 which appeared irregular and have a floss-like appearance with poor flow properties. Although the presence of ETOl within dispersed phase even in small volume resulted in formation of a more stable o/w emulsion as in FLF1, but it is associated with a low drug encapsulation efficiency this may be due to that the microspheres droplets may remain in liquid state for a longer period of time and drug could be easily diffuse along with ethanol across the non-precipitated droplet surface to aqueous phase resulted in lower drug content[19].

Effect of polymer: drug ratio

The effect of increasing the polymer concentration versus a constant concentration of drug within the dispersed phase was studied by preparing formulas **FLF9-FLF12** using different polymer: drug ratios (2:1, 3:1, 4:1 and 5:1) respectively, as illustrated in table 1.

The analyzed results for the prepared microspheres indicated that increase in polymer concentration caused a significant ($p<0.05$) increase in percentage yield, entrapment drug efficiency, percentage buoyancy, particles size, and particles sizes shown in table 2,the same finding was observed by khan A. I *et al*[21] and Bansode*et al*[22].

These results were expected, since the increase in polymer concentration at a constant speed, will result in a fast formation of microspheres and less loss of materials during the process and so increase % yield of microspheres. On the other hand, the increase in % entrapment at same rpm. This can be explained by due to the presence of sufficient amount of polymer that can entrap the drug molecules also increasing of polymer: drug ratio was found to be associated with an increase in viscosity of external phase medium. The increased viscosity of the medium at a higher polymer concentration results in enhanced interfacial tension and diminished in shearing efficiency. This results in a formation of larger and more regular particles [23]. Such significant increase in particles size was associated with high entrapment drug efficiency and percentage buoyancy [21, 22].

Effect of stirring speed and stirring time

The formulas FLF10A and FLF10B were prepared to study these effects. The results indicated that increase in stirring speed from 500 to 1000 rpm (FLF10A) resulted in a significant decrease ($p<0.05$) of % yield which may be due to increasing in a turbulence of agitated emulsion during the formulation procedure

leading to more microspheres to stick to beaker wall [24]. The particles size were insignificantly decreased with increasing in stirring speed ($p>0.05$) which may be due to agitation speed (1000rpm) was not enough to break up the bulk of the polymer into more fine droplets due to a relatively high viscosity of internal phase. The buoyancy and entrapment drug efficiency were also not significantly affected ($p>0.05$) since these properties depend on the particles size. On the other hand the increase in stirring time from 1hr to 2.5hrs, as given by FLF10B, resulted in a significant effect on the physical characteristics of the prepared microspheres in particularly causing an increase in particles size which may be due to that some particles will aggregate or agglomerate along with increasing the stirring time and also a significant decrease in percentage yield which may be due to the high loss by sticking into beaker throughout the formulation procedure whereas the buoyancy percentage and entrapment efficiency were not highly affected as illustrated in table 2.

In-vitro drug releases studies

The lafutidine floating microspheres of formulas **FLF6**, **FLF9, FLF 10, FLF 11, FLF12**, **FLF10A,** and **FLF10B** were subjected to in-vitro drug release study as they consider being the best formulas based on their higher percentage of (yield, entrapment drug efficiency, and buoyancy). In addition, the choice of such formulas was allowed to study the effect of increasing the polymer : drug ratio (**FLF6-FLF12**), increasing in stirring speed (**FLF10A**) and increasing in stirring time (**FLF10B**) on the In-vitro drug release as shown in figures 1,2and 3 respectively. Regarding the effect of varying polymer: drug ratio, the release data of lafutidine floating microspheres showed a significant effect ($p<0.05$). Such formulas exhibited an increased in release retardation, for both the first hour and for whole drug release profile, along with increasing in polymer concentration. This may be attributed to that the increased of the polymer matrix thickness at higher concentrations giving rise to an increase in diffusion path length. This may decrease the overall drug release from the polymer matrix in spite of high solubility of lafutidine in the acidic medium. Furthermore, smaller microspheres were formed at lower polymer concentrations with larger surface area exposed to dissolution medium, giving rise to faster drug release [25].

Table 2: The formulation characteristics for lafutidine floating microspheres formulas prepared at different (emulsifying agent Concentration, volumes of DCM, polymer : drug ratios, stirring speed and stirring time)**.**

Formula code	% yield	% entrapment efficiency	% buoyancy	Particles size
FLF1	77.5	52.6±1.01	84.2±2.925	210.348± 28.374
FLF2	72	31.2±2.2	75±2.25	190.205± 23.662
FLF3	70.4	27±1.39	64.5±1.885	120.411± 21.554
FLF4	NO YIELD	----------	----------	----------
FLF5	NO YIELD	----------	----------	----------
FLF6	80.46	62.3±1.36	88±1.87	350.361± 35.7714
FLF7	75.2	52±2.18	75.3±1.338	220.276± 31.884
FLF8	74	38±2.09	71±3.12	180.561± 29.2204
FLF9	83.5	79.3±2.05	90±1.114	390.912± 41.35401
FLF10	86.4	88.4±1.022	95±1.087	420.55± 43.9906
FLF11	86.8	89.6±1.088	96.5±1.15	580.376± 45.442
FLF12	86	91.2±1.21	96.8±1.22	650.32± 46.98803
FLF10 A	75	87.3±1.33	93±1.56	390.466± 45.85904
FLF10 B	77.4	81.6±1.12	87.5±1.789	510.572± 52.631

The results represent mean ± S.D., n=3

On the other hand, the release data in the case of microspheres prepared at a higher agitation speed (**FLF10A**) show a non-significant ($p>0.05$) difference from the drug release of formula (**FLF10**) as indicated by figure 2. This may be due to that the agitation speed used was inadequate to produce a significant effect on the particles size. Whereas the increase in stirring time was found to have a significant effect ($p< 0.05$) on the lafutidine release profile. A faster release fashion was exhibited by formula (**FLF10B** in compare with **FLF10**). More than 90% of lafutidine dose was released within 9hrs and 14hrs respectively as seen in figure 3. This may be due to a higher porous microspheres surface that

may be developed when the agitation was continued for prolonged period of time.

From the release data that had been obtained and discussed, formulas **FLF10** or **FLF10A** were found to be the best formulations as it releases lafutidine in a sustained manner with no burst and constant fashion over an extended period of time (after 14 hrs). which prolonged the gastric retention time at the upper part of GIT and thereby increasing the lafutidine bioavailability.

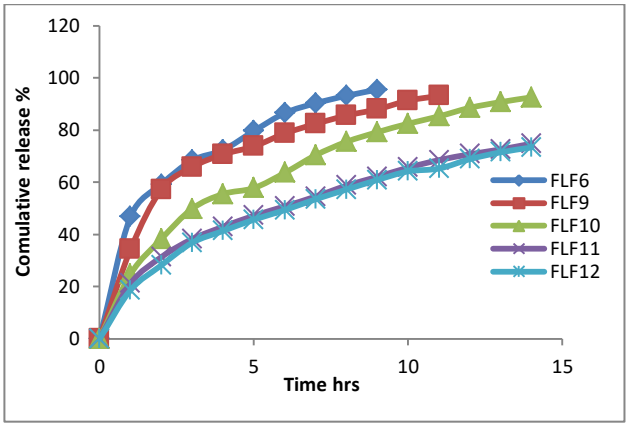


Figure 1: The release profiles of prepared LAF floating microspheres formulas (FLF6, FLF9, FLF10, FLF11 and FLF12) using (EC: LAF) ratios (1:1, 2:1, 3:1, 4:1 and 5:1) respectively in 0.1 N HCl pH 1.2 at temperature 37°C (The results represent mean ± S.D., n=3)

Surface morphology study

Surface topography, particle size, and morphology of the floating microspheres were investigated with a scanning electron microscope (SEM). In this sense, the selected formulas (**FLF10** and **FLF10A**) that provide the sustained, regular and prolonged drug release (≥ 14hrs.) were subjected to SEM study in order to ensure their spherical morphology, porosity, and homogeneous drug distribution within the polymer matrix.

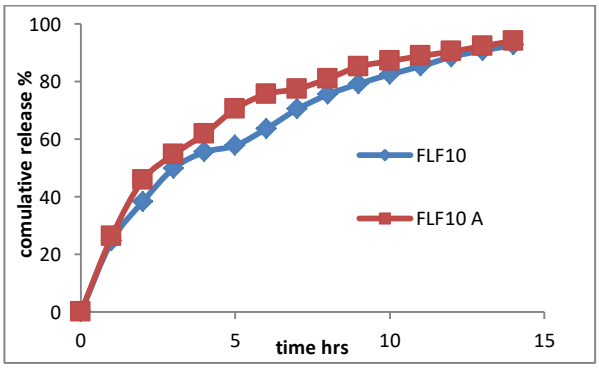


Figure 2: The release profiles of prepared LAF floating microspheres formulas (FLF10 and FLF10A) using EC: LAF of (3:1) ratios, at 500 rpm and 1000 rpm respectively in 0.1NHCl pH 1.2 at temperature 37°C (The results represent mean ±S.D., n=3)

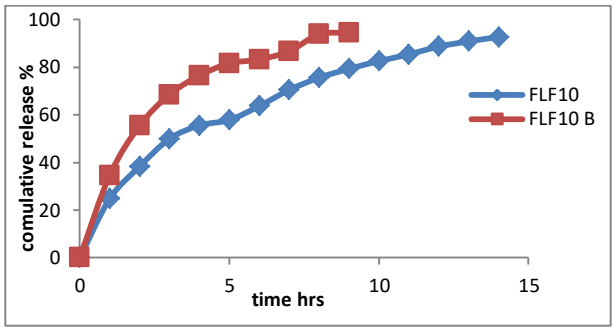
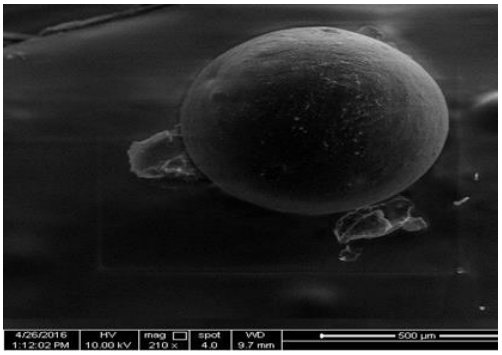


Figure 3: The release profiles of prepared LAF floating microspheres formulas (FLF10 and FLF10 B) using EC:LAF of (3:1) ratios, at 500 rpm for 1hr and 2.5 hrs respectively in 0.1NHCl pH 1.2 at temperature 37°C (The results represent mean ±S.D., n=3).

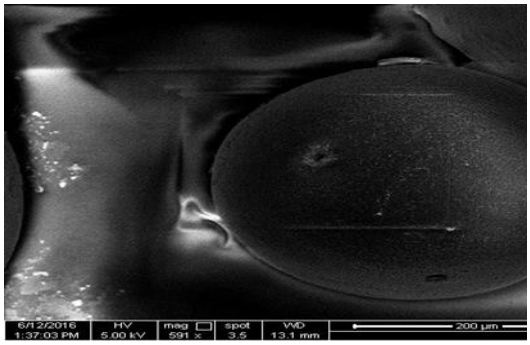
The results indicated that microspheres were spherical, regular in shape, completely closed and had smooth, rugged surface with only a few crystals deposited on it, which is probably a drug that is responsible for an initial release and gives indicative for homogeneous distribution of drug molecules within the polymer matrix. The results also reveal porosity developed at the surface as seen with figures4.The surface porosity is crucial in microspheres prepared with ethyl cellulose. Since the drug dissolution and diffusion were occurred through these pores prior to it is released into the bulk dissolution medium [12].

Fourier-Transform Infrared Spectroscopy (FTIR)

The FTIR spectra obtained for lafutidine (LAF), EC, physical mixtures of (EC-LAF) and (EC-LAF) loaded floating microspheres (formula **FLF10**) are shown in figure 5.



(A)



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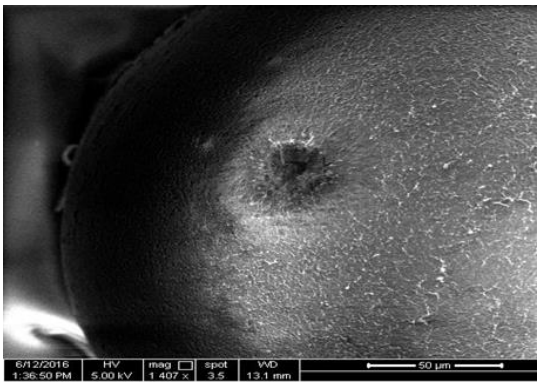
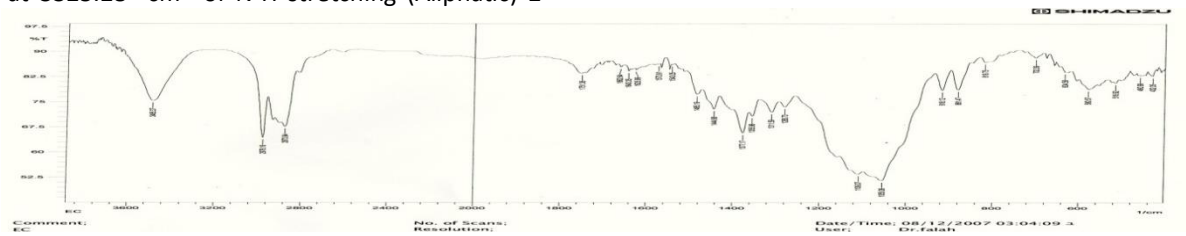


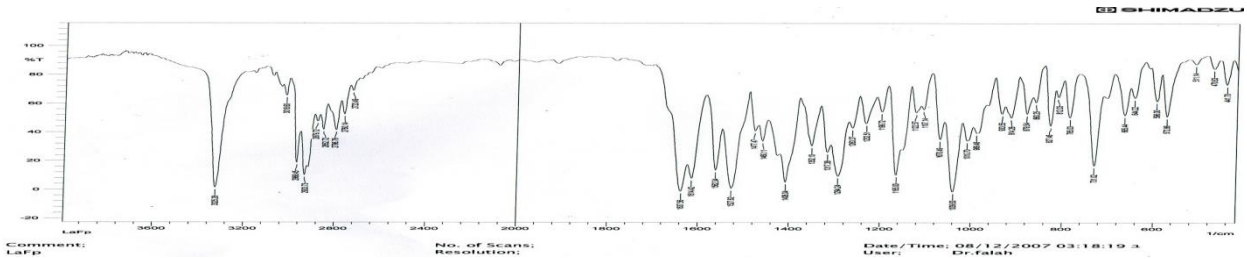
(C)

Figure 4: A-C. SEM photomicrograph of EC-LAF load Floating microspheres (FLF10 & FLF10A)(A-C)

The IR of pure lafutidine show characteristic sharp peaks at 3325.28 cm^{-1} of N-H stretching (Aliphatic) 2° amide, alkene (=C-H) stretching vibration at 3018.6 cm^{-1}, alkane stretching (-CH2 aliphatic and cyclic) vibration at 2852.72 cm^{-1}, C-H stretching (Aromatic) at 2933 cm^{-1}. Also exhibited C=O stretch at 1736.5 cm^{-1} due to saturated ketone and C=C stretching at 1637.56 cm^{-1}. For functional groups like S=O stretch and –C-S stretch showed vibrations at 1039.63cm^{-1} and 731.02 cm^{-1} respectively [26,27]. For EC, the FTIR spectrum shows sharp peaks at 3485.37cm^{-1} of O-H alcoholic stretching, an alkane (CH3-H, CH2-H aliphatic) at 2976.16 cm^{-1} and 2873cm^{-1}. All of the detected peaks were still observed within the physical mixture of EC/LF. In addition, most of the peaks are still observed within the IR spectrum of EC-LF loaded microspheres, which indicate the compatibility and absence of any chemical interactions between drug and polymer.



(A)



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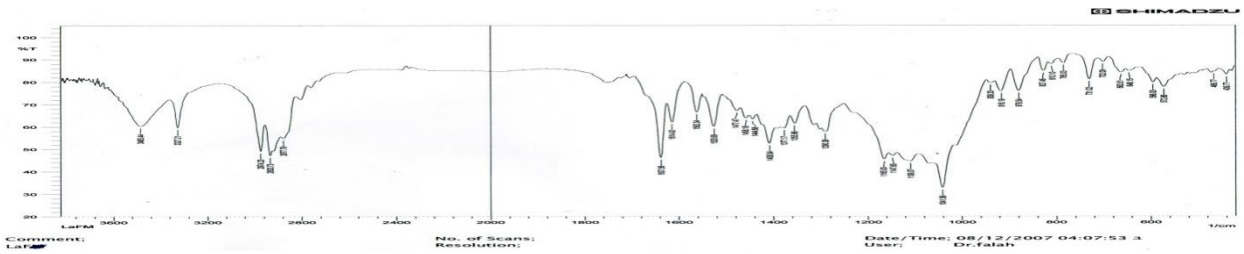
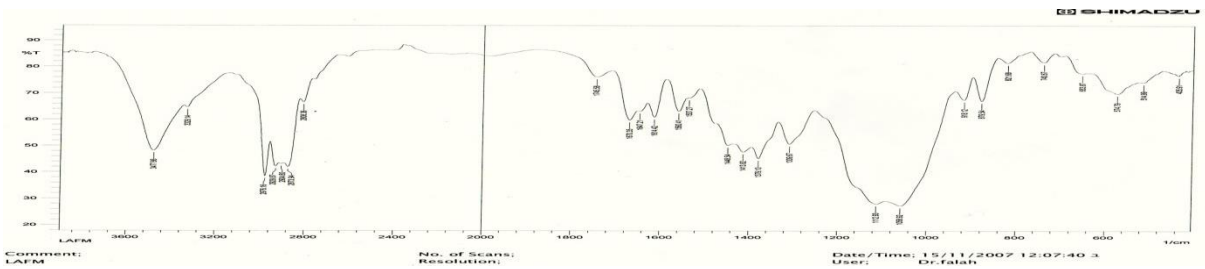


(C)



(D)

Figure 5: FTIR specrum of (A) pure lafutidine, (B) ethyl cellulose, (C) EC/LAF physical mixture and (D) LAF-EC floating microspheres

Differential Scanning Colorimetry (DSC)

Differential scanning calorimetry was carried out to determine the possible interaction between drug and polymer. The thermograms of pure lafutidine, EC/lafutidine physical mixture are shown in figure6a and b, while figure 6c shows the thermograms of loaded floating microspheres of EC-lafutidine.

The DSC of lafutidine shows a single sharp endothermic peak at 101.03 °C corresponding to its melting transition temperature. While the DSC of EC/lafutidine physical mixture still show a sharp endothermic peak for lafutidine at 100°C and small exothermic peak at 205.5°C for EC.

The peak of the drug did not appear in the thermogram of drug microspheres. This may indicate that the drug was uniformly dispersed at the molecular level in the microspheres [28, 29] or may be due to the conversion of the drug from crystalline to semi-crystalline or amorphous state. The same finding was observed by *Jithan Aukunuru et al* [30]. From the results, we can indicate that no interaction between drug and polymer was observed.

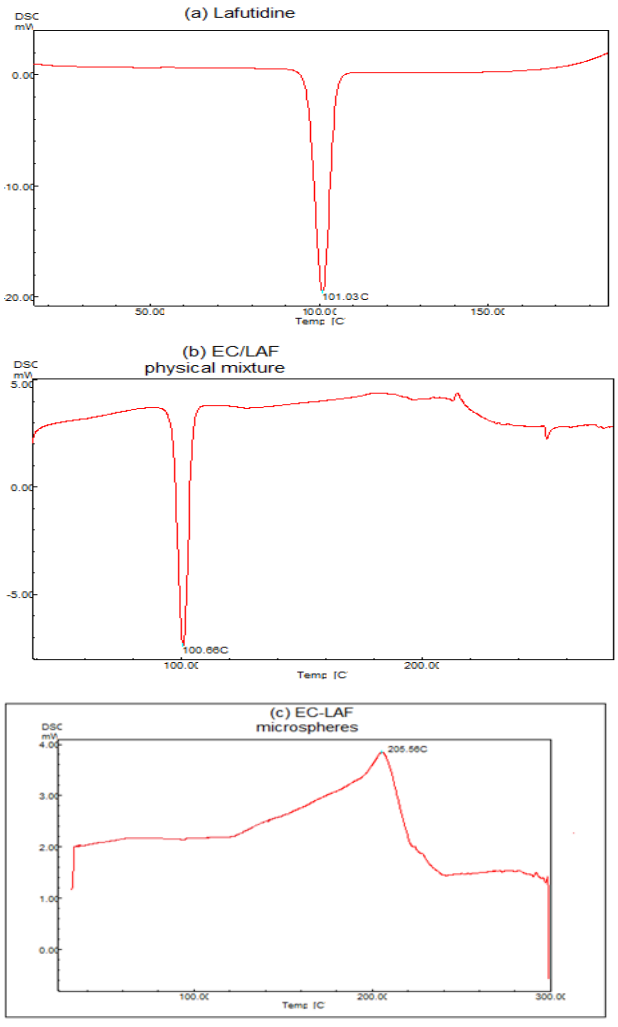


Figure 6: DSC thermo grams of pure lafutadine (a), EC/LAF physical mixture (b) and EC-LAF floating microspheres (c)

CONCLUSION

On the basis of obtained results, one can conclude that EC can be used for the formulation of lafutidine loaded floating microspheres successfully by emulsion solvent evaporation technique. Overall results suggest that most variables (emulsifying agent concentration, type, and volume of dispersed phase, polymer: drug ratio, stirring speed and stirring time) had a significant effect on the physical characteristics along with the drug release profile of the formulated microspheres. On the basis of data obtained from in vitro dissolution studies, it can be concluded that FLF10 and FLF10A are promising formulations suitable for the sustained release of lafutidine for gastro retention purpose that may be giving rise to enhance the bioavailability of lafutidine since they exhibited a prolonged drug release fashion for about 14 hours.

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