Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 3 Issue 2 February 2019

Research Article

Floating Microsponges as Gastro Retentive Drug Delivery System Containing Lafutidine to Treat Gastric Ulcer

Sunil T Galatage[1], SG Killedar[2], JK Saboji[3], Imrankhan M Bhaishaikh[4]*, Vivek P Kadam[5], Nilesh N Gurav[6] and DA Bhagwat[7]

[1]*Sant Gajanan Maharaj college of Pharmacy Mahagaon, Shivaji University, Kolhapur, India*

[2] *Principal, Sant Gajanan Maharaj college of Pharmacy Mahagaon, Shivaji University, Kolhapur, India*

[3]*Principal, K.L.E Society's College of Pharmacy, Karnataka, India*

[4]*K.L.E'S College of Pharmacy, Nipani, Karnataka, India*

[5]*MD Karveer Pharma, Kolhapur, India*

[6]*Senior Scientist Ajanta Pharma, India*

[7]*BVCP College of Pharmacy Kolhapur India*

***Corresponding Author:** Imrankhan M Bhaishaikh, *K.L.E'S College of Pharmacy, Nipani, Karnataka, India*.

Received: December 29, 2018; **Published:** January 08, 2019

Abstract

This research work was carried out to measure the gastro retentive efficacy of micro sponges via optimization of targeted floating lafutidine microsponges for improved site specific absorption for gastric ulcer. Modified quasi emulsion solvent diffusion process was used to fabricate microsponges. The effect of different levels of ethyl cellulose and polyvinyl alcohol concentration, selected as independent variables was determined on the % entrapment efficiency, % buoyancy and % cumulative drug release. Modified rosette rise apparatus was used for *In vitro* release and the release data best fitted zero order models and mechanism of drug release is independent of concentration of drug. The optimized formulation (MS5) demonstrated favourable % entrapment efficiency (92.83 ± 1.8), % buoyancy (86.30 ± 1.8) and % cumulative drug release (85.7 ± 1.2). SEM revealed spherical and porous micro sponges. DSC confirmed molecular dispersion of the drug in the microsponge' polymeric matrix. This study presents a new approach based on floating ability of microsponge for treatment of gastric ulcer.

Keywords: Floating Microsponge; Lafutidine; Quasi Emulsion; Gastric Ulcer

Introduction

The ulcer preventive and the H_2 receptor blocking activity of lafutidine have been demonstrated in numerous antiulcer pre-clinical trials. Lafutidine is newly found histamine H_2 receptor antagonist [1]. Lafutidine produce gastroprotective effect which is related to its antisecretory activity and its ability to activate a sensory neuron-dependent mechanism of defence [2]. It has been reported to increased action on the gastric mucosal defensive capacity and enhancement of mucosal blood flow via capsaicin-sensitive sensory neurons there by providing gastro protective effects even against necrotizing agents such as nonsteriodal anti-inflammatory drugs. The gastro protective action of lafutidine includes increase in mucin biosynthesis via stimulation of nitric oxide production, increasing the thickness of the surface mucus gel layer, and maintaining gastric mucosal blood flow and bicarbonate response. Lafutidine has been found to be effective in subjects with Helicobacter Pylori infections and it induces an increase in intragastric pH. The efficacy of lafutidine has been proven clinically that it balances both the aggressive and the defensive factor in the management of acid peptic disorders [3]. Lafutidine has a powerful receptor binding affinity which is 2-80 times higher than other representative H_2-receptor blockers e.g. famotidine, ranitidine, and cimetidine [4].

In clinical study lafutidine (LAFT) is proved that it is inhibits day-time (i.e., postprandial) as well as night time gastric acid secretion. Despite these promising biological effects of lafutidine, a major drawback with lafutidine is its extremely low solubility in aqueous solutions which leads to low bioavailability. Its low aqueous solubility, which impairs its dissolution in upper gastric fluid producing problems to prepared systems including short half-life. It is determined that lafutidine degrades in neutral, alkaline and photolytic condition but remains stable in acidic condition [5]. Tak-

ing in to consideration the reasons attributable to poor bioavailability of lafutidine, it would be advantageous to design a formulation which prolongs gastric residence time in stomach. Various strategies have been undertaken to deliver lafutidine in gastric cavity by oro-dispersible tablets [6]. These systems have potential for targeting drug molecule to its targeted site but have low drug loading capacity. Microsponges offer an efficient drug delivery system for stomach specific delivery with high drug loading capacity. Microsponges have the ability to entrap wide range of active material due to its numerous interconnected pores and can adsorb high quantity of active pharmaceutical ingredients on its surface and load into the bulk of particles [7]. This system provides maximum efficiency, extended product stability, reduced side effect and modifies drug release favourably [8].

In oral application, the microsponges system has been shown to increase the rate of solubilization of poorly water soluble drugs by entrapping drugs in pores of microsponges.as these pores are very small, the drug in effect reduced to microscopic particles and the significant increase in the surface area thus greatly increase the rate of solubilization [9].

This paper is the first report on development highly efficient lafutidine floating microsponges system with high drug loading capacity using biocompatible, safe and inexpensive polymers ethyl cellulose and eudragit S 100 to target gastric ulcer as a site specific targeted drug delivery system.

Materials and Methodology

Materials

All the materials used in the formulations, evaluation and other experiments are listed below. The chemicals used were of laboratory reagent grade and were used as they were procured. The distilled water was used in all experiments.

	Materials	Suppliers
Drug	Lafutidine	Swapnroop pharma. Ahamadabad, Gujrat.
Polymer	Ethyl cellulose	Himedia Laboratories (Mumbai)
Polymer	Eudragit S 100	Evonikindustries, Mumbai
Chemicals	Ethanol	Loba chem. Pvt. Ltd. (Mumbai)
	Polyvinyl alcohol	Merck Specialities (Mumbai).
	Sodium chloride	Loba Chemie Pvt. Ltd. Mumbai
	Span 80	Karnataka Fine Chem.
	DCM	Loba Chemie Pvt. Ltd. Mumbai

Table 1: List of chemicals and reagents used with supplier.

Method of preparation

Floating Microsponges were prepared by quasi-emulsion solvent diffusion technique using sodium chloride solution as porogen.Solution of ethyl cellulose, Eudragit S100 and lafutidine was prepared in ethanol and dichloromethane (1:1 organic phase). 1.5% (w/v) aqueous solution of the porogen was prepared and sufficient amount of span 80 was added to it with agitation to obtain 1.5% (v/v) dispertion. The porogen solution was uniformly emulsified in polymeric solution, to form a w/o emulsion. An aqueous polyvinyl alcohol solution (aqueous phase) was prepared separately and previously prepared w/o emulsion was emulsified in it. This w/o/w emulsion was stirred on magnetic stirrer for 8 h. The dispersed droplets were solidified in the aqueous phase by evaporation of the solvent. The microsponges were filtered, dried at 60^0C in the hot air oven and stored in desiccator till use [10,11].

Formulation code	Lafutidine (mg)	Eudragit S-100 (mg)	Sodium chloride (% w/v)	Ethyl cellulose (mg) (X_1)	PVA (% w/v) (X_2)	DCM: Ethanol	Water (ml)
MS1	200	100	1.5	300	0.5	1:1	80
MS2	200	100	1.5	600	0.5	1:1	80 80
MS3	200	100	1.5	900	0.5	1:1	80
MS4	200	100	1.5	300	1.0	1:1	80
MS5	200	100	1.5	600	1.0	1:1	80
MS6	200	100	1.5	900	1.0	1:1	80
MS7	200	100	1.5	300	1.5	1:1	80
MS8	200	100	1.5	600	1.5	1:1	80
MS9	200	100	1.5	900	1.5	1:1	80

Table 2: Formulation of Floating Microsponge of Lafutidine.

Evaluation

Melting point determination [12]

Melting point of drug sample was determined by melting point apparatus. The small quantity of drug was taken in a capillary tube sealed at one end and was placed in digital melting point apparatus and temperature range at which the drug melts is noted.

UV spectroscopy-determination of lambda max: [13]

Most drugs absorb light UV wavelength (200-400nm), since they contain aromatic double bonds. The solution containing 10µg/ml of lafutidine was prepared and scanned over the range of 200-400 nm against 0.1 N HCL as blank using shimadzu double beam UV spectrophotometer. The maximum wave length obtained 286 nm in the graph was considered as λmax for the pure drug.

Solubility test [14]

Knowing Solubility criteria of drug is important to check whether it is soluble or not. Take Acetic acid, Ethanol, 0.1N HCL and Methanol 10 ml each in separate beaker and add 100mg of drug in each beaker and check the solubility by stirring it.

Particle size analysis [15]

Particle size of the prepared floating micro sponges was determined by optical microscopy. The optical microscope was fitted with an ocular micrometer and a stage micrometer. The eyepiece micrometer was calibrated. The particle diameters of 100 floating micro sponges were measured randomly by optical microscope and their mean particle size and standard deviation was calculated.

Percentage Production Yield: [16]

The practical percentage yield was calculated from the weight of floating micro sponges recovered from each batch in relation to the sum of the initial weight of starting materials. The percentage yield was calculated using the following formula:

The practical percentage yield was calculated from the weight of floating micro sponges recovered from each batch in relation to the sum of the initial weight of starting materials. The percentage yield was calculated using the following formula:

$$\% \text{ yield} = \frac{\text{Practical Mass (flot. microsponges)}}{\text{Theoretical Mass (Polymer + Drug)}} \times 1$$

Dug content: [17]

Prepared floating micro sponges of drugs were assayed spectrophotometrically for the drug content at the maximum wavelength with proper dilution of formulations taking suitable solvent as blank. Taking accurately weighted 50 mg of prepared micro sponges and crushed it and mixed in a beaker containing 100 ml 0.1 NHCL and stirred it at 75 rpm for 2 hrs. Filtered it taken supernant filtrate and observed at 286 nm using UV spectroscopy and calculated drug content using following formula.

$$\% \text{ Drug Content} = \frac{\text{Practical Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

Determination of drug loading efficiency: [18]

Drug loaded floating micro sponge (50 mg) was digested with 100 ml of 0.1N HCL at room temperature for 12 h. After filtration and suitable dilution, lafutidine present in the solution was determined at 286nm using a UV visible spectrophotometer. Drug loading in the micro sponge was estimated by using following formula.

% E = Actual drug content/Total amount of drug × 100 Where, %E = % Drug entrapment Efficiency of floting. Microsponges.

% Buoyancy-[19]

% buoyancy was carried out using 0.1 N HCl containing 1% span 20 as a dispersing medium. Micro sponges were spread over the surface of 900 ml of dispersing medium at 37± 0.5oC. A paddle rotating at 100 rpm agitated the medium for 8 hrs. Each fraction of micro sponges floating on the surface and those settled down were collected at a predetermined time point. The collected samples were weighed after drying. The % buoyancy was determined by following equation.

% Buoyancy = weight of micro sponges floating on the surface/ initial total weight of micro sponges× 100

In vitro drug release studies for lafutidine loaded floating microsponges: [20]

In vitro drug release studies were performed with a USP (type 2) dissolution apparatus. Samples of floating micro sponges containing 10 mg of lafutidine were tested in 0.1N HCL solution. The

rotational speed was set at 75 rpm and temperature for the dissolution medium was set at 37ºC. Samples (1 ml) were withdrawn at predetermined time points (1, 2, 3, 4, 5, 6, 7 and 8 hrs.) and for each withdrawal the corresponding volume was replaced with fresh 0.1N HCL of the same temperature. Samples were filtered (PTFE O.45µm) and assayed spectrophotometrically at 286 nm.

FTIR spectroscopy [24]

IR study was carried out to check compatibility between drug and excipients. An IR spectrum of lafutidine and along with excipients, this final complex was determined by Fourier Transform Infrared spectrophotometer using KBR dispersion method. The base line correction was done using dried potassium bromide. Then the spectrum of dried mixture of drug and potassium bromide was run. FT-IR spectrum of lafutidine was compared with FT-IR spectra of lafutidine with polymer. Disappearance of lafutidine peaks or shifting of peak if any of the spectra was studied.

Scanning calorimetry (DSC) [13]

DSC was performed in order to assess the thermotropic properties and thermal behaviour of the drug and the complex compacts prepared. About 5 mg of the sample were sealed in the aluminium pans and heated at the rate of 10°C/min, covering a temperature range of 40°C to 3000C under nitrogen atmosphere of flow rate 30 ml/min.

Scanning electron microscopy (SEM) [22]

Surface morphology of pure drug and MS5, before and drug release was visualized by scanning electron microscopy. The samples were coated with gold under argon atmosphere using gold sputter module VG microtech, west sussex, UK in high vacuum evaporator and observed under various magnifications (100-1000×) with direct data capture of the images.

Stability testing-[23]

Micro sponges equivalent to 50mg of lafutidine were filled in hard gelatin capsules size 0. The filled capsules were manually packed in blister and the samples were maintained in a stability chamber under accelerated storage conditions, 40 ± 2oC and 75 ± 5% relative humidity for three months with humidity and temperature control. The samples were analysed for Physical changes, buoyancy, % drug content and %CDR at 0, 30, 60, and 90 days and results were noted.

Kinetic release data [24]

For studying the release kinetics, all formulations are fitted in the mathematical models. In order to describe the kinetics of the release process of drug in all formulations, various equations were used, such as zero-order rate equation, first order Equation, Higuchi's Classical diffusion model which describes the system where release rate is independent of the concentration of the dissolved species.

Results and Discussion

Melting point determination

Melting point of lafutidine in literature is 96-100ºC after estimation by capillary method, it was found to be 98ºC which indicates purity of drug sample.

UV SPECTROSCOPY: - DETERMINATION OF Λ_{MAX}:

The λ_{max} of Lafudine was determined in 0.1N HCL which was scanned between 200-400 nm in the UV spectrophotometer. It was found to be 286 nm.

Figure 1: λ_{max} of lafutidine.

Solubility test

Solubility criteria of drug are important to check whether it is soluble or not. by Taking Acetic acid, Ethanol, 0.1N HCL and Methanol 10 ml each in separate beaker and add 100mg of drug in each beaker and check the solubility by stirring it the results where It was freely soluble in acetic acid, soluble in methanol, sparingly soluble in ethanol and practically insoluble in water.

Particle size

The particle size of the micro sponges ranged between from91.2 µm to 168.9 µm. when both ethyl cellulose and PVA were at high

levels the formulation exhibited maximum particle size of 168.9 µm MS-9 and when both ethyl cellulose and PVA were at low levels the formulation exhibited minimum particle size of 91.2 µm MS-1. Considering the design, for a given level of PVA, as the level of ethyl cellulose to be incorporated increased, particle size increased. The particle size increase is attributable to viscous organic phase produced at higher strengths of ethyl cellulose that formed larger sized emulsion droplets and consequently larger micro sponges. As the level of PVA increased, the emulsion droplets could not be easily divided into smaller droplets particles that resulted in larger micro sponges. Results are shown in Table 3.

Percentage product yield

The formulation MS-3 was highest yielding product (85.1%) containing high level of ethyl cellulose and low level of PVA and low yielding product MS-7 containing low level of ethyl cellulose and high level of PVA(MS-7 63.12%). Furthermore, for a given same level of PVA, on increasing the level of ethyl cellulose the product yield increased. As described in literatures high level of ethyl cellulose retards the diffusion of organic phase to aqueous phase that delays polymer precipitation and provides more time for droplet formation thus increasing yields. On the other hand less, viscous organic phase (low level of ethyl cellulose) causes rapid mixing and faster removal of solvent that reduces the coalescence time and solidification of drug and polymer before droplet formation decreasing the yield. Results are shown in Table 3.

Drug content uniformity

The percentage of drug content for formulated Floating micro sponge was found to be 83.02 ± 1.5 to 92.83 ± 2.4 % of lafutidine. The highest drug content was found in MS-5 92.83%. The results were shown in following table 3

Bulk density –(GM/CC)

Bulk density of all floating micro sponges was determined. It ranges from 0.103 g/cc to 0.382 g/cc. Formulation MS-1 shows more bulk density 0.382 g/cc and formulation MS-9 shows 0.103 g/cc. The density of floating micro sponges was considerably lower than that of SGF (1.004 g/cc) that imparted them buoyant character. The results were shown in following table 3.

Drug entrapment efficiency

The Entrapment efficiency of all formulations was found in the range of 61.94 ± 1.7% to 86.74 ± 2.1%. Among these highest loading efficacies was found to be for MS-5 formulation which is 86.74 %. At constant level of PVA and variations in ethyl cellulose level, entrapment efficiency showed bell shaped pattern, it was peaking at mid-level. Formulation MS1, MS4, MS7 made same level of ethyl cellulose and 0.5%, 1.0%, 1.5% PVA exhibited close entrapment efficiencies of 69.33%, 66.18%, 61.94% respectively affirming adsorption as dominant mode of drug incorporation. The results were shown in following table 3

Percentage buoyancy of floating microsponges

The *In vitro* buoyancy test was carried out to investigate buoyancy of prepared floating micro sponges. The floating microsponges formulations MS-1 to MS-9 showed good floating ability range from 77.90% to 87.11%. *In vitro* buoyancy of microsponges can be corelated to low density (0.4 g/cc) of ethylcellulose and that of the formulations. The microsponges formed with high level of ethyl cellulose were more buoyant than those with low level of ethyl cellulose. The microsponges made with high level of PVA were less dense than those made with low level of PVA. The results were shown in following table 3.

Formulation code	% Yield	Particle size (µm)	Bulk density	Drug content (%)	Drug Loading Efficacy o(%)	BUOYANCY (%)	% CDR 8 hrs.
MS-1	73.83 ± 2.2	92.89 ± 18.25	0.382 ± 0.2	83.07 ± 1.5	69.33 ± 3.5	73.99 ± 1.4	92.2 ± 1.8
MS-2	76.33 ± 2.7	105.43 ± 16.97	0.316 ± 0.2	90.41 ± 2.8	73.71 ± 2.8	78.90 ± 1.9	81.26 ± 1.4
MS-3	85.00 ± 1.8	144.84 ± 12.50	0.239 ± 0.3	88.35 ± 2.4	65.55 ± 2.9	81.64 ± 1.6	73.31 ± 1.4
MS-4	68.33 ± 2.4	108.26 ± 20.37	0.281 ± 0.2	82.21 ± 1.5	66.18 ± 2.3	75.59 ± 2.3	90.1 ± 1.3
MS-5	78.77 ± 1.6	134.05 ± 13.21	0.198 ± 0.1	92.83 ± 1.8	86.74 ± 1.8	86.30 ± 1.8	85.7 ± 1.2
MS-6	82.50 ± 2.1	140.18 ± 13.56	0.136 ± 0.2	84.00 ± 2.3	68.08 ± 2.3	84.14 ± 1.7	70.19 ± 2.5
MS-7	63.00 ± 1.7	135.01 ± 14.67	0.216 ± 0.2	83.02 ± 1.7	61.94 ± 1.7	76.39 ± 2.1	76.81 ± 2.4
MS-8	72.33 ± 1.9	145.38 ± 20.59	0.165 ± 0.3	90.76 ± 2.4	70.30 ± 2.4	81.96 ± 2.4	71.95 ± 2.1
MS-9	78.51 ± 2.3	169.72 ± 16.31	0.103 ± 0.2	88.03 ± 1.4	65.17 ± 1.4	87.11 ± 2.0	67.98 ± 1.5

Table 3: Evaluation data of lafutidine loaded microsponges prepared by quasi emulsion solvent diffusion method.

Characterization of optimized formulation (MS5)

Scanning electron microscopy (SEM)

Morphology of the floating microsponge was investigated by scanning electron microscopy. Microsponge of lafutidine were spherical and their surface was smooth and devoid of cracks giving them good appearance. The uniformly spherical shaped microsponges (MS5) were visualized at low magnification (100×) that on higher magnification (1000×) revealed tiny pores on its surface. The drug crystals were not visible on the surface indicating its molecular dispersion in the polymeric matrix (interpreted in DSC). The SEM data obtained on the drug-loaded floating microsponge are shown in figure 2 and 3.

Figure 2: SEM of microsponge formulation MS-5.

Figure 3: Surface Morphology SEM of microsponge formulation MS-5.

Differential scanning calorimetry (DSC)

The results of DSC analysis showed that the melting temperature for pure drug, Eudragit S100 and Ethylcellulose were 96.6˚C, 245.10˚C and 202.14˚C. The integrity of drug was unaffected when developed in to microsponges, this is confirmed by DSC of formulation where the composite melting peaks of pure drug, Eudragit S 100 and ethyl cellulose were found to be at 99.2˚C, 248˚C and 205.53˚C respectively indicating compatibility between drug polymer and processing conditions. Appearance of no new peak and absence of any potential shift suggested compatibility of lafutidine with polymers and was confirmed by diffuse reflectance infrared Fourier transform spectroscopy.

Figure 4: DSC of pure lafutidine.

Figure 5: DSC of lafutidine loaded floating microspongems-5 formulation.

FTIR spectroscopy

FTIR spectroscopy is a powerful technique, which is used for identification of drug substances. After comparing FTIR peaks of lafutidine with standard, it is confirmed that the obtained sample is lafutidine. All the characteristic peaks of lafutidine were present in spectra at within the respective wavelengths. Thus, indicating compatibility between drug and polymers. It shows that there was no significant change in the chemical integrity of the drug.

Figure 6: FT- IR spectra of pure lafutidine.

Figure 7: FT-IR Spectra of MS-5 formulation.

Release kinetics

In-vitro drug release study of floating microsponge of lafutidine shows 67.98% to 92.30% drug release within 8 hrs. From these results it is evident that as the amount of hydrophobic polymer (EC) increases, drug release decreases. MS-1 fabricated with low level of ethyl cellulose formed small size microsponges that can be associated with higher surface area and shorter path length leading to higher release rate. From the results it seen that the drug release mechanism from the formulations was found to be follows Zero order kinetics, in which the rate of drug release is independent of concentration of drug. This further strength the suitability of developed Floating Microsponge of lafutidine.

The *In vitro* release kinetic data was applied to various kinetic models like zero-order rate kinetics, first-order, Higuchi's equations, Peppa's model and hixon crowell model to predict the drug release kinetic mechanism.

Cumulative drug release V/S. time. (zero order model)

Figure 8: % (zero order model).

LOG % cumulative drug remaining V/S. time.(first order model)

% Cumulative drug released V/S. square root of time (Higuchi's Model)

Time (HRS.) V/S cube root of % drtrelease.(hixon crowell model)

LOG % cumulative drug released V/S. LOG time. (peppasmodel)

Figure 9: LOG %. (first order model).

Figure 10: (Higuchi's Model).

Figure 11: Hixon Crowell model.

Figure 12: LOG % cumulative drug released V/S. LOG time. (Peppasmodel).

Stability

Stability study carried out for 0 to 90 days. On physical observation of the stored samples there was found that no change in colour and shape of microsponges. The drug content and percentage buoyancy did not change significantly ($p > 0.05$) on storage. The stored formulations were also subjected to *In vitro* drug release study and compared. For comparison of *In vitro* release profiles. Similarity factor (f2) is emphasized by USFDA (Gohel., *et al.* 2005) that was calculated by Pheq bootstrap V1.1software (30–688, Krakow, Poland) with 5000 bootstrap at 90% confidence interval. Similarity factor was (f2) found to be more than 60 indicating similarity between release profiles of microsponges at different storage periods. The studies suggest physical and chemical stability of floating microsponges of lafutidine for a period of three months under test conditions. Results were shown in following table 4.

Time (Days)	Physical changes	% Buoyancy	% Drug content	%CDR
0	-	86 ± 0.94	92.83 ± 1.26	85.70 ± 1.2
30	No change	85 ± 0.89	92.35 ± 1.10	86.12 ± 1.4
60	No change	84 ± 1.04	91.24 ± 1.15	84.46 ± 1.7
90	No change	84 ± 1.15	90.41 ± 1.20	85.68 ± 1.5

Table 4: Stability study of lafutidine loaded formulationms-5.

*Each value represents MEAN ± S.D. of three observations.

Conclusion

The expediency of microsponges as floating gastro retentive system was affirmed by successfully development of lafutidine loaded gastro retentive microsponges to provide sustained release of drug at the site of action. The high drug loading capacity of microsponges offered a convenient approach for fabricating in to a conventional capsular system to heal gastric ulcer. For scientific as well as economic reasons, such delivery system have potential advantages which include enhanced therapeutic response, predictable rate of release, extent of absorption and improve patient acceptance. This study presents a new approach based on floating ability of microsponges for treatment of gastric ulcer.

Acknowledgement

The authors are kindly thankful to Swapnroop Durgs and Pharmaceuticals, Ahemdabad, Gujarat for providing Lafutidine as a gift sample. The authors are also thankful to Principal SGMCP Mahagaon, Department of Pharmaceutics SGMCP Mahagaon and Trustees of SGMCP Mahagaon for providing required guidance and support.

Conflict of Interest

Myself Mr. SUNIL T.GALATAGE, as the author of the manuscript and don't have a direct financial relation with the commercial identities mentioned in your paper that mingt lead to a conflict of interest for any of the authors.

Bibliography

1. Sanjay K., *et al*. "A Comparative Evaluation of Lafutidine and Rabeprazole in the Treatment of Gastritis and Peptic Ulcer: A Double-blind, Randomized Study in Indian Patients". *British Journal of Medicine and Medical Research* (2013): 1187-1198.

2. Edelsbrunner M., *et al*. "Afferent signalling from the acid challenged rat stomach is inhibited and gastric acid elimination is enhanced by lafutidine". *Biomed Central* (2009): 1-11.

3. Dewan B and Shah D. "A Study to Evaluate the Symptomatic Efficacy and Safety of Lafaxid TM (Lafutidine 10mg) in Patients with Acid Peptic Disorders in India". *British Journal of Medicine and Medical Research* 3.4 (2013): 821-831.

4. Dewan B and Chimata R. "An open label, randomized, crossover bioequivalence study of lafutidine 10 mg under fasting condition". *World Journal of Gastrointestinal Pharmacology and Therapeutics* 1.5 (2010): 112-118.

5. Fule R and Amin P. "Development and evaluation of lafutidine solid dispersion via hot melt extrusion: Investigating drug-polymer miscibility with advanced characterization". *Asian Journal of Pharmaceutics* 9 (2014): 92-106.

6. Hemalatha P., *et al*. "Formulation and evaluation of oro-dispersible tablets of lafutidine". *Der Pharmacia Lettre* 7.5 (2015): 226-235.

7. Orlu M., *et al*. "Design and evaluation of colon specific drug delivery system containing flurbiprofen microsponges". *International Journal of Pharmaceutics* 318 (2006): 103-117.

8. Nokhodchi A., *et al*. "Factor Affecting the morphology of benzoyl peroxide microsponges". *Micron* 38 (2007): 834-840.

9. Kaity S., *et al*. "Microsponges a novel stratergy for drug delivery system". *Journal of Advanced Pharmaceutical Technology and Research* (2010): 283-290.

10. Srivastava., *et al*. "Colonic luminal surface retentive meloxicam microsponges delivered by erosion based colon targated matrix tablet". *International Journal of Pharmaceutics* 427 (2012): 156-162.

11. HH Willard., *et al*. "Instrumental Methods of Analysis 4th Edition Affiliated East-WestPress Pvt. Ltd., New Delhi, (1977): 496.

12. Arthur I Vogel. "Elementary Practical Organic Chemistry. Part I: Smaal ScalePreparations". 2nd Edition. 76.

13. Indian pharmacopoeia 2007, Indian Pharmacopoeia Commission, Ghaziabad 2 (2007): 1165-1167.

14. kumar P., *et al*. "Development and Validation of UV Spectrophotometric method for estimation of Lafutidine in bulkand Pharmaceutical dosage form". *International Journal of Drug Development and Research* 4.1 (2012): 325-329.

15. Satyanarayanapattnaik and kalpanaswami. "Effect of casting solvent on crystallinity of ondanestron intradermal films". *IJP* (2001): 106-110.

16. Arya P and Pathak K. "Assessing the viability of microsponges as gastro retentive drug delivery system of curcumin: Optimization and pharmacokinetics". *International Journal of Pharmaceutics* 460 (2014): 1-12.

17. Kaundal A., *et al*. "A Review on Microsponges Drug Delivery System". *International Journal of Advances in Pharmaceutical Sciences* 4 (2014): 177-181.

18. Kapoor D and Rakesh P. "Formulation, Optimization and Evaluation of Floating Microspheres of Captopril". *Asian Journal of Biomedical and Pharmaceutical Sciences* 2.9 (2012): 1-10.

19. Kumar H., *et al*. "Gastroretentive Ethyl Cellulose Floating Microspheres containing Ranitidine Hydrochloride". *International Journal of Drug Development and Research* 4(2012): 315-321.

20. Yasunori S., *et al*. "In vitro and in vivo evaluation of riboflavin-containingmicroballoons for a floating controlled drug delivery system in healthy humans". *International Journal of Pharmaceutics* 2004 275 (2004): 97-107.

21. Arthur I Vogel. "Elementary Practical Organic Chemistry. Part I: Smaal Scale Preparations". 2nd Edition. 76.

22. Yerram ., *et al*. "Preparation and Evaluation of Microsponge Loaded Controlled Release Topical Gel of Acyclovir Sodium". *International Journal of Biopharmaceutics* 3 (2012): 96-102.

23. Mohan V., *et al*. "Formulation and Evaluation of Microsponges for Topical Drug Delivery of Mupirocin". *International Journal of Pharm Tech Research* 5.3 (2013): 1434-1440.

24. Aloorkar N., *et al*. "Microsponges an innovative drug delivery system". *International Journal of Pharmaceutical Sciences and Nanotechnology* 5.1 (2012): 1597-1606.

Volume 3 Issue 2 February 2019