International Journal of Advanced Technology in Engineering and Science www.ijates.com

Volume No.03, Special Issue No. 02, February 2015 ISSN (online): 2348 – 7550

EFFECT OF SUPER DISINTEGRANTS ON SOLUBILITY AND DISSOLUTION RATE OF LAFUTIDINE

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ABSTRACT

The objective of the present work is to prepare solid dispersions of the Lafutidine with different pharmaceutical excipients (sodium starch glycolate, croscarmellose sodium, polyplasdone XL) and to study the effect of these excipients on the solubility and dissolution rate of lafutidine. Lafutidine is yellowish white crystalline powder practically insoluble in water. Due to very poor solubility, its bioavailability rate is limited by dissolution. In this study, an attempt has been made to enhance the solubility and dissolution rate of Lafutidine by solvent evaporation method, which is a solid dispersion technique by superdisintegrants (sodium starch glycolate, croscarmellose sodium, polyplasdone XL) as a carrier. Solid dispersions were prepared using different ratios of drug and carriers by solvent evaporation method and further evaluated for its drug content and rate of dissolution. Solid state characterization was carried out by Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD) and Scanning electron microscopy (SEM). The dissolution rate of Lafutidine from solid dispersion was higher compared to pure drug. Among all the formulations, solid dispersion with sodium starch glycolate and croscarmellose sodium shown highest dissolution rate. This study concluded that the solubility and dissolution rate can be improved by these Superdisintegrants.

Keywords: Dissolution Rate, Lafutidine, Solubility, Solvent Evaporation, Super Disintegrants.

I INTRODUCTION

Bioavailability of drugs administered orally for systemic effect depends on two key phenomenon which occur post administration of that drug. First is dissolution of the drug in the gastrointestinal fluid to produce a solution of the drug and second, transportation of the dissolved drug across the gastrointestinal membrane. Each of these two steps can be a rate limiting factor. The Biopharmaceutical Classification System (BCS) divides drugs into one of four classes according to their solubility and permeability[1-2]. The focus of this study will concern itself with drugs in BCS Class II. Increasing the solubility of these APIs will also increase the bioavailability of the drug in the body. One important factor that affects the solubility of any chemical is its surface area or in other words the area that is presented for the process of solubilization. Surface area can be increased by reducing the particle size.

Solid dispersion is frequently used to improve the dissolution rate of poorly water-soluble compounds. By adsorbing drug molecules onto the surface of adsorbents with large surface areas, the total surface area of the drug is increased, and the drug may even be transformed from crystalline form to amorphous form. By

adsorbing a surfactant onto the crystal surface of poorly water-soluble drugs, dissolution rate can also be enhanced. This technique also used to improve the bioavailability of poorly soluble compounds for enhancing the dissolution profiles of these compounds

Lafutidine (LAFT) a newly developed histamine H2-receptor antagonist, inhibits daytime (i.e., postprandial) as well as nighttime gastric acid secretion in clinical studies. It is practically insoluble in water and has low bioavailability. LAFT has a very low aqueous solubility, which impairs its dissolution in upper gastric fluid producing problems to prepared systems [1]. Overall, these characteristics hinder its therapeutic application by delaying the absorption rate and thereby onset of action or activity [2]. Together solubility, permeability and dissolution rate of a drug are essential factors for determining its oral bioavailability [3]. Literature reports generally revealed the fact that drug materials with a very low aqueous solubility will show dissolution rate limited absorption and hence poor bioavailability. Improvement of aqueous solubility in such a case is a valuable assignment to improve therapeutic efficacy [4]. However there is no literature on the enhancement of solubility of LAFT with superdisintegrans. Subsequently there is a need to deliver LAFT in formulation with increased solubility and improved dissolution profile. For the current study we selected sodium starch glycolate, croscarmellose sodium, polyplasdone XL. They act as Solubilizing Agent. The super disintegrants acts as hydrophilic carrier for poorly water insoluble drug. Superdisintegrant makes enough pressure in the pores of the tablets as to produce an efficient disintegration. Hydrophobic drugs can be improved by solid deposition of the drug upon hydrophilic, strongly swelling carriers like the super disintegrants sodium starch glycolate, Crosscarmellose, and crosspovidone. This increased in dissolution is because of micronized drug particles are fairly evenly distributed on relative large hydrophilic carrier particles prevent reagglomeration and increase the drug dissolution rate as on effect of the large effective surface for dissolution.

Thus, in this study dispersions of LAFT were prepared using sodium starch glycolate, croscarmellose sodium, polyplasdone XL as carriers by solvent evaporation method and the effect of these excipients on the solubility and dissolution rate were evaluated. Subsequently, prepared dispersions were characterized by scanning electron microscopy, fourier transform infrared spectroscopy and powder X-ray diffraction.

II MATERIALS AND METHODS

2.1. Materials

LAFT was obtained as a generous gift from Dr. Reddy's Laboratry, Hyd, India. croscarmellose sodium obtained from DFE Pharma, Germany, sodium starch glycolate obtaind from JRS Pharma,Germany, Polyplasdone XL obtained from BASF Corporation,Mumbai, India. Dichloromethane obtained from Qualikems, Mumbai, India, Methanol(hplc grade) from Sigma Aldrich, Mumbai, India. All other chemicals used were of analytical grade or equivalent quality.

2.2. Methods

2.2.1. (A). Construction of Calibration Curve of Lafutidine In Water

For the construction of calibration curve stock solution was prepared by dissolving 100 mg of accurately weighed drug dissolved in methanol (10ml) and make up with water (l mg/ml). 1mLof the stock solution was

pipetted out into a 10mL volumetric flask and volume was made up with water (100µg/ml). From this working stock 10 µg/ml concentration was prepared and scanned in a range of 200-400 nm to find the absorption maxima. Based on the absorbance obtained λ_{max} would be fixed, remaining dilutions were made with water to get concentrations ranging from 4-20 µg/ml, was constructed at and a calibration curve absorption maxima obtained.

2.2.1. (B). Construction of Calibration Curve of Lafutidine in Methanol

For the construction of calibration curve stock solution was prepared by dissolving 100 mg of accurately weighed drug dissolved and make up with methanol (l mg/ml). 1ml of the stock solution was pipetted out into a 10ml volumetric flask and volume was made up with water (100µg/ml). From this working stock 10 µg/ml concentration was prepared and scanned in a range of 200-400 nm to find the absorption maxima. Based on the absorbance obtained λ_{max} would be fixed, remaining dilutions were made with methanol to get concentrations ranging from 4-20 µg/ml, was constructed at and a calibration curve absorption maxima obtained.

2.2.2. Solution Stability Studies for Lafutidine Using UV Spectrophotometry

Solution stability studies was performed by determining absorbance values of the prepared dilution from the above step at different time points such as 1, 3, and 6h after preparation of the solution. This was done to determine the stability of the method in conducting of dissolution studies or other studies over a period of 24 h.

2.2.3. Prepartion of Solid Dispersion by Solvent Evaporation Method

Solid dispersions of Lafutidine were prepared with Lafutidine: Carriers (Primojel (sodium starch glycolate), Ac-di-sol (croscarmellose sodium), and polyplasdone XL (cross linked polyvinyl pyrrolidone)) in 1:0.5 and 1:1 weight ratio by solvent evaporation method. Methanol and Dichloromethane 1:1 ratio used as solvent for solid dispersions. Briefly, required amounts of drug was dissolved in solvent then dispersed the carrier mixed thoroughly and evaporate the solvent by using rotary flash evaporator at 40°c with 50 rpm/1h. The obtained solid mass was dried in desiccator and pulverized and store in a screw-cap vial at room temperature until further use.

Table 1: Composition of solid dispersions prepared by solvent evaporation method

S.NO	SOLID DISPERSION SYSTEM	RATIO OF
1	Lafutidine : sodium starch glycolate (SD1)	1:0.5
2	Lafutidine : sodium starch glycolate (SD2)	1:1
3	Lafutidine : croscarmellose sodium (SD3)	1:0.5
4	Lafutidine : croscarmellose sodium (SD4)	1:1
5	Lafutidine : polyplasdone XL (SD5)	1:0.5
6	Lafutidine : polyplasdone XL (SD6)	1:1

2.2.4. Drug Content Determination

For the Lafutidine content determination of the powder, an amount of powder corresponding to equivalent to dose of drug was dissolved in 10 ml of methanol. Keep it for agitation for 1h.Then centrifuge supernant layer filtered. The samples were analyzed with UV spectroscopic method. Each content determination was performed in triplicate and the average and standard deviation were calculated.

2.2.5. In Vitro Dissolution Studies

Dissolution studies of pure Lafutidine, physical mixtures and solid dispersions were performed by using the U.S.Pharmacopeia(USP) XXIV type II apparatus (Electrolab, Mumbai, India) at the paddle rotation speed of 50 rpm in 900 ml of distilled water as dissolution media at 37±0.5°C. A sample equivalent to 10 mg of Lafutidine of the prepared systems was placed in dissolution medium. During the release studies, samples of 5 ml were collected after 2, 5, 10, 20, 30, 45 and 60 min using a syringe and were replaced with the same volume of release medium. The samples were subsequently analyzed by UV spectroscopic method. Experiments were performed in triplicate. The dissolution profile was examined and valuated for amount of drug released in initial 5min (Q5min),time taken to release 50% of the drug (T50%), Dissolution efficiency (DE%) afte01r 10and 60 min and mean dissolution time (MDT), mean dissolution rate (MDR), initial dissolution rate (IDR).

Dissolution efficiency (DE%) : DE% at 10 and 60 min were calculated out for all the batches for comparison. The dissolution efficiency (DE) is defined as the area under the dissolution curve up to a certain time(t), expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time.[7]

$$D.E = \frac{\int_0^t y\,dt}{y_{100}\,t} \times 100 \qquad (1)$$

Mean dissolution time-MDT (min): In order to assess the comparative extent of the dissolution rate enhancement from SDs, mean dissolution time (MDT) was calculated. The dissolution data obtained of all the batches were treated according to Equation(2) where i is dissolution sample number, n is number of dissolution sample times, t_{mid} is time at midpoint between time t_i and t_{i-1}, and ΔM is the amount of Lafutidine dissolved between time t_i and t_{i-1}.[8]

$$MDT_{invitro} = \frac{\sum_{i=1}^{n} t_{mid\ \Delta M}}{\sum_{i=1}^{n} \Delta m} \qquad (2)$$

Mean dissolution rate (MDR) can be calculated according to the following equation:

$$MDR = \frac{\sum_{j=1}^{n} \Delta M_j / \Delta t}{n} \qquad (3)$$

Where n is number of dissolution sample times, Δt is the time at midpoint between t_i and t_{i-1} (easily calculated with $(t_i + t_{i-1})/2$) and ΔM_j is additional amount of the drug dissolved between tj and t-1.

Initial dissolution rate (IDR, %dissolved/min) was computed over the first 5 min of dissolution.

2.2.6. Solid State Characterization

Solid state study was performed for Lafutidine, carriers (sodium starch glycolate, croscarmellose sodium, polyplasdone XL), selected batch of solid dispersions and their physical mixtures.

2.2.6.1. X-Ray Diffraction (XRD)

Samples (Lafutidine, carriers (sodium starch glycolate, croscarmellose sodium)) physical mixtures and the solid dispersion in carriers were analyzed using an X' Pert PRO MPD diffractometer with a copper anode (Cu Kα radiation, λ =0.15406 nm, 40 kV, 35 mA).The diffraction pattern was measured with a step size of 0.020° and a dwell time of 32.8 s at each step between 3 and 50 2Θ at ambient temperature.

2.2.6.2fourier Transform Infrared Spectroscopy (FTIR)

Samples (Lafutidine, carriers (sodium starch glycolate, croscarmellose sodium)) physical mixtures and the solid dispersion in carriers were conducted using an FTIR Spectrophotometer which was employed to characterize the possible interactions between the drug and the carrier in the solid state. Samples were prepared using KBr (potassium bromide) disk method. Samples of 2mg were lightly ground and mixed with 200mg IR grade dry potassium bromide and then compressed at 10 tonnes in a hydraulic press to form disc. The spectrum was recorded in the range 4000-450 cm^{-1} at room temperature.

2.2.6.3. Scanning Electron Microscopy (SEM)

Samples (Lafutidine, carriers (sodium starch glycolate, croscarmellose sodium)) physical mixtures and the solid dispersion in carriers were examined by means of QUANTA 200 ESEM scanning electron microscope. The powders previously fixed on a brass stub using double-sided adhesive tape and then were made electrically conductive by coating, in a vacuum. The picture were taken at an excitation voltage of 20 Kv and different magnifications.

III RESULT AND DISCUSSION

3.1(a) Calibration Curve of Lafutidine in Distilled Water

The calibration curve of Lafutidine was plotted in water at wave length of 215 nm (which was obtained by scanning in the above step) in the concentration range of 1-20µg/ml which is shown in Fig1 and corresponding values are recorded in Table 2. A straight line was obtained with regression coefficient of 0.9915, with an equation of y=0.046x-0.0065 which is used for calculation of concentration of Lafutidine in unknown samples.

Table 2: Absorbance values of Lafutidine in water

Concentration(µg/ml)	Absorbance
0	0
4	0.1525
8	0.4183
12	0.5778
16	0.7569
20	0.8934

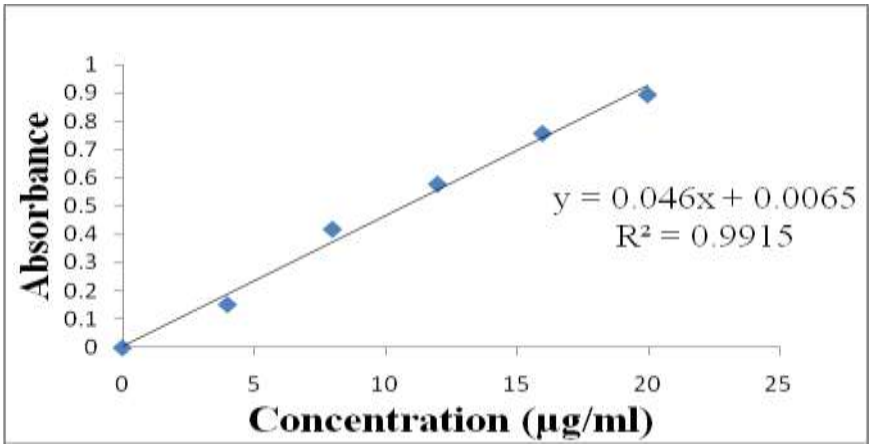


Figure 1: Calibration curve of lafutidine in water

3.1(b) Calibration Curve of Lafutidine in Methanol

The calibration curve of Lafutidine was plotted in methanol at wave length of 215 nm (which was obtained by scanning in the above step) in the concentration range of 4-20µg/ml which is shown in Fig2 and corresponding values are recorded in Table 3. A straight line was obtained with regression coefficient of 0.9958, with an equation of y=0.0455x-0.0172 which is used for calculation of concentration of Lafutidine in unknown samples.

Table 3: Absorbance values of Lafutidine in methanol

Concentration(µg/ml)	Absorbance
0	0
4	0.194
8	0.425
12	0.552
16	0.743
20	0.919

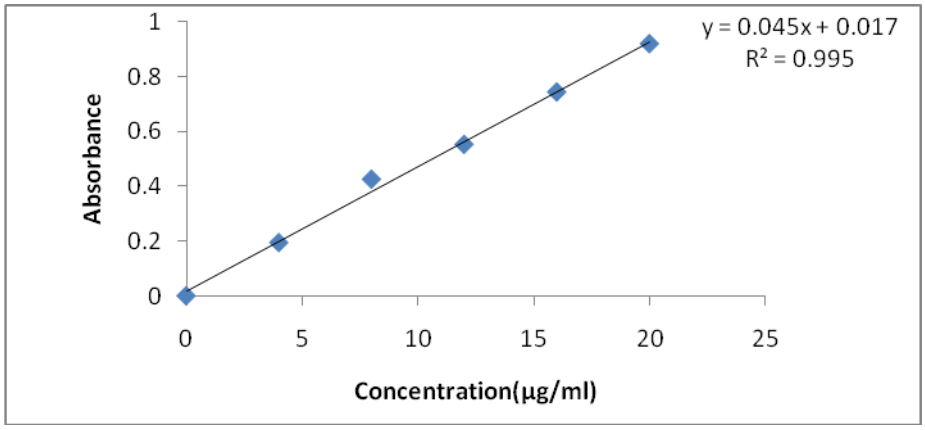


Figure 2: Calibration curve of lafutidine in methanol

3.2. Solution Stability Method of Lafutidine Estimation in UV Spectro Photometry

Absorbance of 12µg/ml concentrations which were used to prepare calibration curve were determined at various time intervals ranging from 1hr to 6hr. Standard deviations were determined for the absorbance values obtained which was less than 0.001 for all the absorbance values indicating stability of drug in the standard solution and stability of method in determining the concentration of unknown samples during dissolution studies. Standard deviations and absorbance values obtained were represented in Table. 4.

Table 4: Stability indicating absorbance values

Time(hr)	Absorbance
0	0.5703
1	0.5640
3	0.5610
6	0.5516

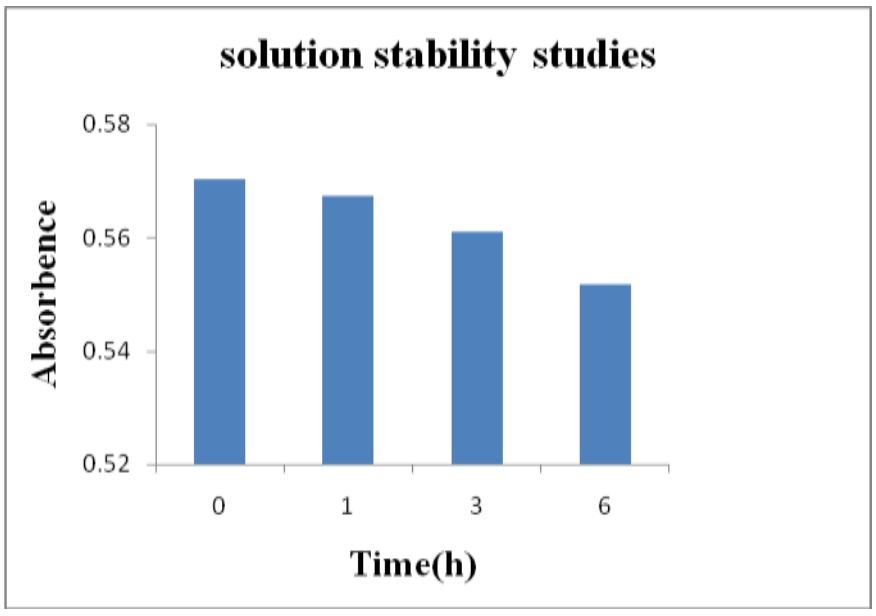


Figure 3: Solution stability study graph of lafutidine

3.3. Drug content

The percentage of drug content was determined for the physical mixture and solid dispersions. The value ranged from 95.30±0.863% to 101.54±0.927 % for physical mixtures and solid dispersions as shown in table .indicating high content uniformity of physical mixtures and solid dispersions.

Table 5: Drug content in percentage, each value represents mean ± S.D.(n=3)

Formulation code	Drug content (%)	Formulation code	Drug content (%)
SD1	97.94±0.289	SD5	95.80±0.348
SD2	99.31±0.498	SD6	97.30±0.863
SD3	91.46±0.691	PM1	92.48±0.830
SD4	101.54±0.927	PM2	93.87±0.491

3.4 In Vitro Dissolution Study

The dissolution behaviour of pure Lafutidine, physical mixtures and solid dispersions prepared with sodium starch glycolate, croscarmellose sodium, polyplasdone XL using solvent evaporation method fig 4 and Fig 5. It is clear that the pure lafutidine has lowest dissolution rate and all the studied physical mixtures and solid dispersion formulations had a higher dissolution rate where the fastest dissolution rate was obtained for the sample when the ratio of drug carrier was 1:1(w/w). The pure drug showed a release of 52.83% at the end of 1h, while SD showed 107.05% drug release in 1h. The percent drug dissolution increased with carriers. Physical mixture (PM) also showed an improved dissolution rate as compared with pure drug.

Table 6 and Table 7 in vitro release data and summarizes the percentage drug dissolved in 5 min (Q5) and 60 min (Q60), dissolution efficiency at 10 min (DE10) and 60 min (DE 60), MDT (mean dissolution time), MDR (mean dissolution rate), IDR (initial dissolution rate),and $t_{50\%(min)}$ (time taken to release 50% of the drug) for pure drug, physical mixtures and solid dispersions.

The pure drug showed 22.46% (Q5) and 52.83% (Q60) drug release. In solid dispersion, Q5and Q60 and DE% increased with an increase in ratio. The highest dissolution rate was exhibited by drug/carrier SD (1:1). However, slight enhancement in the dissolution rate with physical mixture was observed in comparison to pure drug.

The MDT for lafutidine profile was 14.56min, and MDT was decreasing to greater extent by all the solid dispersions with increasing carrier concentration while minimum MDT 8.92 min was seen in solid dispersion with sodium starch glycolate.

Time taken to release 50% of lafutidine from pure drug was found to be 48.5 min while from the solid dispersion (SD1& SD2 was found 2 min,SD3&SD4 was found 3,2 min)and the physical mixture(PM1,PM2 was 27.5,20min) was greater decreased with carriers.

To facilitate comparison between free drug, solid dispersions and physical mixture, IDR, MDR were calculated. From those values, release rates of lafutidine were always higher from solid dispersion compared with pure drug and physical mixtures.

The enhancement in the dissolution of lafutidine from solid dispersion can be attributed due to several factors, like reduced crystallinity, particle size reduction, increased wettability and solubility by hydrophilic carriers.

Table 6: Dissolution parameters for solid dispersions of lafutidine

PARAMETERS	Q5	DE10	DE60	MDT	MDR	IDR	t50%min
PURE DRUG	22.461±1.69	43.60±5.98	63.00±3.77	14.27±2.79	3.64±0.262	5.88±0.955	48.5
SSG (1:0.5) (SD1)	70.07±4.67	63.30±4.01	88.10±4.49	8.92±1.64	9.61±0.65	14.01±0.93	2
SSG (1:1) (SD2)	75.46±1.77	66.50±5.22	90.64±5.15	7.28±0.15	10.84±0.28	15.09±0.35	2
CCS (1:0.5) (SD3)	72.71±4.100	64.06±5.34	87.31±1.75	9.39±1.22	9.18±1.28	14.54±0.82	3
CCS (1:1) (SD4)	85.07±9.88	72.50±7.56	93.00±9.06	7.30±3.02	10.20±0.98	17.01±1.97	2
POLYPLASDONE (1:0.5) (SD5)	38.08±4.37	32.82±8.87	49.80±9.54	22.9±6.77	4.61±0.677	6.34±0.998	13.5
POLYPLASDONE (1:1) (SD6)	37.22±2.85	30.90±5.60	56.61±5.93	20.46±1.63	4.90±0.722	7.54±2.09	9.5
PM-CCS (1:1)	34..04±1.74	30.51±1.68	48.45±1.25	11.83±0.73	4.37±0.21	6.80±0.34	20
PMSSG(1:1)	35.26±2.20	30.29±1.34	54.19±1.94	12.72±0.96	4.49±0.19	7.05±0.44	27.5

Q: Percentage drug released at 5min.

DE: Dissolution efficiency at 10 and 60 min.

MDT: Mean dissolution time.

MDR: Mean dissolution rate.

IDR: Initial dissolution rate.

$T_{50\%}$ (min): time taken to release 50% of the drug.

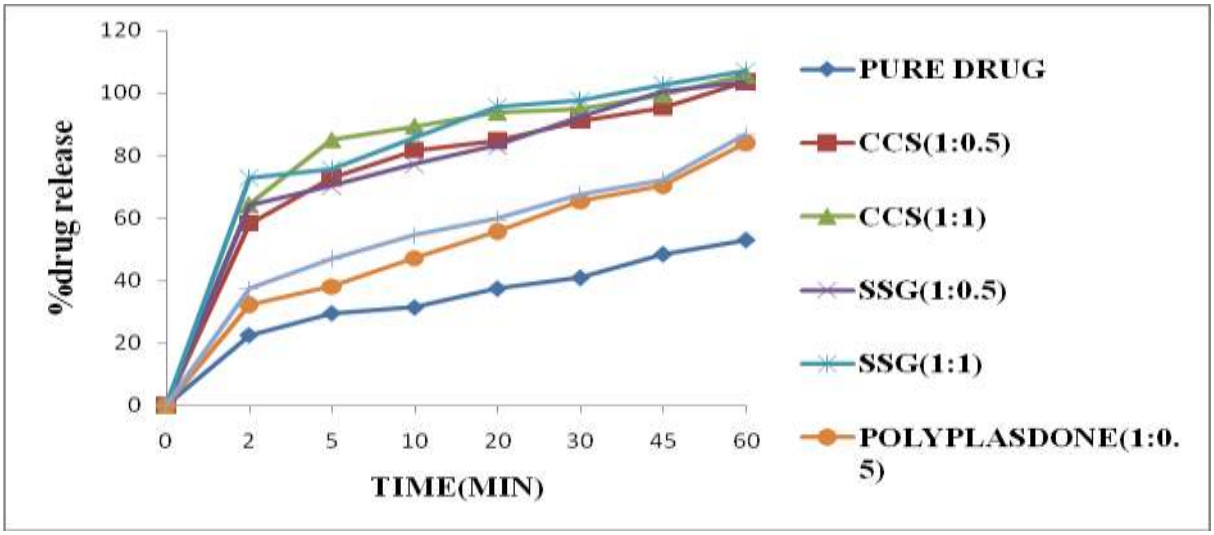


Figure 4: In vitro release profile of lafutidine solid dispersions

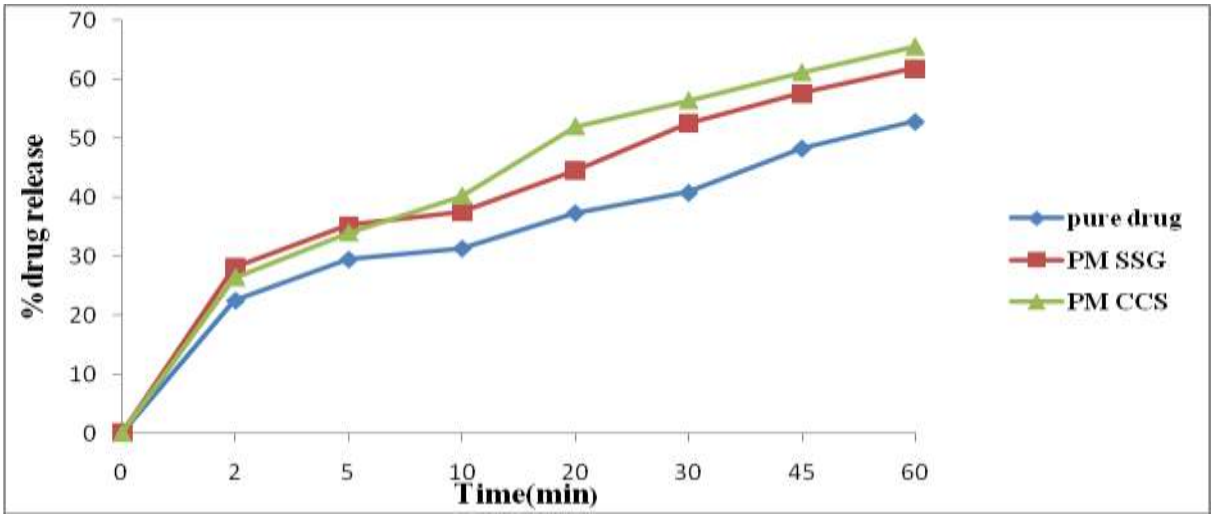


Figure 5: In vitro release profile of lafutidine physical mixtures

3.5. Solid State Characterization

3.5.1. Fourier Transform Infrared Spectroscopy

Drug excipient compatibility is an important parameter to be determined since they play a crucial role in stability of formulation. Drug excipient compatibility studies give the information of physical and chemical interaction which may be deterioration to the formulation and cause toxic reactions when consumed by the patient. Corresponding results shown in Fig.6.

FTIR spectra of pure Lafutidine characteristic sharp peaks of alkenes stretching (-C-H and CH2) vibration at 3324.32- 3016.48 cm^{-1} and alkane stretching (-CH_3, -CH_2 and -CH) vibration at 2853.73 cm^{-1}. Also exhibited C=O stretch at 1738.2 cm^{-1} due to saturated ketone and C=O-NH stretching at 1635.90 cm^{-1}. A selective stretching vibration at 1561.57 cm^{-1} and 1525.80 cm^{-1} for primary and secondary amine was also observed. For functional groups like S=O stretch and –C-S stretch showed vibrations at 1041.78 cm^{-1} and 729.57 cm^{-1} respectively.

The sodium starch glycolate spectrum showed a characteristic broad spectra of O-H stretching vibration from 3300 to 3600cm^{-1} , C-H stretching from 2800-2900 cm^{-1},and C-O stretching from 1000-1200cm^{-1}. Croscarmellose sodium 3429(broad), 3040 (broad), and 1106 (intense), 1410(intense) due to stretching of O-H, C-H, C-O groups, respectively. The IR spectrum of polyplasdone XL shows important bands at 1639 cm^{-1} and 1121 cm^{-1} respectively which are indicative of C=O stretching and =C-H bond stretching shows at 3367 cm^{-1}.

The characteristic peaks of Lafutidine and carriers sodium starch glycolate, croscarmellose sodium, polyplasdone XL were observed in both solid dispersions and physical mixture. This suggest that there is no significant interaction between the drug and carrier.

3.5.2. X-Ray Diffraction Analysis

The XRD pattern of pure Lafutidine, pure carriers (sodium starch glycolate, croscarmellose sodium, polyplasdone XL) ,SD(1:1) and corresponding PM was shown in Fig 7.

The diffraction pattern of Lafutidine showed high intensity peaks at 2 theta values of 7.134°, 20.567°, 21.215° and 23.102°. Sharp intense peaks may be due to presence of crystalline form of the drug. The diffraction pattern of sodium starch glycolate exhibited intensity peaks at 11.516°, 17.353° and 24.293°.croscarmellose sodium and exhibited intensity peaks at 32.00°, 34.134°, and 22.794 °. Whereas the XRD pattern of prepared physical mixtures and solid dispersions exhibited a reduction in both number and intensity of peaks compared to plain drug indicating the decrease in crystallinity or partial amorphization of the drug. The solid dispersion showed significant decline in the peaks suggesting that it more amorphous than the physical mixture.

Moreover, no other peaks than those that could be assigned to other to pure sodium starch glycolate, croscarmellose sodium were detected in the PMs and SDs, indicating that reduced chemical interaction in the solid state between the two entities. Results of this study imply that lafutidine is present in decreased crystallinity from in the solid dispersion.

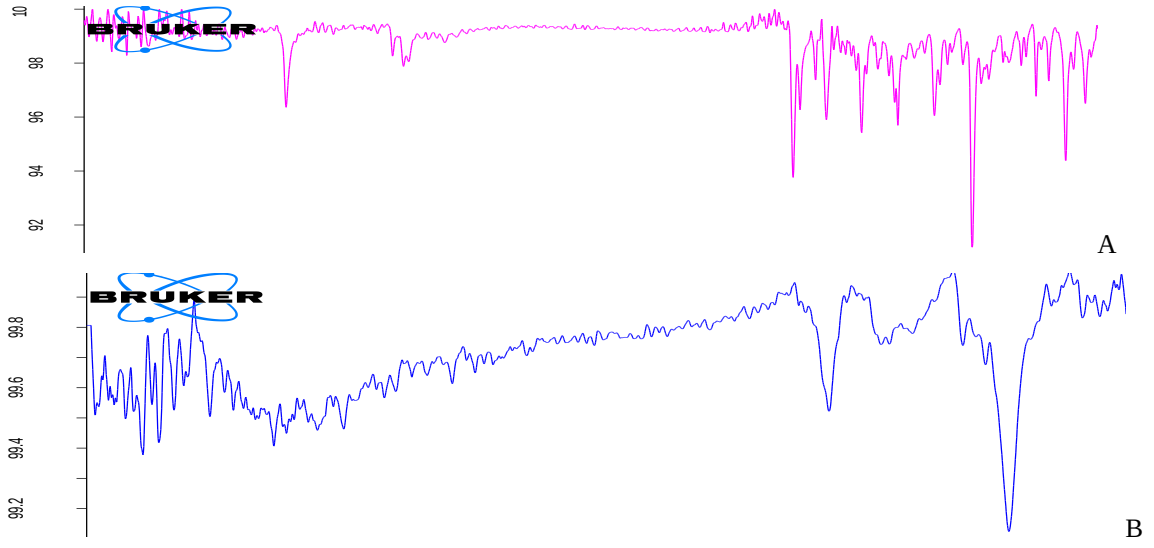
3.5.3. Scanning Electron Microscopy

The scanning electron micrographs of Lafutidine, pure carriers (SSG, CCS) SDs (1:1) and corresponding PM were shown in Fig 8.

Pure lafutidine appears crystals with smooth surface. SSG and CCS appears irregular shape and smooth surfaced particles.

The physical mixture of the drug and carrier weight ratio 1:1 showed clearly the adherence of lafutidine particles on the surface of SSG and CCS due to physical mixing. The solid dispersions of lafutidine with SSG and CCS appeared as a uniform and homogeneously mixed mass with wrinkled surface.

From SEM photomicrographs, it can be speculated that lafutidine existed in very fine crystalline form with reduced particle size, increased surface area and closer contact between the hydrophilic carriers would improve the wettability of the drug which may lead to enhanced drug solubility and dissolution rate.



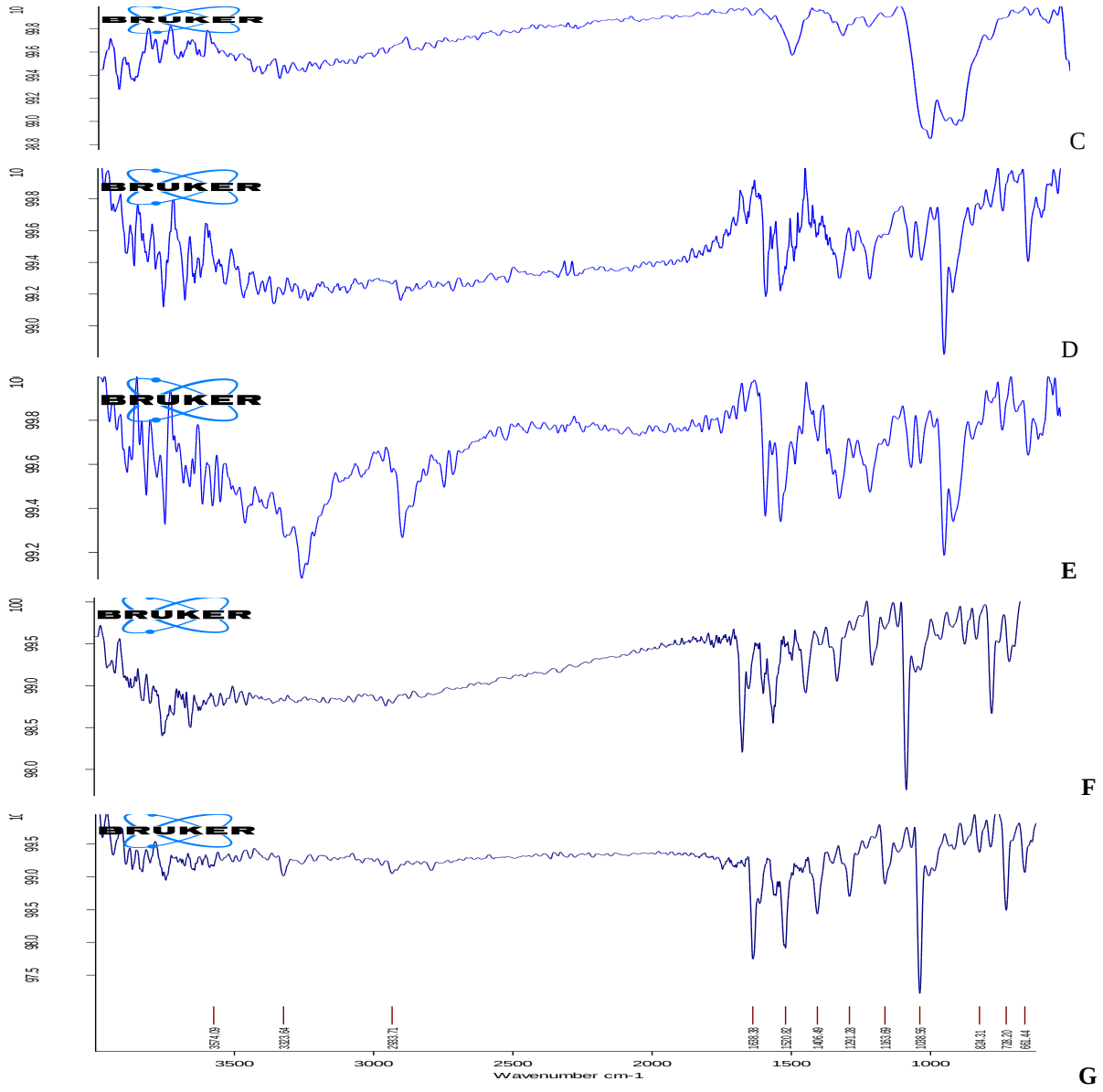
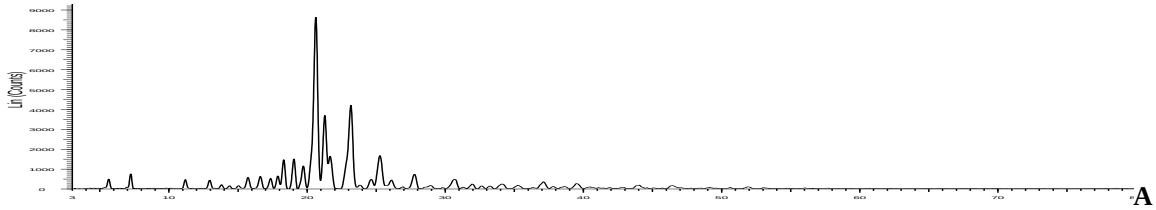


FIGURE 6: FTIR SPECTROGRAM OF (A) LAFUTIDINE, (B)SODIUM STARCH GLYCOLATE, (C) CROSCARMELLOSE SODIUM, (D) LAFUTIDINE WITH CROSCARMELLOSE SODIUM SOLID DISPERSION 1:1 (E) LAFUTIDINE WITH SODIUM STARCH GLYCOLATE SOLID DISPERSION 1:1, (F) PHYSICAL MIXTURE OF SODIUM STARCH GLYCOLATE(1:1), (G) PHYSICAL MIXTURE OF CROSCARMELLOSE SODIUM (1:1).



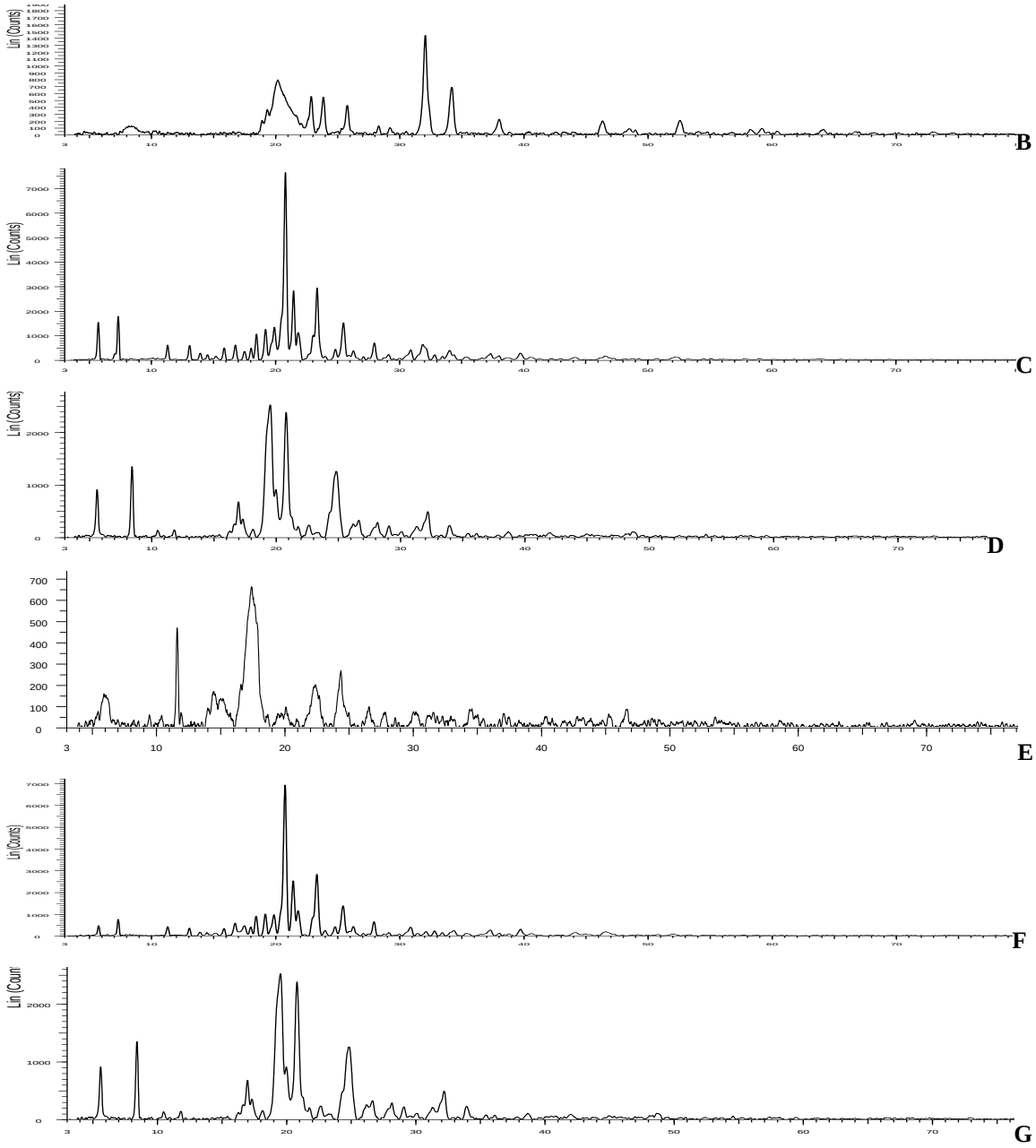
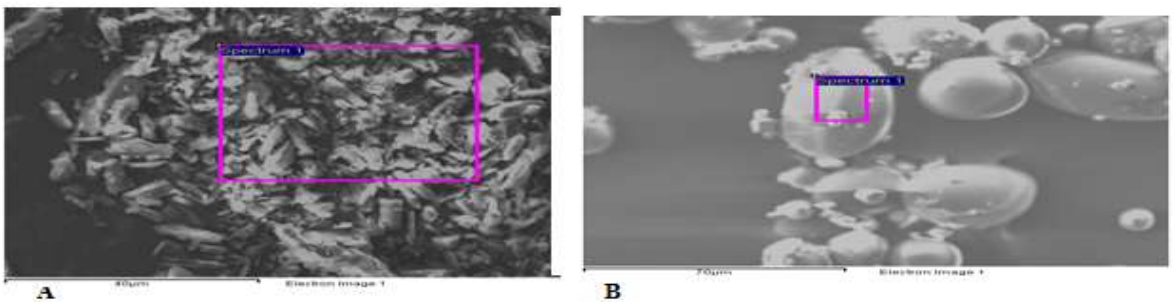


FIGURE 7: X-RAY DIFFRACT GRAMS OF (A) LAFUTIDINE, (B) CROSCARMELLOSE SODIUM, (C) LAFUTIDINE WITH CROSCARMELLOSE SODIUM PM 1:1, (D) SD OF LAFUTIDINE WITH CROSCARMELLOSE SODIUM 1:1,(E) SODIUM STARCH GLYCOLATE, (F) LAFUTIDINE WITH SODIUM STARCH GLYCOLATE SODIUM PM 1:1, (G) SD OF LAFUTIDINE WITH SODIUM STARCH GLYCOLATE 1:1.



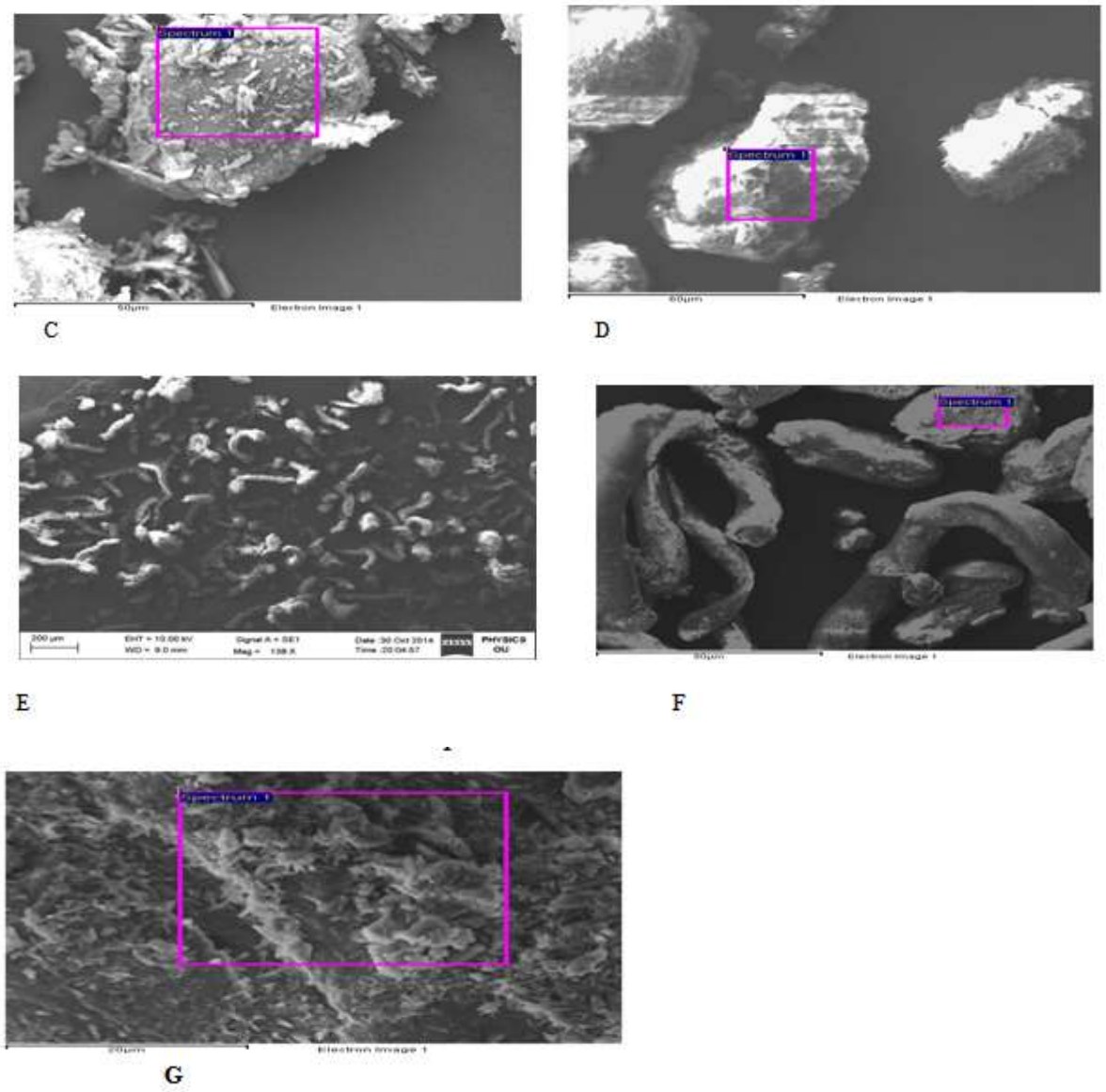


FIGURE 8: SEM PICTURES OF (A) LAFUTIDINE, (B)PURE SODIUM STARCH GLYCOLATE, (C) LAFUTIDINE-SSG PM AT 1:1 RATIO AND (D) LAFUTIDINE-SSG SDS AT 1:1 RATIO, (E) LAFUTIDINE-CCS PM AT 1:1 RATIO (F) PURE CROSCARMELLOSE SODIUM, AND (G) LAFUTIDINE-CCS SDS AT 1:1 RATIO.

IV CONCLUSION

The solid dispersion of Lafutidine were prepared by maintaining constant drug concentration and increasing carrier(SSG, CCS, Polyplasdone XL) concentration by solvent evaporation method. The drug content of solid dispersions and physical mixtures was obtained 95-101.2%. *In vitro* dissolution rate of drug from solid dispersions was higher compared to pure drug lafutidine. The pure drug showed a release of 52.83% at the end of 1 h, while SD showed 107% drug release in 1 h. The percent drug dissolution increased with an increase in the ratio of carriers. Physical mixture (PM) also showed an improved dissolution rate to a significant extent as compared with pure drug. The dissolution parameters MDT, MDR, IDR and $t_{50\%}$(min) was caluculated.IDR

showed improved dissolution characteristics of solid dispersion compare to pure drug. Solid –state characterization (FTIR, DSC, SEM studies) indicated decrease in crystallinity of the drug with no interaction between drug and carriers. The solubility and dissolution rate of lafutidine can be enhanced by the use of solid dispersions of lafutidine with carriers. From the result of the present study, it can be concluded that the solubility and dissolution rate of the lafutidine was improved with the solid dispersions of croscarmellose sodium and sodium starch glycolate.

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