doi.org/10.36721/PJPS.2022.35.6.SP.1779-1786.1

Formulation and assessment of controlled release tablets of famotidine by using eudragit RL 100 polymer

Tehmina Rabani[1], Syed Umer Jan[1*], Ghulam Razaque[1], Rahman Gul[1], Kamran Ahmad Khan[2], Faisal Rashid[2] and Muhammad Tufail[2]

[1]Faculty of Pharmacy & Health Sciences, University of Balochistan, Quetta, Pakistan
[2]Faculty of Pharmacy, Department of Pharmaceutics, Gomal University, D. I. Khan, Pakistan

Abstract: Controlled release" in drug release kinetics denotes reproducibility and predictability, implying that drug release from delivery devices follows a kinetically predictable and repeatable rate profile from dose to dose. In the current study controlled release tablets of famotidine were prepared by direct compression technique using Eudragit RL 100 polymer. Four different formulations of controlled release tablets of famotidine as (F1, F2, F3 and F4) were prepared by adding different drug to polymer ratio. The pre compression and the post compression of the formulation, characteristics were compared. All results obtained were within the specified standard limits. FTIR studies showed that both the drug and the polymer were compatible. *In vitro* dissolution study were conducted by Method II (Paddle Method) in phosphate buffer (pH 7.4), at 100rpm. Power law kinetic model was applied for drug release mechanism. The difference similarity of the dissolution profile was determined. The formulation F1 and F2 were released 97 and 96 % in 24 hours and other formulations F3 and F4 were released subsequently 93% and 90% in 24 hours. The results showed that incorporation of Eudragit RL 100 in the formulation of controlled release tablets prolong the drug release rates for 24 hours. The release mechanism was Non-Fickian diffusion mechanism. It was deducted from the current study that the Eudragit RL 100 can be efficiently incorporated in the formulation of controlled release dosage forms with predictable kinetics.

Keywords: Famotidine, polymer; control release tablets, Eudragit RL 100, paddle method.

INTRODUCTION

Drug delivery is the process of transportation of an active pharmaceutically active substance to living organisms to have therapeutic effect (Pedro *et al.,* 2019). The delivery of drugs seeks to deliver the API to the correct location, in the correct amount, and at the correct time. Various drug delivery systems have been developed in order to achieve an effective and safe medication concentration. The primary goal of drug delivery systems is to deliver precise API concentrations to the site of action in order to generate the desired healing effect or reaction in the body (Scicluna *et al.,* 2020). The term "controlled release" in drug release kinetics denotes reproducibility and predictability, implying that drug release from delivery devices follows a kinetically predictable and repeatable rate profile from unit to unit. Spatial placement refers to the distribution of a drug to a particular tissue or organ, whereas temporal delivery refers to the control of the drug rate to the targeted tissue. The oral route is the most prevalent and routinely utilized route for medication administration. Oral medicine administration is mostly done with tablet dose forms (Thabet *et al.,* 2018). Their appeal stems from the ease with which they may be prepared on an industrial scale as well as patient compliance. These tablets mostly use immediate or traditional release dose formulations. Because of the numerous doses of the drug, immediate release given dosage forms of pharmaceuticals frequently display drug plasma concentration variations, peak concentration and subsequently decline. Immediate release multiple dosage necessitates a strict monitoring of the dosing routine by the patient in order to get optimal therapeutic assistance; conversely, may lead to noncompliance and missing of timed doses, compromising therapeutic and specific goals of the procedure (Williams *et al.,* 2018). For individuals on a chronic treatment procedure, controlled release drug delivery systems with a low dose frequency and as a result, less side effects provide more convenience, improved patient compliance, and more consistent tablet consumption, all of which are significant (Laracuente *et al.,* 2020).

Since many years, polymer science has a key function in the development and manufacture of novel dosage forms. Polymers' uses have expanded from coating agents, adjuvant, emulsifying and suspending agents and adhesives to encapsulating agents, drug carriers, thickness and viscosity enhancers, stabilizers, disintegrates and bioadhesives as a result of advancements in polymer sciences (Kulkarni *et al.,* 2012). The primary goal of polymeric systems is to achieve spatial and temporal control of medication delivery (Marguet *et al.,* 2013). Cellulose derivatives, PVP, Carbomers, Eudragits, and other polymers are employed in the manufacture of matrix tablets (Debotton *et al.,* 2017). Eudragit is a quaternary

**Corresponding author:* e-mail: suj55@yahoo.com

ammonium-grouped copolymer of (ethyl acrylate and methyl acryl ate) with a little concentration, methyl acrylic acid ester. Due to their existence in salt form, ammonium groups are making the polymer porous. The granules are colourless and transparent to hazy, with a mild amine-like odor. It is insoluble in water, has a limited permeability, and belongs to the Eudragit family of pH-independent polymers. It expands when it comes into contact with water, allowing the integrated medicines to diffuse via swelled matrix and released from formulation. Its release retarding feature makes it ideal for controlled release medication delivery systems (Werber *et al.,* 2017). Famotidine is a best antagonist for the histamine H 2 receptor. Controlling pentagastrin-stimulated and basal stomach acid production, famotidine is 20 times additional power than cimetidine and 7.5 times more potent than ranitidine on a weight basis. Famotidine 20mg twice daily or 40mg at bedtime has been established in clinical studies to be an effective alternative to conventional cimetidine dosages for therapeutic gastric ulcers and standard ranitidine and cimitidine doses for therapeutic duodenal ulcers. famotidine 20mg dose taken at night as a preventative measure lowers the risk of duodenal ulcer reappearance (versus placebo) (Hsu *et al.,* 2017).

Famotidine 40mg given at bedtime was as effective as ranitidine 300mg, extra powerful than cimetidine 800mg in inhibiting nocturnal and pentagastrin-stimulated acid production in healthy participants. In healthy patients, famotidine 5mg was indicated to be both equally effective and 66 percent more effective than cimetidine 300mg against pentagastrin-stimulated acid secretion. In individuals with duodenal ulcers, single night dosages of famotidine 20 or 40 mg and ranitidine 150 or 300 mg had no statistically significant differences in daytime and nocturnal pH and mean acid ratio (Campoli *et al.,* 1986).

The aim of the study was to formulate and assessment of controlled release tablets of famotidine by using eudragit RL 100 polymer, direct compression into controlled release tablets, in vitro evaluation, investigation of release mechanism and dissolution profiles comparison with reference formulations. The development of controlled release tablets might extend the drug release rates up to 24 and this might reduce the dosage frequency of the selected drugs and ensure compliance of the patient as compare to conventional tablets.

MATERIALS AND METHODS

Materials

Famotidine, Eudragit RL 100 (Gifted by Martin Dow, Marker Pvt., Ltd), Analytical balance (Shimadz, Germany), Dissolution Apparatus (pharma Test, D-63512, Germany), Single Punch Tablet Machine (Erweka, AR 400, Germany), disintegration Apparatus (Pharma Test, Germany), friabilator (Erweka, TA3R, Germany) Hardness Tester (Erweka, Apparatus TB24, Germany), UV-Vis Spectrophotometer (Shimadzu, 1601, Japan), Mechanical sieve shaker (Mainland, HY 200,china) FTIR (Shimadzu, 8400, Germany). SEM (Hitachi S-3400N type-II Japan). All the instruments, chemicals and other reagents were provided by the University of Balochistan.

Methods

Precompression analysis

Standard calibration curve

Accurately weigh 20mg of famotidine into 50ml volumetric flask in phosphate buffer, dissolved and dilute up to the mark. Pipette out 1ml of this solution in 50ml volumetric flask dilute with phosphate buffer up to the mark. Consecutive dilutions consisting of 0.312, 0.625, 1.25, 2.5, 5, 10 and 20 ug/ml were prepared from the standard stock solutions. Measure the absorbance at 267nm, cell path length 10mm (1cm) using filtered phosphate buffer solution pH 7.4 as a blank.

Solubility analysis

Solubility of famotidine was conducted by taking 100mg of active drug (famotidine) which was incorporated in volumetric flask of 100ml having different solvents (0.1 N Hcl glacial acetic acid and distilled water) at different temperatures i.e. 25ºC, 37ºC and 40ºC respectively, The samples were covered with aluminium foil to protect from atmosphere and other contaminant factors and finally kept for 24 hours in shaker separately in water bath for solubility studies. After the required time the sample were analysed on UV spectrophotometer for absorbance at wavelength of 265nm. All the procedures were done in triplicate.

Particle size analysis

Particle size analysis were done with different sieves having pore sizes 0-40 ,40-60 60-80,80-100,100-120, µm by using the mechanical sieve shaker.

Sieve No.	Percent weight retained (%, n=3)
0-40	5.2
40-60	7.8
60-80	9.5
80-100	25.5
100-120	52

Pre compression studies

Angle of Repose

Correctly weighed powders were taken in a funnel. Height of the funnel was adjusted accordingly that the powder touches the tip of the funnel just at the apex of the heap. The funnel was placed and the powder was allowed to pass freely via the funnel onto the surface. Diameter and height of the powder cone were calculated and angle of repose was measured by utilizing the given formula.

$\tan\Theta = h/r$

Bulk density and tapped density

10gms of powder was taken and placed in 10ml measuring cylinder. Later observing the first volume the cylinder was tapped continuously 100 times or as specified in procedure up till no more change in volume was observed. By utilizing the given formula and calculated the bulk density (BD) and tapped density (TD).

Bulk density = Mass (M) / Bulk Volume (Vb)

Tapped density = Mass (M) / Tapped volume

Carr's compressibility index

This test was performed for the evaluation of the powder bulk and tapped density at rate on which it was filled. The carrs index was determined by using the following formula (Khan *et al.,* 2022).

Carr'sindex (%) = TD-BD/TD×100

Fourier transform infrared spectroscopy (FTIR)

This technique was used to check compatibility of drug and polymer on prepared formulations. Pure drug, all polymers used and the combination of drug and polymers were taken to confirm the identity of the drug and to detect the interaction of the drug with the recipients**.** A simple FTIR (Shimadzu, 8400, Germany) was used at 4000 to 750 cm^{-1} wave number.) (Samiullah *et al.,* 2020).

Scanning electron microscopy (SEM)

This characterization was conducted to analyze the particle size of the given samples of pure drug (famotidine) and polymers (Eudragit RL 100) individually and mixture of drug with polymers. All the samples individually and in combination were placed separately on aluminum paramount and sprinkled with gold palladium. Accelerating voltage of 10KV was passed through the samples for scanning from the working distance of about 10-25mm.(Samiullah *et al.,* 2020).

Formulation of tablets

Tablets were formulated with varying amounts of polymer (Eudragit RL 100) and Famotidine was kept constant 40mg. Pilot batches of 130 tablets were formulated using filler (Avecil), lubricants (magnesium stearate, talc). Different concentrations of polymers were added to analyze its effects on drug release patterns. The formulations are given in table 1.

Preparation

The controlled release tablets of famotidine (600mg) were formulated by direct compression technique. The drug (famotidine) and Eudragit RL 100 were weighed as per respective drug to polymer ratio. The drug, polymers and filler were blended through mortar and pestle for through mixing. Mixing was repeated again. The blended mixture after passing through sieve No 32 then lubricated. Mixed powder for through mixing pass via the same sieve by utilizing single punch machine finally prepared mixture of dry powder were compressed into tablet.

Physical evaluation of tablets

The different formulation physical evaluation characterizations were conducted such as weight variation, thickness, diameter, hardness and friability.

Weight variation test

This test was conducted to ensure that each tablets contained the same or proper quantity of active ingredient. The test was conducted by weighing 20 tablets one by one on analytical balance and the average weight was determined. The tablets passed the test if not more than two of the individual weights deviated from the average weight by more than the percentage deviation and not deviated by more than twice that percentage. A maximum difference of 5% is allowed for tablets weighing >324mg.

Thickness and diameter

Tablets thickness was assessed by the diameter of the die, the required quantity filling the die cavity, the pressure or force used in compression and the compaction characteristics of the fill material. The thickness and diameter of 20 tablets were determined in millimeters by automatic hardness tester. Thickness of tablets should be controlled within ±5% limits of a standard range depending on the size of the tablet (Gabbott *et al*., 2016).

Hardness test

Tablet hardness is defined as the load required to crush a tablet placed on its edges. This parameter is used to control tablet manufacturing process. Tablets must have sufficient strength to withstand the rigors during handling packaging and transportation. Hardness is related to solubility an increased or too much hardness of tablets fails to disintegrate the tablets within required time which ultimately affects the therapeutic efficacy which cannot be achieved in required time. The tablet hardness was measured by placing the tablets between two anvils of the hardness tester pressure was applied to the anvils and the crushing strength which caused the tablet to break was recorded. The hardness of the tablets should not be more than 5kg out of 20 tablets only 2 tablets are allowed to exceed the limit (Gabbott *et al.,* 2016).

Friability test

This test was conducted for the determination of physical strength of uncoated compressed tablets during the process of manufacturing handling, packaging, shipping and consumer use where the tablets undergo the process of abrasion and mechanical shock without crumbling. The weight variation and content uniformity problem also arises if the tablet powder, chip or fragments**.** Friabilator in which 20 pre-weighed tablets were closed in the plastic chamber of apparatus revolved at 25rpm as the tablets fall 6 inches in every turn they undergoes the process of abrasion and shock. After 4 minutes or 100 revolutions the tablets were taken out and the weight loss was compared with initial weight.

Table 1: Formulations of tablets

Formulation	Famotidine (Active Drug)	Eudragit RL100	Talc	Mg-Stearate	Avecil (102)	Total weight of tablets
F1	40mg	260mg	8.5mg	10.5mg	281mg	600mg
F2	40mg	250mg	8.5mg	10.5mg	291.mg	600mg
F3	40mg	240mg	8.5mg	10.5mg	301mg	600mg
F4	40mg	230mg	8.5mg	10.5mg	311mg	600mg

Table 2: Solubility studies of famotidine by using various solvent

S. No	Solvent used	Temperature	
1	Distill water	37^0C	0.251
2	Distill water	25^0C	0.229
3	Distill water	40^0C	0.301
4	Phosphate Buffer 7.4	37^0C	0.812
5	Phosphate Buffer 7.4	25^0C	0.829
6	Phosphate Buffer 7.4	40^0C	0.802
7	0.1 N HCl	37^0C	0.799
8	0.1 N HCl	25^0C	0.725
9	0.1 N HCl	40^0C	0.862

Table 3: Flow characteristics

Formulations	Angle of repose	Hausner's ratio	Compressibility index (%)
F1	24.6±0.116	1.324±0.016	10.18±0.014
F2	25.3±0.132	1.187±0.014	12.15±0.032
F3	26.2±0.138	1.121±0.162	11.22±0.011
F4	26.2±0.138	1.123±0.032	13.43±0.042

Table 4: Physical tests of CR tablets of Famotidine using Eudragit RL 100

Code	Thickness (mm)	Diameter (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation (mg)
F1	3.1±0.008	13.1±0.125	9.0±0.543	0.01±0.014	600±0.139
F2	3.12±0.003	13.1±0.148	10±0.654	0.013±0.012	600±0.128
F3	3.11±0.006	13.1±0.123	9.5±0.865	0.01±0.124	601±0.229
F4	3.14±0.032	13.1 ±0.091	9.4±0.465	0.011±0.035	602±0.332

Table 5: Drug release mechanisms

Formulations	Power Law		
	R^2 value	n-value	Mechanism of drug release
F1	0.8539	0.6132	ANFD
F2	0.9107	0.7621	ANFD
F3	0.8838	0.8424	ANFD
F4	0.8997	0.9135	ANFD

ANFD; Anomalous non-fickian diffusion

Table 6: Dissolution profiles comparison

Formulations	Difference and Similarity factors	
	f1	f2
F1 vs reference	19.8	38
F2 vs reference	18.89	36
F3 vs reference	20.13	33
F4 vs reference	23.84	32

The weight loss by abrasion was a measure of tablet friability. The value is expressed in percentage. Acceptable limits for the weight loss shall not be more than 1% (Sirimamilla *et al.*, 2013).

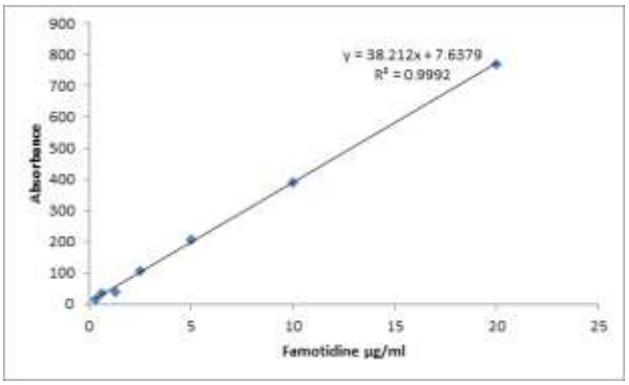

Fig. 1: Standard calibration curve of Famotidine

Fig. 2: FTIR spectra of famotidine
http://www.ijrpc.com/files/12-4170.pdf

In-vitro evaluation

This test was conducted through USP method-II (Paddle type) by utilizing dissolution apparatus. The dissolution medium used was phosphate buffer having pH 7.4 at constant temperature 37^{+}.2ºC. The speed of the rotation was kept constant at 100 rounds per minute. After different time intervals 5ml of the samples were taken each at 5 minutes ,10 minutes,30 minutes,1 hour ,3 hours ,6 hours,12 hours,18 hours and 24 hours. These samples were collected and filtered separately and analyzed by UV- visible spectrophotometer at 265nm. The released percentage of the different formulations were analyzed and were calculated from the standard curve of Famotidine at 7.4 pH . All these analysis were repeated three times. The absorbance were noted at 265nm and the results were tabulated and also the reference drug was evaluated through same procedure.

Effect of drug-to-polymer ratio

All four controlled release Famotidine formulations (F1, F2, F3 and F4) were formulated by various drug to polymer ratios and were checked .The drug concentration was fixed, while the ratio of polymer varies. The release kinetics were also investigated.

Determination of drug release kinetics

The evaluated in vitro data was used in mathematical model Power Law to check the release of drug, famotidine which is shown in following formula accordingly.

$M_t / M_\infty = K\, t^{n}$

Similarity and difference factors

The similarity and difference factor were determined of control release famotidine tablets with standard (Optifam by Martin Dow) with 1-15 being acceptable range of difference factor (f1) and 50-100 (f2) is the range of similarity factor.

$f_1 = \{[\sum t = 1^{n} (R_t\text{-}Rt)]/ [\sum_{t=1}^{n} Rt]\} \times 100$
$f_2 = 50 \times \log \{[1 + (1/n) \sum_{t=1}^{n} (R_t\text{-}Rt)^{2}]^{-0.5} \times 100\}$

STATISTICAL ANALYSIS

Statistical analysis of the kinetics results were performed on DD solver. (Microsoft excel 2007).SPSS version 21, IBM, USA) was used for drug release calculation (Gul *et al.*, 2019). All the formulations data were applied to the Kinetics Model and the results were calculated (Samiullah *et al.*, 2020).

RESULTS

All the results statistically found significance. Standard calibration curve of the famotidine was constructed by plotting its dilutions concentration against its absorbance and obtained straight line as shown in fig. 1.

Solubility of famotidine

Solubility in various solvents at different temperatures were determined. It showed good solubility in 0.1N HCl and phosphate buffer pH 7.4. as indicated in the table 2.

Fig. 3: FTIR of famotidine with Eudragit RL-100

Flow properties

The pre-compression studies were analyzed accordingly and it was concluded after the tabulation of the results that in F1 the angle of repose was 24.6±0.116 , in F2 it was 25.3±0.132, in F3 26.2±0.138 and in F4 was 26.2±0.138. These results indicated that all the values when compared with the standards were within the limits accordingly. The flow properties of all four formulations were checked according to the standard procedure. The results showed in table 3 that all the flow properties were within the limits specified as per the standards.

Fourier transform infrared spectroscopy (FTIR)

FTIR was conducted and it was observed that there was no incompatibility of the drug and additives as given in figs. 2 and 3.

Scanning electron microscopy (SEM)

The SEM was used to study the morphology of the drug, the drugs have irreuglar shapes were observed under electron microscope because of its hydrophobic nature, the polymers Eudragit RL-100 always shows the layers on the surface of tablets as indicated in fig. 4 (B).

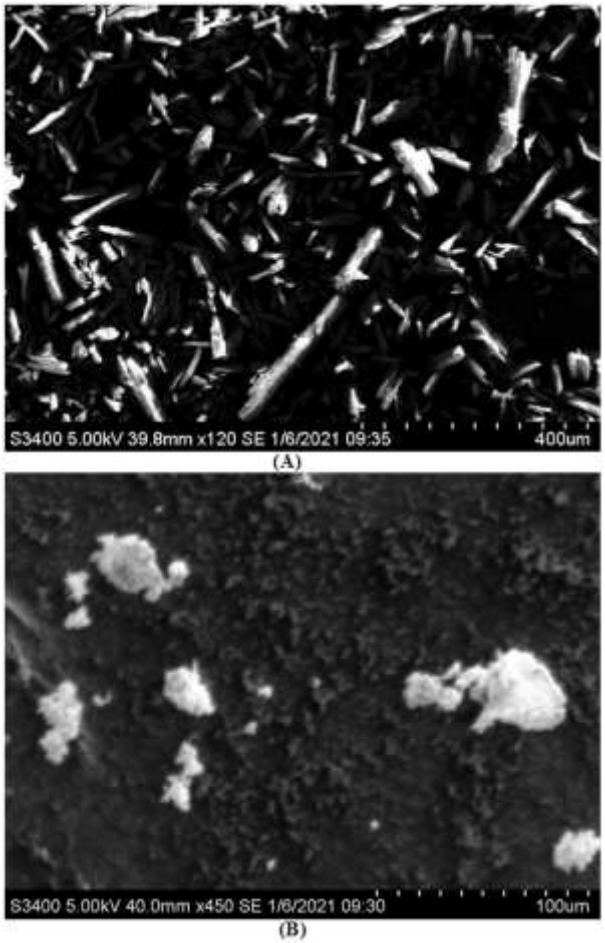

Fig. 4: SEM (A) illustrate that surface morphology of the drug Famotidine, while (B) display surface morphology of Eudragit RL 100 at different magnificent powers.

Physical characteristics

The thickness of all the formulations were checked according to the specified standards ranging between 3.1±0.008mm to 3.14±0.032mm and diameter 13.1 ±0.091mm which was within standard limits. The hardness test of the all the four formulations ranged between 9.0±0.543kg/cm^2 and 10±0.654kg/cm^2 which was within standard limits. The values of friability test measured was found to be 0.01±0.014% to 0.011±0.035% indicating good resistance of the tablets as given in table 4.

Drug release

The drug release of all the formulation with different drug to polymer ratio was checked by using dissolution apparatus Pedal method having 6 stations. The medium used was Phosphate buffer having pH 7.4. The apparatus was run at 100 rpm. The temperatures were kept 37^{o}C±2. The absorbance was checked at 265nm as standard**.** The release rates were checked in different time intervals i.e. 0.5hr, 1hr, 2hrs, 4hrs, 8hrs, 16hrs and 24hrs. The formulation having drug to polymer ratio were 1:6.5, 1:6.25, 1:6, 1:5.75 (F1, F2, F3, F4). The release profiles were observed and tabulated where F1 showed 94% formulation F2 95%, F3 96% and F4 97%.

The results confirmed that increase percentage in polymer concentration extended the drug release rate of the controlled release formulations. It is indicated in fig. 5, that among the four formulations (F) of famotidine the F1 in which the polymer quantity was more as compared to the other formulations the release rate was decreased (94%) and the F4 having the decreased concentration of polymer showed increased drug release (97%) in 24hours.

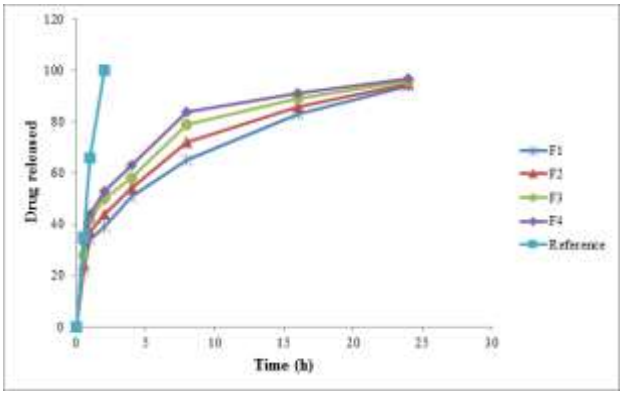

Fig. 5: Famotidine release profiles from CR tablets with Eudragit RL 100 (after 24 hrs)

Drug release mechanism

All the formulations of CR tablets of famotidine were checked through the power law by putting the standard formula as showed in table 5. It was concluded that all the formulations mechanism of release were followed by Anomalous non-fickian diffusion.

Similarity and difference factor

The dissolution profile of controlled release tablets were compared with immediate release reference tablets. The results showed that f1 values of all the four controlled release tablets of famotidine were not in acceptable range which is (1-15) and indicated difference from the dissolution study of reference standard tablets. Likewise the f2 values of these four controlled release formulations of famotidine tablets also indicated difference from dissolution study of the reference standard as the normal values ranging from (50-100) (Khan *et al.,* 2018). It was noted that the test formulations were not similar with

immediate release reference tablets in terms of dissolution patterns. Results are given in table 6.

DISCUSSION

CR tablet of famotidine were developed by direct compression method. These CR depends on polymer Eudragit RL 100. Four different drug to polymer ratio of controlled release tablets of famotidine were prepared (F1, F2, F3, F4).The ratio used was (1:6.5, 1:6.25, 1:6 1:5.75). The pre compression tests of the formulations were performed accordingly with SEM and FTIR, Post compression characteristics of the CR famotidine tablets were checked and compared with the standards. The results showed that both the pre compression and post compression studies were in the specified standard limits. The findings of FTIR were incorporated and it was observed that there was compatibility of drug with polymer. Scanning electron Microscopy were also checked. The physical characteristics of the all formulation were checked and concluded that all the formulations met the standards specified in the Pharmacopeia. The presence of Eudragit RL 100 extended the release of drug up to 12 hours and 24 hours simultaneously. As it was also mentioned this polymer extended release rate of CR tablets up to 24 hrs by (Khan *et al.,* 2018). This is due to the hydrophobic nature of Eudragit RL 100 which act as the retardant to the solvent molecules and so existence of its layer on the surface of tablets prevents the penetration of the solvent into the system and extends the drug release.

The concentration of polymer had a great effect on the rates of drug release. Increase in concentration of polymer increases the retardation and decreases the release of drug. Among the four controlled release formulation of famotidine F1 in which the drug to polymer ratio is more i.e. 1:6:5 the retardation is more and the drug release is less (i.e. 94%) similarly in F2 formulation the polymer concentration is less (1:6.25) as compare to the F1 and so retardation is less and drug release is more (95%). In F3 the drug to polymer ratio becomes less i.e. (1: 6) and the drug release is 96%. In F4 the concentration of the drug to polymer ration is (1:5.75) and the release is 97%.

Drug release mechanism of the controlled release tablet of famotidine is indicated by n-values of power law (n=0.5); indicates quasi Fickian diffusion, n>1; indicates anomalous non-fickian diffusion and when n=1; it indicates non-Fickian zero order kinetics.

The n-values of all the four controlled release directly compressed Eudragit RL100 based tablets ranging from 0.6132 - 0.9135 anomalous non-Fickian diffusion was the method through which drug was release. These findings are in confirmation with authors (Karetal *et al.,* 2009).

The results of controlled release tablets of F1 formulation showed that f1, values is 19.8 and occurs in acceptable range (1-15) and indicated difference from dissolution study of the reference standard. The f2 values of the formulation F1 is 38 which indicated similarity with reference standard dissolution study as the f2 limit is from 50- The results confirmed that when a slight increase in polymer the release rate decreases and decrease in polymer ratio increases the release rate of the famotidine. It is observed among all these formulations the F4 having drug to polymer ration decrease showed increased in drug release in 24 Hours.

CONCLUSION

In the present study famotidine were prepared by mixing polymer Eudragit RL100 and expedients. The Pre compression and post compression test were showed accurate results when compared with the standards. The compatibility studies were also done with the help of FTIR and compared there was no compatibility among the drug and polymers. were also checked with polymers by FTIR The results confirmed that when a slight increase in polymer the release rate decreases and decrease in polymer ratio increases the release rate of the famotidine. It is observed among all these formulations the F4 having drug to polymer ration decrease showed increased in drug release in 24 Hours.

ACKNOWLEDGMENTS

The authors are thankful to Martin Dow, Marker Pharmaceuticals Pvt. Ltd, for providing drug and polymers for my project. The authors are additionally giving their gradtidues to the department of Pharmaceutics, University of Balochistan, for providing reagents and chemicals.

REFERENCES

Al Husban F,Gabbott IP, Al Husban F and Reynolds GK (2016). The combined effect of wet granulation process parameters and dried granule moisture content on tablet quality attributes. *Eur. J. of Ph & Bioph.*, **106**: 70-78.

Campoli-Richards DM and Clissold SP (1986). Famotidine. *Dr. J.*, **32**(3): 197-221.

Debotton N and Dahan A (2017). Applications of polymers as pharmaceutical excipients in solid oral dosage forms. *Med. Res. Rev.*, **37**(1): 52-97.

Gul R, Jan SU, Ahmed Mahmood, Amanullah Khan, Jhan Nusrat, Rahman R, Sherani S and Tariq N (2019). Effect of thyme oil on the transdermal permeation of pseudoephedrine HCl from topical gel. *Dissolution Tech*., 26(4): 18-23

Hsu PI, Wu DC, Tsay FW, Cheng JS, Liu CP, Lai KH and Kao SS (2017). Histamine-2 receptor antagonist cannot prevent recurrent peptic ulcers in patients with

atherosclerotic diseases who receive platelet ADP receptor antagonist monotherapy: A randomized-controlled, double-blind and double-dummy trial. *Off. J. ACG.*, **112**(2): 282-289.

Khan KA, Khan GM, Jan SU and Mehsud S (2018). Formulation and *in vitro* evaluation of directly compressed controlled release tablets designed from the co-precipitates. *Pak. J. Pharm. Sci.*, **31**(2): 455-461.

Khan KA, Zizzadoro CD, Cerbo A, Pugliese N, Khan GM, Ghazanfar S and Farid A (2022). Preparation and *in vitro* evaluation of controlled-release matrices of losartan potassium using ethocel grade 10 and carbopol 934P NF as rate-controlling polymers. *Polym. J.*, **14**(15): 2993.

Kulkarni S, Butte D and Rathod S (2012). Natural polymers A comprehensive review. *Int. J. Res. Pharm. Biomed. Sci.*, **3**(4): 1597-1613.

Laracuente ML, Marina HY and McHugh KJ (2020). Zero-order drug delivery: State of the art and future prospects. *J. CR.*, **327**: 834-856.

Marguet M, Bonduelle C and Lecommandoux S (2013). Multicompartmentalized polymeric systems: Towards biomimetic cellular structure and function. *Chem. S. Rev.*, **42**(2): 512-529.

Pedro SN, Freire MG, Freire CS and Silvestre AJ (2019). Deep eutectic solvents comprising active pharmaceutical ingredients in the development of drug delivery systems. *Ex. Op. DD.*, **16**(5): 497-506.

Samiullah, Syed UJ, Rahman G, Syed J and Asmathullah (2020). Formulation and evaluation of transdermal patches of pseudoephedrine HCl. *Int. J. App. Pharm*., **12**(3):121-127.

Scicluna MC and Vella-Zarb L (2020). Evolution of nanocarrier drug-delivery systems and recent advancements in covalent organic framework drug systems. *J. ANM.*, **3**(4): 3097-3115.

Sirimamilla N (2013). Formulation and evaluation of atorvastatin calcium immediate release tablets using super disintegrants (Doctoral dissertation, KK College of Pharmacy, Chennai, Tamil Nadu, India (Thesis).

Thabet Y, Klingmann V and Breitkreutz J (2018). Drug formulations: Standards and novel strategies for drug administration in pediatrics. *J. Cl. Pharm.*, **58**: S26-S35.

Werber JR, Bull SK and Elimelech M (2017). Acyl-chloride quenching following interfacial polymerize-tion to modulate the water permeability, selectivity, and surface charge of desalination membranes. *J. Mem Sci.*, **535**: 357-364.

Williams DJ, Habib AG and Warrell DA (2018). Clinical studies of the effectiveness and safety of antivenoms. *Tox. J.*, **150**: 1-10.