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SOLUBILITY ENHANCEMENT OF POORLY WATER SOLUBLE DRUG LAFUTIDINE BY LIQUISOLID COMPACT TECHNIQUE

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ABSTRACT

Solubility of the drug play a very significant role in the pharmaceutical formulation also affect their pharmaceutical action and its bioavailability. Bioavailability of hydrophilic drug is lower as compare to hydrophobic drug, that's why to improve bioavailability of hydrophobic drug need some modification to increase the solubility. In the present study solubility of Lafutidine was modified by using liquisolid compact technique. Liquisolid compact technique is the technique in which dispersed system ornon-volatile liquid system is converted into dry, non-adherent and free flowing powder with proper selection of carrier and coating material. This technique has an ability to alter the dissolution rate of formulation. Carrier used in present study in Avicel 102 and coating material Aerosil 200, also PEG 400 used as a non-volatile solvent. Formulation of tablet was carried out by direct compression of the formed dry powder by the addition of required additives. IR study confirmed that no interaction occurred between drug and excipients and in final formulation also. The in-vitro released of formulation is not less than 74% (F1) and more than 88.58% (F9) within 45 min. according to result it is observed that the solubility and bioavailability of hydrophilic drug Lafutidine is increased after its modification by liquisolid compact technique as compare to normal and also increased the stability of the drug and formulation.

INTRODUCTION

The physicochemical property of the drug plays a very significant role in the performance of the activity and other also. One of these the solubility of the drug impact the major role in the overall activity of the drug. As per the BCS classification the drug is classified on the basis of the drug solubility and permeability, most of the newly developed drug belong to the BCS class II, which having the high permeability and low solubility property[1,2].The low solubility of the drug directly impart the dissolution and bioavailability of the drug that mean low solubility low in the drug activity. In modern drug discovery there in continually increased in the development of the lipophilic drug that mean poor water soluble drug, at current condition more than 60% of the of the active constituent Available in the market[3,4]. To overcome these solubility problem of the drug various approaches are used like used of Nano particle, solid dispersion, micronization, self-emulsification, liquisolid compact, complexation, etc.[3,5,6]. The liquisolid technique is define as the formulation formed by the conversion of liquid drug, drug suspension or drug solution in non-volatile solvent into dry, non-adherent, free flowing and compatible powder mixture by blending the suspension or solution with selected carrier and coating material. Liquisolid compact technique have an ability to change the dissolution rate of the drug and its formulation. Liquisolid technique has been used to increase the dissolution rate of the poorly water soluble drug[4, 7]. Lafutidine is used as an antacid as well as anti-ulcerative

agent. It is freely soluble in acetic acid and practically insoluble in water. Lafutidine is the h2 receptor antagonist with persistent effect on suppression of gastric acid secretion. It also protect gastric mucosa, accelerated mucosa reconstitution, increased gastric mucosal blood flow and gastric mucus[8].

Material and Method

Lafutidine was provided by Ajanta pharma, lactose, DCP (anhydrous), colloidal silica, Avisel pH 102 and 101, talc, magnesium stearate, PEG, PEG 400 and 200, and methanol was collected from the laboratory of analytical grade.

Solubility Study:

For the saturation solubility study of Lafutidine were carried out in different solvents likes PEG-400, PEG-200 and PEG. Lafutidine were mixed in different nonvolatile solvent and mixed using vortex mixture for half ahr. and collected in the vial. Then vial were placed in the mechanical shaker for the 24hr at 32^0C. The saturation condition should be maintained during the shaking of the vials. Then the sample remove from the shaker are diluted with the solvent and absorbance were taken at the recorded wave length in UV-Spectroscopy[9, 10, 11]. And the abs. were recorded down.

Calculation of liquid load factor (Lf):

In the present work the aim of the formulation is to develop the tablet formulation. To attain the optimal solubility of Lafutidine in vehiclePEG 200, PEG 400 and PEG was used and Aerosil 200 was selected as a coating material. For the calculation of the liquid load factor the different ration of the carrier and coat material are selected and the mixture was blended for the 10 min. the flowability of the different ration was carried out by using flowmeter[12]. These liquid/ carrier ratio is known as liquid load factor and calculated by fallowing formula[14]:

Lf= W/Q

Were,

W is amount of liquid medication and

Q is amount of carrier material

Preparation of liquisolid powder:

The liquisolid powder was formulated in three main steps

Step 1: The desired quantity of the drug and liquid vehicle (PEG, PEG 200, PEG 400) were mixed the calculated weight of resulting liquid medication was incorporated into the calculated quantity of the carrier material (Avicel, PH 102, DCP, lactose) and mixed thoroughly.

Step 2: then the resulting mixture was blended with the calculated amount of the coating material (Aerosil 200) using a standard mixing process to form simple admixture. Several factor of carrier: coat ratio ranging from 4 to 1 was employed.

Step 3: to the above binary mixture disintegrant like sodium starch glycolate and other remaining additive such as talc and magnesium stearate added according to their application and mixture for a period of 10 to 20 min. in mortar. The final mixture was compressed using the tablet machine to achieve tablet form[7, 14, 15]. The formulation table for the Lafutidine tablet is given in table no. 1

EVALUATION:

Characteristic of powder:

1. **Bulk density:**Bulk density is the ratio of mass of powder to the bulk volume. The powder was passed through the 40# sieve mesh, 10g of power was collected and introduced into the 25ml measuring cylinder. Volume occupied by the powder was recorded. The bulk density were calculated by the fallowing formula[16]:
   Bulk density = weight of powder (g) / bulk volume (ml)
2. **Tapped density:** The powder available in the measuring cylinder in above study, the measuring cylinder were tapped until the powder compacted completely. The tapped density value were calculated by using fallowing formula[16]:
   Tapped density = Weight of powder/ Tapped volume
3. **Angle of repose:** The angle of repose of individual batch was determined by the funnel method. The funnel was fixed above the surface area ata the distance of 2.5 cm. with the help of stand.

The accurately weight quantity of powder was allow to pass throught the funnel on to the graph paper until the powder is touch to the tip of funnel. Angle of repose was calculated by using the fallowing formula[16]:

$$\text{Tan } \Theta = 2h/D$$

Where, Θ = angle of repose,
h = height of the heap,
D = diameter of the heap

4. **Hausner's ratio:**Hausner's ratio was used for the flow property of the powder. It was calculated by fallowing formula[16]:
   Hausner's ratio = tapped density (g/cm^3)/ Bulk density (g/cm^3)
5. **Carr's index:** The compressibility of individual blend were calculated using fallowing formula[16]:
   Carr's index = (Tapped density – Bulk density /Tapped density) x 100

Characteristic of Lafutidine Tablet:

1. **Weight variation:** 20 tablet of each formulation type were weighted individually, the average weight was calculated and each of the individual tablet was compared and weight deviation were recorded and percent weight variation was calculated[17].
2. **Friability:** Take the no. of tablets equivalent to the 6.5g and placed into the friabilator. The friabilator was operate at25rpm for 4 min. then the tablet was weighted again and noted down. The loss in the weigh due to abrasion or fracture was noted and % friability was calculated by fallowing formula[17]:
   $F\ \% = (W_0 - W) / W_0 \times 100$
3. **Hardness:** The hardness of the tablet can be measured by the various apparatus, here Monsanto harness tester was used. Tablet from each batches were selected. Each tablet was held along its axis between two jaws of the tester and scale was observed to zero. A constant force was applied by rotating the knob until the tablet was fractured[17]. The hardness were noted down in kg/cm^2
4. **Disintegration test: (15.** Y.B.A. Bakar**)** The disintegration apparatus was used for the testing of disintegration test. Placing each of tablet in each basket with the disc. 0.1N HCL (1.2 pH) is used as a buffer[17].
5. **Drug content:** Two tablet from each batch was selected, weighted and crushed. The equivalent quantity of 5 mg of Lafutidine was accurately weight from crushed powder and transferred into the 100ml volumetric flask containing 20ml of 0.1N HCL, further diluted up to 100ml. filtered through whatman filter paper. Absorbance was noted down at 284nm by using UV- visible spectrophotometer[17].
6. ***In-vitro* drug released study:** *In-vitro* drug released study of Lafutidine tablet was carried out by USP dissolution apparatus type II at 50rpm. One Lafutidine tablet was placed in each flask of apparatus containing 900ml of dissolution media having the pH 1.2.The temperature is maintained the $37 \pm .0.5^0$C. 5ml sample were withdrawal ate the fixed time interval and analyzed by the UV-Spectrophotometry at284nm[17].
7. **IR Study:** Infra-red spectra was carried out of Lafutidine, physical mixture of Lafutidine and Aerosil 200, mixture of Lafutidine and avicel 102, mixture of Lafutidine and DCP, mixture of Lafutidine and lactose and mixture of Lafutidine and sodium starch glycolate by using standard procedure for the study of IR[17].IR spectra for the formulation was performed after the conformation that their not any kind of interaction occurred in between drug and excipients, spectra are shown in fig.1.

RESULT AND DISCUSSION:

For the possible interaction study of tablet of Lafutidine were mainly identify by the performing the FT-IR Spectroscopy study. The result prove that the Lafutidine is show the characteristic with Aerosil 200, Avicel 102, DCP, lactose, sodium starch glycolate and formulation as per show in the fig no. 1 respectively. From the saturation solubility study it was observed that Lafutidine has a maximum solubility in PEG-400 and minimum solubility in PEG-200 and PE as per given in the table no.2. The liquisolid powder of Lafutidine was prepared by the simply adsorption method with the help of vehicle and carrier material.

Table no. 1: formulation table for the Lafutidine tablet.

Formulation	LS1	LS2	LS3	LS4	LS5	LS6	LS7	LS8	LS9
Drug (mg)	5	5	5	5	5	5	5	5	5
PEG 400	-	-	-	7.6	11	-	7.6	7.6	7.6
PEG 200	7.6	7.6	7.6	-	-	7.6	-	-	-
R value	4:1	4:1	4:1	4:1	4:1	4:1	4:1	4:1	4:1
Lf value	0.0028	0.0028	0.0028	0.0028	0.0042	0.0028	0.0028	0.0028	0.0028
Avicel 102	70	70	-	-	70	70	70	70	70
Avicel 101	-	-	70	70	-	-	-	-	-
DCP	240	240	240	240	237	240	240	-	240
Lactose	240	-	-	-	-	240	-	240	-
Colloidal silica	17	-	-	-	17	17	17	17	-
Arosil 200	-	17	17	17	-	-	-	-	17
SSG	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Magnesium stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Talc	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Total weight	350	350	350	350	350	350	350	350	350

Table no.2: saturation solubility of Lafutidine

Sr. No.	Non-volatile solvent	Solubility mg/ml
1	PEG 400	2.763
2	PEG 200	1.155
3	PEG	1.005

Table no. 3: Characteristic study of Lafutidine powder.

Batch code	Bulk density	Tapped density	Hausner's ratio	Carr's index	Angle of repose (Θ)
LS1	0.983±0.02	1.19±0.00	1.23±0.02	17.23±0.10	26.56±0.75
LS2	1.07±0.02	1.25±0.10	1.2±0.01	17.48±0.01	31.381±1.15
LS3	0.097±0.01	1.21±0.10	1.40±0.10	4.46±0.02	29.16±0.14
LS4	0.098±0.01	1.196±0.01	1.22±0.01	18.18±0.10	30.06±0.31
LS5	0.966±0.03	1.21±0.01	1.11±0.01	17.5±0.1	30.89±0.26
LS6	0.983±0.02	1.2±0.01	1.12±0.01	17.5±0.1	26.56±0.75
LS7	1.05±0.05	1.96±0.15	1.03±0.01	13.42±0.01	27.19±0.02
LS8	1.03±0.03	1.25±0.01	1.23±0.01	19.16±0.01	30.12±0.89
LS9	1.016±0.03	1.20±0.01	1.21±0.01	10.74±0.01	26.63±0.62

Fig1: Infrared spectrum of formulation

Table no. 4: characteristic of Lafutidine tablet.

Batch code	Hardness Kg/cm^2	Thickness (cm)	% Friability	Weight variation (mg)	Disintegration time	Drug content (%)
LS1	5.36±0.68	3.47±0.02	0.52	Passes	4.44±0.04	87.70±0.05
LS2	4.91±0.12	3.49±0.05	0.62	Passes	4.23±0.07	88.23±0.020
LS3	5.63±0.71	3.01±0.02	0.50	Passes	4.55±0.02	88.76±0.015
LS4	6.12±0.36	3.98±0.04	0.61	Passes	4.36±0.01	89.30±0.01
LS5	4.36±0.21	4.12±0.05	0.49	Passes	3.59±0.01	89.82±0.01
LS6	5.89±0.36	3.97±0.05	0.58	Passes	3.52±0.03	90.36±0.01
LS7	4.39±0.82	4.19±0.09	0.67	Passes	4.56±0.01	90.90±0.01
LS8	4.33±0.59	3.48±0.02	0.60	Passes	4.44±0.52	91.44±0.02
LS9	4.84±0.19	4.19±0.09	0.41	Passes	4.59±0.07	91.96±0.1

Table no. 5: In-vitro release study of Lafutidine tablet.

% cumulative drug release									
Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5	36.68± 1.29	37.04± 0.85	43.91± 1.53	38.89± 1.58	54.97± 1.89	52.30 ±1.68	37.36± 1.37	63.12± 1.18	48.56 ±1.60
10	42.63± 1.71	45.63± 0.87	50.49± 1.51	51.10± 1.78	62.75± 1.62	69.35 ±1.81	55.04± 0.94	67.47± 0.78	63.64 ±0.88
15	46.23± 1.44	57.23± 1.48	3.52±1 .90	56.93± 0.95	67.36± 0.96	72.13 ±1.10	64.14± 1.22	77.88± 1.64	66.42 ±1.08
30	54.89± 1.04	70.51± 0.49	74.10± 1.90	69.03± 0.51	73.60± 1.43	81.65 ±1.07	76.92± 1.05	82.86± 1.60	79.51 ±1.12
45	74.49± 0.54	76.84± 1.94	77.63± 1.55	77.78± 0.65	79.54± 1.43	84.50 ±1.18	84.1 ±0.46	86.78± 1.02	88.58 ±0.94

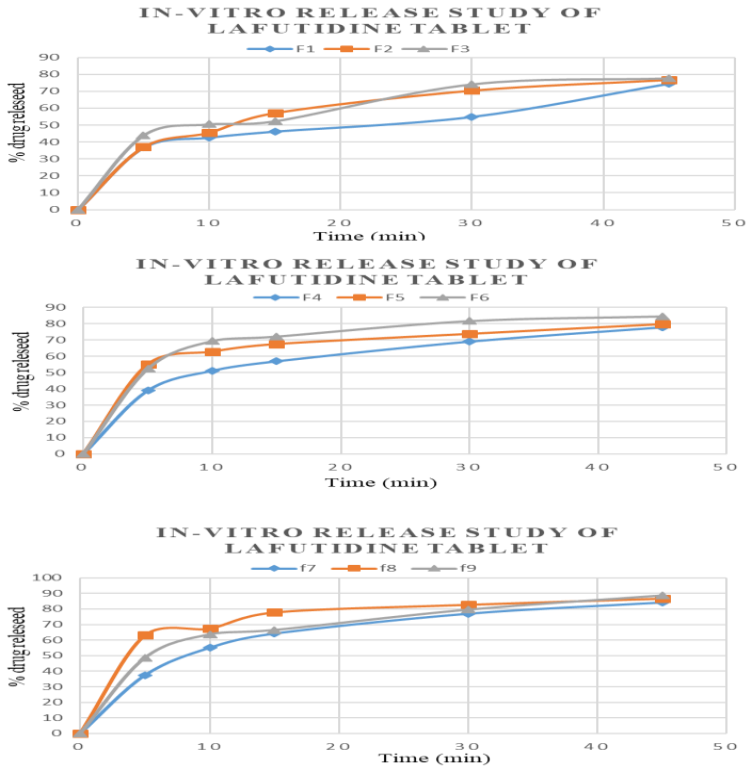

Fig.2: In-vitro released study of Lafutidine tablet (F1-F9)

The powder was triturated with additives and by direct compression method the Lafutidine tablet was formulated. The powder and tablet was evaluated and the result of liquisolid powder and tabletwere given in table no. 3 and 4 respectively. From the tapped density, Bulk density, Hausner's ratio, Carr's index and Angle of repose it was found that the liquisolid powder of Lafutidine has a good flowing property. The hardness of the tablet was measured by the Monsanto hardness tester and the hardness of the tablet was found to be 4.3 to 6.2 kg/cm^2, and % friability is less than 1%. Weight variation of the tablet is passable for all the batch, disintegration time of the tablet was found to be in between the 3 to 5 sec. and percentage Drug contain was found to be in range as shown in the table no.4. The infra-red spectroscopy study clear that the absence of the interaction between the drug and excipients that is in their physical mixture, and final formulation also as shown in the fig.1. The cumulative drug released of the drug is depend on the polymers and its concentration available in formulation, percent released of tablet is shown in table no. 5 it was observed that the released in in between 75 to 90% within the 45 min. as shown in fig.2.

REFERENCES:

1. Lam M, Ghafourian T, Nokhodchi A. Liqui-pellet: the emerging next-generation oral dosage form which stems from liquisolid concept in combination with pelletization technology. AAPS PharmSciTech 2019;20: 231.
2. Loftsson T, Brewster ME. Pharmaceutical applications of cyclodextrins: basic science and product development. J pharm pharmacol. 2010;62(11):1607–1621.
3. Karmarkar, Liquisolid technology for dissolution rate enhancement or sustained release. Expert Opin. Drug Deliv. 2010;7(10):1227-1234.
4. Dissolution enhancement of tadalafil by liquisolid technique mei lua , haonan xinga , tianzhi yangb , jiankun yua , zhen yanga , yanping suna and pingtian dinga. Pharm J. Tech. 2016;6(6):1-14.
5. Chiou, Pharmaceutical applications of solid dispersion systems. J pharm sci. 1971;60:1281-302.
6. Savolainen, et al. Evaluation of polar lipid-hydrophilic polymer microparticles. Int j pharm 2003;262:47-62.
7. Javadzadeh, Liquisolid technique as a new approach to sustain propranolol hydrochloride release from tablet matrices. International Journal of Pharmaceutics 2008;362:102–108.
8. Dolas, Formulation and evaluation of gastroretentive floating tablets of Lafutidine. Journal of Drug Delivery & Therapeutics. 2018;8(5):393-399.
9. Sun, et al. Preparation and Pharmacokinetics Evaluation of Solid Self-Microemulsifying Drug Delivery System (S-SMEDDS) of Osthole. AAPS PharmSciTech 2018;19:2301–2310.
10. Balata, Self-emulsifying drug delivery systems as a tool to improve solubility and bioavailability of resveratrol. Drug Design, Development and Therapy 2016;10:117–128.
11. Korni, Voodikala S, Gonugunta CSR, Jayanti V. Liquisolid technique: an approach to enhance the dissolution rate of olanzapine.Indian J Pharm Sci. 2018;80(6):1003-1010.
12. Kala, Shastri DH, Shelat PK. Design and Characterization of Buccoadhesive Liquisolid System of an Antihypertensive Drug. Hindawi Publishing Corporation Journal of Drug Delivery 2015; 9:1-10.
13. Spireas, Sadu S. Enhancement of prednisolone dissolution properties using liquisolid compacts. International journal of pharmaceutics. 1998;166(2):177–188.
14. Kulkarni .Liquisolid Systems: A Review. International Journal of Pharmaceutical Sciences and Nanotechnology 2010;3(1).
15. Hire, Barhate HA, Bhambere DS, Erande AS. Liquisolid technology: a novel approach for enhancement of solubility and bioavailability. International Journal of Institutional Pharmacy and Life Sciences 2016; 6(1).
16. Kushwaha, Singh PM.Role of naturally isolated pear starch on the bioavailability of famotidine. Journal of Drug Delivery & Therapeutics 2019; 9(3):430-435.
17. Bakar, Revisiting dispersible milk-drug tablets as a solid lipid formulation in the context of digestion, International Journal of Pharmaceutics 2018;5173(18):308..