ejpmr, 2020,7(4), 476-486

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

ENHANCEMENT OF SOLUBILITY OF VILAZODONE DRUG BY LIQUI-SOLID COMPACT TECHNIQUE

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Article Received on 01/02/2020 **Article Revised on 21/02/2020** **Article Accepted on 12/03/2020**

ABSTRACT

The aim of present work is to enhance the solubility rate of Vilazodone by using liqui-solid compacts. Liquisolid compacts were formulated using PEG 400 as a non volatile solvent along with avicel and aerosol as carrier and coating materials in R:2 ratio, by direct compression method. Totally nine formulations were formulated using different ratios of carrier to coating material, and the concentration of super disintegrant. Drug and Excipient compatability studies revealed that the drug and excipients were found to be compatable and there weren't any interactions between them. Prepared formulations were evaluated for pre-compression and post compression parameters. All the studies revealed that the all parameters were found to be in acceptable range for the Liquisolid compacts. From the *in-vitro* studies we can say that formulation F9 shows best drug release of 97.32% within 40 minutes where as all the other formulations takes about 50-60 minutes to release the drug. Based on the regression values it was concluded that the optimized formulation F9 follows First order kinetics.

KEYWORDS: Vilazodone, FTIR, PEG 400, CCS, SSG, MCC and aerosol.

INTRODUCTION

Solubility of drugs is a major factor in the design of pharmaceutical formulations lead to variable oral bioavailability. Dissolution is an important factor for absorption of drugs especially in case of water insoluble or poorly water soluble drugs. The rate limiting step for most of the pharmaceutical formulations is dissolution. Various methods used to increase the solubility of poorly water soluble drygs are solid dispersions, inclusion complexes with β- cyclo dextrins, micronization, an eutectic mixtures and spray drying technique.[1]

Many suitable formulation approaches have been developed to increase the solubility of poorly water soluble drugs. Micronization technique is the most commonly used approach to improve drug solubility due to an increase in surface area, but the agglomeration tendency of micronized hydrophobic drugs makes it less effective to circumvent the solubility problem, especially when the drug is formulated into tablets or encapsulations. Solid dispersion has gained an active research interest for improving drug dissolution in the past few decades, however its commercial application is very limited and only a few products, such as Kaletra and Gris-PEG have become commercially available. The reason mainly lies on its poor stability during storage and lack of understanding of its solid state structure.[2]

The new developed technique by spire as liquisolid system improves the dissolution properties of water insoluble or poorly soluble drugs. The term liquisolid system (LS) is a powdered form of liquid drug formularted by converting liquid lipophilic drug or drug suspension or solution of water insoluble solid drug in suitable non volatile solvent systems, into dry looking, non- adherent, free flowing and readily compressible powdered mixtures by blending with selected carrier and coating materials.[3]

Various grades of cellulose, starch, lactose, etc. are used as the carriers, where as very fine silica powder is used as the coating material. The good flow and compressible properties of liquisolid may be attributed due to large surface area of silics and fine particle size of Avicel. Hence, liquisolid compacts containing water insoluble drugs expected to display enhanced dissolution characteristics and consequently improved oral bioavailability.

Solubility

Solubility is the ability for a given substance (solute) to dissolve in a solvent. It is measured in terms of the maximum amount of solute dissolved in a solvent at equilibrium. The resulting solution is called saturated solution.

Poorly Soluble Drugs

Poorly soluble drugs are which dissolves slowly in the Gastro Intestinal tract. These drugs comes under class 2

and class 4 drugs. These classes are according to Biopharmaceutics Classification System (BCS).

Liquisolid Compact Technique

Water insoluble and poorly soluble drugs which are converted to rapid release solid dosage forms. The term Liquisolid compact technique refers to process of immediate (or) sustained release tablets (or) capsules using the Liquisolid system combined with inclusion of appropriate excipients required for Tabletting (or) Encapsulating. Nearly 1/3rd of the drugs are water insoluble drugs. The dissolution rate is the rate limiting factor in drug absorption for class 2 and class 4 drugs according to Biopharmaceutics Classification System (BCS).[4]

More effective than various techniques which have been employed to enhance the dissolution profile and, in turn, the absorption efficiency and bioavailability of water insoluble drugs. Micronization, adsorption on the high surface area carriers, lyophilization, co-precipitation, micro-encapsulation, solubilization by surfactants, solid dispersions, solid solutions. Micronization is the most common method to increase the drug surface area. But this becomes less effective when they are formulated as tablets or encapsulations. The most promising method for promoting dissolution is the formation of liquisolid tablets. A liqusolid systems refers to formulations formed by conversion of liquid drugs, drug suspensions or drug solutions in non-volatile solvents, into dry, non-adherent, free flowing and compressible powder mixtures by blending the suspensions or solution with selected carriers and coating materials. These techniques are carefully selected on the bases of properties of drug, excipients and dosage forms.[5]

DRUG PROFILE[6]

Vilazodone

Description

Vilazodone is a novel compound with combined high affinity and selectivity for the 5-hydroxytryptamine (5-HT) transporter and 5-HT(1A) receptors Label,2. Vilazodone may also be associated with less sexual dysfunction and weight gain. Vilazodone was given FDA approval on January 21, 2011.

Structure

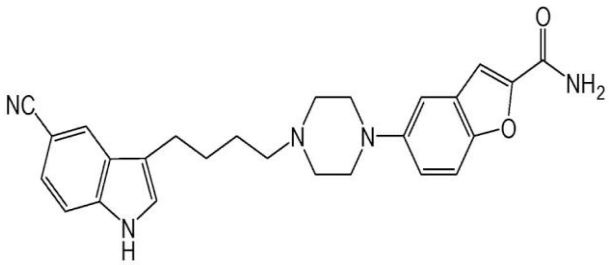

Fig No 1: Srtucture of Vilazodone.

Synonyms: Vilazodona, Vilazodone, Vilazodonum.

Categories: Agents that produce hypertension, Antidepressive Agents, Benzofurans, Central Nervous System Agents, Central Nervous System Depressants, Neurotransmitter Agents, Neurotransmitter Uptake Inhibitors, Piperazines, Psychoanaleptics, Psychotropic Drugs.

CAS number: 163521-12-8.

Weight

Average: 441.5249

Monoisotopic: 441.216475133

Chemical Formula: $C_{26}H_{27}N_5O_2$

IUPAC Name: 5-{4-[4-(5-cyano-1H-indol-3-yl)butyl]piperazin-1-yl}-1-benzofuran-2-carboxamide.

PHARMACOLOGY

Indication: Vilazodone is approved for treatment of major depressive disorder Label,1,2.

Pharmacodynamics.

Vilazodone increases serotonin levels in the brain by inhibiting the reuptake of serotonin while acting as a partial agonist on serotonin-1A receptors Label, 1, 3. Due to this activity vilazodone has sometimes been referred to as a selective partial agonist and reuptake inhibitor (SPARI).

Mechanism of action

Vilazodone selectively inhibits serotonin reuptake in the central nervous system as well as acting as a partial agonist of 5HT-1A receptors. The exact mechanism for how these effects translate to its antidepressant effects are not known Label, though there is an association between these effects and antidepressive activity.

Adverse Effects

Comprehensive structured data on known drug adverse effects with statistical prevalence. MedDRA and ICD10 ids are provided for adverse effect conditions and symptoms.

Absorption: Vilazodone bioavailability is 72% when taken with food.

Volume of distribution: Vilazodone volume of distribution is unknown but large.

Protein binding: 96-99%.

Metabolism: Vilazodone is mainly metabolized by cytochrome P450 (CYP) 3A4 and also to a minor extent by CYP2C19 and CYP 2D6Label, 1. Although the metabolic pathway for vilazodone has not been fully studied, a proposed mechanism for metabolism in rats was published in 2017.

Route of elimination: 1% of the dose is recovered unchanged in the urine and 2% of the dose is recovered unchanged in the faeces.

Half life: 25 hours. Other studies show a half life of 24±5.2h with a single 40mg dose and 28.9±3.2 h with repeated doses.

MATERIALS

Vilazodone was purchased from Spectrum Labs, Hyderabad. Microcrystalline Cellulose, Aerosil,

Propylene Glycol, Tween 80, Sodium Starch Glycolate, Croscarmellose Sodium, Magnesium Stearate, Talc were purchased from B.M.R Chemicals, Hyderabad.

METHODOLOGY

Preformulation studies[7-12]

Solubility studies of pure drug

Solubility study was conducted to determine the effect of different buffers on the drug. An excess amount of the drug was dispersed in 5 ml of different solvents in glass stoppered tubes, respectively. All flasks were closed with stopper and covered with cellophane membrane to avoid solvent loss for 24 hrs in water bath shaker at 37ºC. After reaching equilibrium, the samples were centrifuged (Hermle Z 200 A, Germany) at 3000 rpm for 5 min. Supernatant was filtered through 0.45 µm membrane filter. One ml sample of saturated solution was diluted with suitable solvents and then analyzed by UV spectrophotometer at 240 nm (PG Instruments, T60).

IR Spectra

IR spectra of pure drug Vilazodone, excipients 1:1 compacts were done in potassium bromide pellets at moderate scanning speed between 400 to 4000 cm^{-1}.

Determination of UV spectrum of vilazodone:

10mg of Vilazodone was dissolved in 3ml of methanol and volume was made upto 10ml with buffer. So, as to get a stock solution of 1000 µg/ml concentration. From this 1ml solution was withdrawn and diluted to 10ml to get a concentration of 100µg/ml (SS-II). From this stock solution pipette out 1 ml of the solution and makeup the volume to 10ml using buffer to get the concentration of 10µg/ml concentration, this solution was scanned under UV Spectroscopy using 200-400nm.

Preparation of Standard Calibration Curve for Vilazodone using 6.8pH buffer 10 mg of pure drug was accurately weight and transferred into the 10 ml volumetric flask. The volume was made up using 6.8pH buffer to get a concentration of 1000µg/ml. From this solution, 1 ml was withdrawn into 10 ml volumetric flask and it was diluted to 10 ml with distilled water to get a concentration of 100µg/ml. From this 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml, 1.2 ml were pipetted out into a 10 ml volumetric flask and diluted to 10ml using 6.8pH buffer to get concentrations of 2µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml, 10 µg/ml, and 12 µg/ml respectively. Absorbance of this solution was measured at 240nm using UV Spectrophotometer against blank.

PREPARATION OF LIQUID-SOLID COMPACTS[13-21]

The general method of preparation of liquid-solid:

1. A Drug was at first scattered in the nonvolatile solvent system (PEG-400) named as liquid vehicles with the diverse drug: vehicle proportion.
2. At that point a blend of a bearer or diverse polymers and excipients were added to the above liquid by consistent blending in a mortar. These measure of the carrier and excipients are sufficient to keep up adequate flow and compression properties.
3. To the above binary blend disintegrant and other residual added substances are added by their application and blended for a time of 10 to 20 min in a mortar.
4. The last blend was compacted utilizing the tableting machine to accomplish tablet hardness.
5. Portray the final liqui-solid granules for solvency, dissolution, flowability, compressibility.

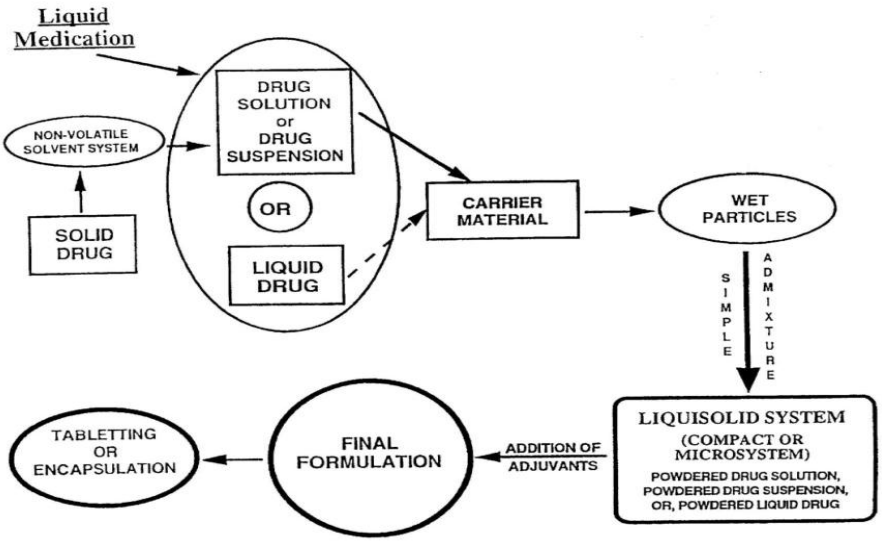

Fig. 2: Depiction of liqui-solid compacts.

Calculation of load factor[15-19]

Application of the mathematical model for designing the liqui-solid systems In this study, PEG 400, Avicel PH 102, Microcrystalline Cellulose (MCC), and Aerosil 200 were used as a liquid vehicle, carrier, coating respectively. The concentration of the drug in a liquid

vehicle was varied and the carrier: coating ratio was kept constant in all formulations (R=1:1 & 1:3). In order to address the flowability and compressibility of liqui-solid compacts, simultaneously, the ‘‘new formulation mathematical model of liqui solid systems" was employed as follows to calculate the appropriate quantities of excipients required for producing liqui-solid systems of acceptable flowability and compressibility. This mathematical model depended on new crucial powders properties (constants for each powder material with the liquid vehicle) called the flowable fluid retention potential (Φ-esteem) and compressible liquid retention potential (ψ-number) of the constituent powders (transporter and covering materials). As indicated by the new theories, the transporter and coating powder materials can hold just certain measures of liquid while keeping up worthy stream and pressure properties. Contingent upon the excipients proportion (R) or the carrier: coating proportion of the powder system utilized, where

$$R=Q/q... (1)$$

As R represents the ratio between the weights of a carrier (Q) and coating (q) materials present in the formulation. An acceptably flowing and compressible liqui-solid system can be prepared only if a maximum liquid on the carrier material is not exceeded; such a characteristic amount of liquid is termed the liquid load factor (Lf) and defined as the ratio of the weight of liquid medication (W) over the weight of the carrier powder (Q) in the system, which should be possessed by an acceptably flowing and compressible liqui-solid system. i.e.:

$$L_f = W/Q... (2)$$

***Spireas et al*., 2000.** Used the Flowable liquid retention potentials (Φ -values) of powder excipients used to calculate the required ingredient quantities, hence, the powder excipients ratios R and liquid load factors L*f* of the formulations are related as follows:

$$L_f = \Phi + \Phi (1/R)... (3)$$

Where Φ and Φ are flowable liquid retention potential of carrier and coating material separately. So, keeping in mind the end goal to ascertain the required weights of the excipients utilized, first, from Eq. (3), Φ and Φ are constants, in this way, as indicated by the proportion of the carrier/coat materials (R), L*f* was ascertained from the straight relationship of L*f* versus 1/R. next, as per the utilized liquid vehicle concentration, different weights of the liquid medication solution (W) will be utilized. Along these lines, by knowing both L*f* and W, the fitting amounts of a transporter (Qo) and covering (qo) powder materials required to change over a given measure of fluid drug (W) into an acceptably streaming and compressible liqui- solid system could be ascertained from condition (1) and (2).

Calculation of Liquid load factor (L_f), Carrier (Q) and Coating (q) materials for the formulations: [Φ and ψ standard values as in Table no. 1.1].

Polyethylene Glycol 400: Weight of 0.4ml, W= Wt. of 0.4 ml of PEG 400= 0.353g= 353mg.

For Ratio: 2 i.e., R:2

L_f = ψ + ψ (1/R)
= 0.242 + 0.653 (1/2)
= 0.568

Q0 = W/L_f
= 353/0.568
= 621.47

R = Q/q

=> q = Q/R

Carrier Material (Q) MCC = 216

Coating Material (q) Aerosil = 216/2 = 108

L_f = Φ + Φ (1/R)
= 0.005 + 3.26(1/2)
= 1.635

Q0 = W/L_f
= 353/1.635
= 215.90

Flow properties

The flowability of a powder is of critical importance in the production of pharmaceutical dosage forms in order to get a uniform feed as well as the reproducible filling of tablet dies, otherwise, high dose variations will occur. In order to ensure the flow properties of the liqui-`solid systems that will be selected to be compressed into tablets and further evaluated, an angle of repose measurements, Carr's index, and Hausner's ratios were adopted.

Angle of repose

The angle of repose of powder blend was determined by the funnel method. The accurate weight powder blend was taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose (θ) was calculated using the following equation.

$$\tan^{-1} = h/r$$

Where h and r are the height and radius of the powder cone.

Bulk density

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 2 gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced into 10 ml measuring cylinder. After that, the initial volume was noted and the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TDB were calculated using the following equations.

LBD = Weight of the powder blend/Untapped Volume of the packing

TBD = Weight of the powder blend/Tapped Volume of the packing.

Compressibility Index

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The formula for Carr's Index is as below:

Carr's Index (%) = [(TBD-LBD) x100]/TBD

Hausner's Ratio

Hausner's ratio was calculated from the equation:
Hausner's ratio = Tapped density/Bulk density.

Table 1: Formulation of Vilazodone Hydrochloride Based Liquisolid Tablets (R:2).

Ingredients	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Vilazodone	10	10	10	10	10	10	10	10	10
MCC	230	228	221	220	216	228	221	220	216
Aerosil	123	118	118	112	108	118	118	112	108
SSG	--	7	14	21	29	--	--	--	--
CCS	--	--	--	--	--	7	14	21	29
Mg.sterate	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	370	370	370	370	370	370	370	370	370

POST COMPRESSION PARAMETERS[22-26]

Weight variation Test

The test was executed according to USP by measuring 20 tablets separately on electric balance, computing the average weight, and contrasting the individual tablet weight with the average. Results are appeared in Table:

Friability Test

The test was performed using Roche friability. The device was rotated at 25 rpm for 100 revolutions. Friability was calculated by using following formula.

$$\%F = 100(1-W_0/W)$$

Whereas, W = Final weight of tablets

W_0 = Original weight of tablets

Hardness

Hardness demonstrates the capacity of a tablet to withstand mechanical stuns while handling. The hardness of the tablets was resolved utilizing Monsanto hardness analyzer. It is communicated in kg/cm^2. Three tablets were arbitrarily picked and hardness of the tablets was resolved.

Drug content estimation

A precisely measure of each preparation was dissolved in little volume of methanol and further diluted in phosphate buffer with pH of 6.8 phosphate buffer. The content of Vilazodone was resolved spectrophotometrically at 240nm utilizing the UV- visible spectrophotometer.

***In-vitro* Drug Release Study**

The dissolution study was carried out using USP II Apparatus (LAB INDIA DS8000). The dissolution medium was 900 ml of pH of 6.8 phosphate buffer kept at 37 ± 5ºC. Vilazodone Tablet were kept in the paddle of dissolution apparatus rotating at 50 RPM. samples of 5ml were withdrawn at indicated time intervals and analyzed spectrophotometrically at 240 nm utilizing Shimadzu 1700 UV- visible spectrophotometer, the samples withdrawn were supplanted by the freshly prepared buffer solution. Every preparation was tried in triplicate and the mean values were computed.

RELEASE KINETICS[24-26]

In the present study, data of the *in-vitro* release were fitted to different equations and kinetic models to explain the release kinetics of vilazodone tablets. The kinetic models used were Zero order equation and First order.

Zero-order model

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation,

$$Qt = Q0 + K0t$$

Where Qt is the amount of drug dissolved in time t, Q0 is the initial amount of drug in the solution (most times, Q0 = 0) and K0 is the zero order release constant expressed in units of concentration/time. To study the release kinetics, data obtained from *in-vitro* drug release studies were plotted as cumulative amount of drug released versus time.

First Order Model

The first order equation describes the release from systems where the dissolution rate is dependent upon the concentration of the dissolving species.

Release behavior generally follows the following first order equation:

$$\text{Log } C = \text{Log } C_o - kt/2.303$$

Where C is the amount of drug dissolved at time t,
C_o is the amount of drug dissolved at t=0 and
k is the first order rate constant.
A graph of log cumulative of % drug remaining vs time yields a straight line.

The pharmaceutical dosage forms following this dissolution profile, such as those containing water-

soluble drugs in porous matrices, release the drugs in a way that is proportional to the amount of drug remaining in its interior, in such way, that the amount of drug released by unit of time diminishes.

RESULTS AND DISCUSSION

Preformulation studies

Saturation Solubility

Saturation solubility was carried out at 25^{0}C using 0.1N HCL, 6.8 phosphate buffer, Propylene glycol, Polyethylene glycol 400 and Tween 80.

Table 2: Solubility data.

Media	Solubility(mg/ml)
0.1N HCl	0.365
pH 6.8 phosphate buffer	0.892
pH 7.4 phosphate buffer	0.715
PG	1.635
PEG 400	2.426
Tween 80	1.056

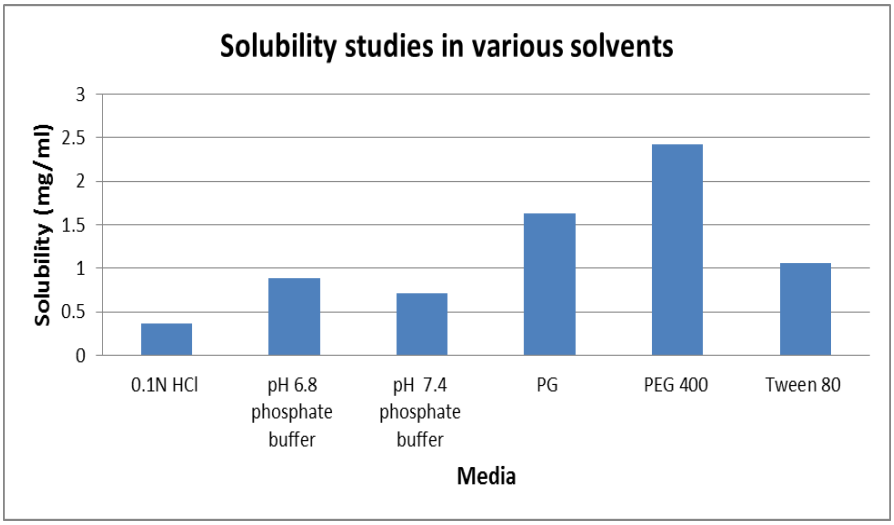

Fig No 3: Solubility Data.

Discussion: From the above conducted solubility studies in various buffers observed say that pH 6.8 phosphate buffer has more solubility when compared to other buffer solutions. So pH 6.8 buffer is used as dissolution medium.

Determination of absorption maximum (λ_{max})

Determination of Viladzodone λ_{max} was done in pH 6.8 buffer medium.

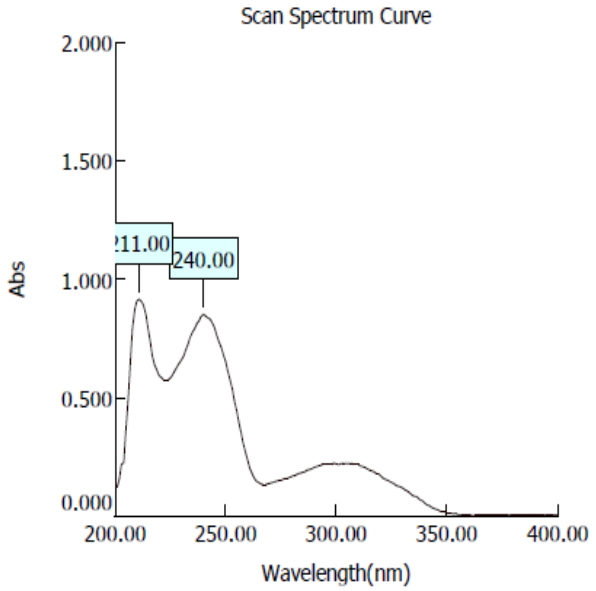

Fig No 4: UV Spectrum of Vilazodone.

Calibration curve of Vilazodone in 6.8pH buffer

Table No 3: Standard graph of Vilazodone in pH 6.8 (λ_{max} 240 nm).

Concentration (µg/ml)	Absorbance
0	0
2	0.153
4	0.348
6	0.502
8	0.672
10	0.819
12	0.986

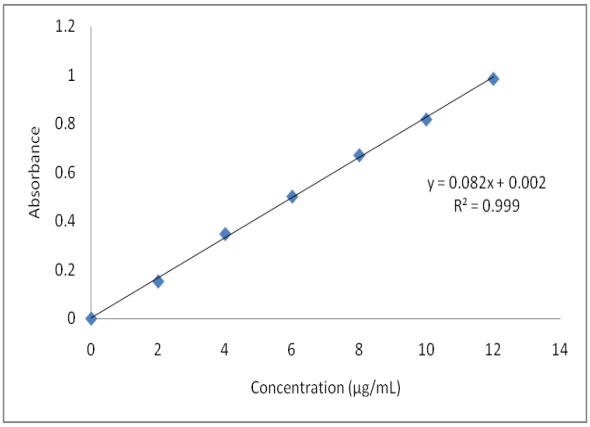

Fig No 5: Standard calibration curve of Vilazodone in pH 6.8 buffer.

DISCUSSION

The linearity was found to be in the range of 2-12 µg/ml in pH 6.8 buffer. The regression value was 0.999 indicating the method obeys Beer-lamberts' law.

Drug excipient compatibility

Drug and excipient compatibility was confirmed by comparing spectra of FT-IR analysis of pure drug with that of various excipients used in the formulation.

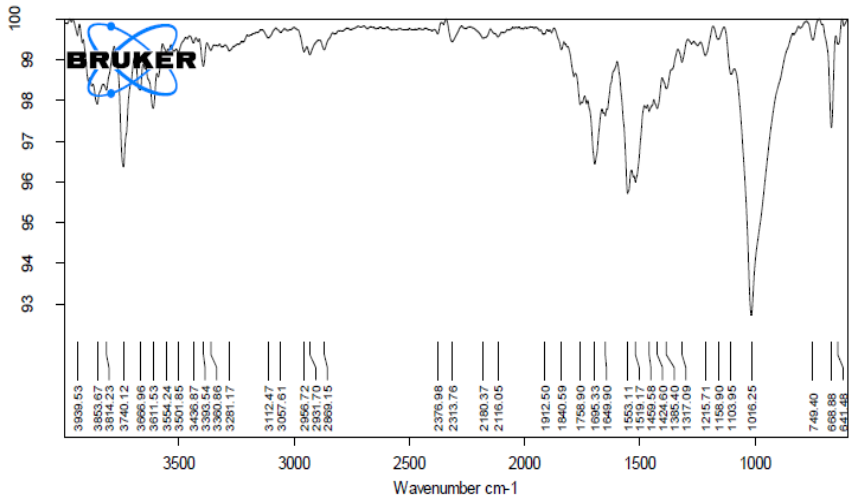

Fig No 6: IR spectrum of Vilazodone.

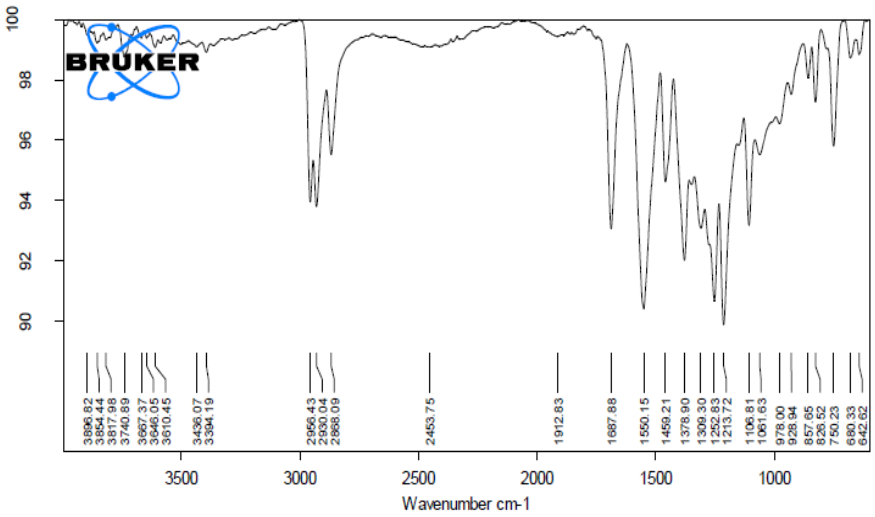

Figure No 7: IR spectrum of Vilazodone Optimised Formulation.

Discussion: Form the drug excipient compatibility studies we observe that there are no interactions between the pure drug (Vilazodone) and optimized formulation (Vilazodone + excipients) which indicates there are no physical changes.

Precompression parameters of all the Vilazodone liqui-solid comapcts Formulations:

Table No 4: Flow Properties of Tablet Blend.

Formulation code	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	28.96	0.468	0.538	13.01	1.15
F2	29.45	0.478	0.542	11.81	1.13
F3	28.05	0.469	0.539	12.99	1.15
F4	27.06	0.482	0.569	15.29	1.18
F5	25.19	0.498	0.554	10.11	1.11
F6	29.86	0.459	0.562	18.33	1.22
F7	30.25	0.462	0.559	17.35	1.21
F8	28.46	0.481	0.574	16.20	1.19
F9	29.32	0.459	0.529	13.23	1.15

Discussion

A flow property plays an important role in pharmaceuticals especially in tablet formulation because improper flow may cause more weight variation. Values of Carr's Index (Compressibility) below 15% usually give rise to good flow properties but readings above 25% indicate poor flow properties. It was found that the compressibility values of the powders were below 25% and hence they exhibit good flow characteristics.

Values of angle of repose are rarely 20^{o} and values up to 40^{o} indicate reasonable flow properties. Above 50^{o} however the powder flows only with great difficulties. Dynamic angle of repose measurements can be replicated with relative standard deviations of approximately 2%.

They are particularly sensitive to changes in particle size distribution and to the moisture content, and they provide a rapid means of monitoring significant batch to batch differences in these respects.

The angles of repose of the powders were in the range of 25^{0} to 29^{0}, which indicate a good flow property of the powders. Here the angle of repose was found to be below 40^{o} this shows that the reasonable flow property of powders.

Post compression parameters

Table No 5: Evaluation studies.

Formulation code	Weight variation (%)	Hardness (kg/cm^2)	Fraibility (%)	Thickness (mm)	% Drug content
F1	3.26	3.56 ± 0.02	0.22 ± 0.09	3.96 ± 0.02	96.15±0.16
F2	2.59	3.42 ± 0.09	0.15 ± 0.22	3.85 ± 0.01	98.06±0.52
F3	3.18	3.29 ± 0.06	0.49 ± 0.61	4.02 ± 0.06	95.35±0.97
F4	4.16	4.02 ± 0.12	0.82 ± 0.16	4.01 ± 0.03	96.48±0.56
F5	2.68	3.98 ± 0.43	0.65 ± 0.45	3.98 ± 0.06	99.89±0.29
F6	2.69	3.78 ± 0.02	0.32 ± 0.02	3.99 ± 0.09	99.45±0.36
F7	3.49	4.21 ± 0.14	0.54 ± 0.24	4.08 ± 0.04	98.16±0.21
F8	2.98	4.05 ± 0.09	0.41 ± 0.18	3.94 ± 0.08	97.42±0.85
F9	2.35	3.68 ± 0.05	0.78 ± 0.06	3.99 ± 0.05	98.46±0.46

Discussion: The appearance of vilazodone tablets was smooth and uniform on physical examination. The hardness of prepared tablets of viladozone was found to be 3.29 to 4.21 ± 0.52 kg/cm^2.

The thickness and weight variation were found to be uniform as indicated by the low values of standard deviation. The thickness of the prepared tablets were found to be in the range of 3.85 to 4.08nm respectively. Friability values less than 1% indicate good mechanical strength to withstand the rigors of handling and transportations.

The drug content of vilazodone tablets was quite uniform. The average drug content of the was found to be within the range of 95.35 to 99.89% and the low values of standard deviation and coefficient of variation (< 2) indicate uniform distribution of the drug within the prepared vilazodone tablets.

***In vitro* Dissolution studies**

Table No 6: *In-vitro* drug release data of formulation F1 to F9.

Time (mins)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	16.35±0.42	26.18±0.15	32.49±0.46	40.52±0.15	46.18±0.42	40.85±0.16	46.21±0.15	52.16±0.26	59.32±0.36
10	24.05±0.59	36.29±0.24	39.52±0.21	49.19±0.23	50.86±0.36	49.36±0.24	53.19±0.20	68.36±0.41	72.15±0.15
15	35.16±0.63	43.04±0.63	46.02±0.85	56.18±0.42	59.36±0.12	56.75±0.36	62.04±0.63	75.46±0.52	79.63±0.02
20	39.56±0.12	49.78±0.62	50.36±0.36	63.25±0.42	66.48±0.82	63.85±0.15	69.45±0.25	80.15±0.63	82.63±0.36
30	46.05±0.01	56.31±0.94	59.78±0.20	69.85±0.18	70.25±0.31	69.23±0.25	70.36±0.51	87.46±0.15	90.24±0.52
40	56.19±0.04	62.49±0.25	68.41±0.63	76.49±0.56	79.61±0.02	76.35±0.85	79.32±0.63	92.53±0.02	97.32±0.15
50	60.58±0.25	70.06±0.36	79.34±0.79	83.46±0.02	87.16±0.63	79.32±0.96	86.32±0.42	98.46±0.63	
60	65.28±0.63	76.15±0.21	86.49±0.01	90.35±0.16	95.36±0.10	82.49±0.31	96.35±0.15		

Discussion

In vitro release studies were carried out in USP dissolution test apparatus-II employing paddle stirrer at 50 rpm and 900 ml of pH 6.8 buffer as dissolution medium. The *in vitro* dissolution data of all the designed formulations are shown and dissolution profiles depicted in figures.

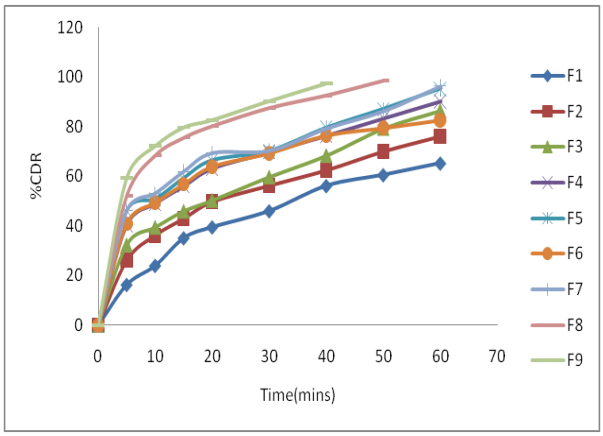

Fig No 8: Dissolution parameters for the formulations F1-F9.

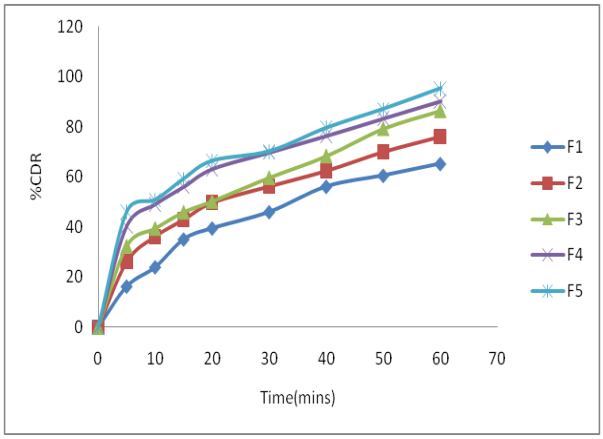

Fig No 9: Dissolution parameters for the formulations F1-F5.

Discussion

From the above *in vitro* drug release studies it was observed that the formulations F1 formulated using PEG-400 as a non volatile solvent by taking R=2, without super disintegrant shows 65.28% drug release at the end of 60 minutes, whereas F2 to F5 formulations were prepared by using SSG as a super disintegrant in different ratios like 2-8% of the total tablet weight. F5 formualtion shows maximum drug release at the end of 60 minutes.

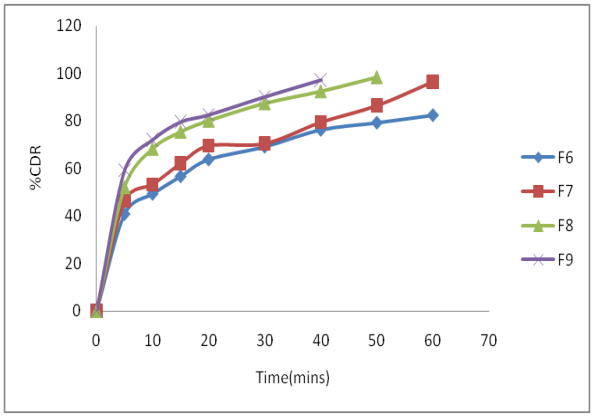

Fig No 10: Dissolution parameters for the formulations F6-F9.

Discussion

F6 to F9 formulations were prepared by using CCS as a super disintegrant in different ratios like 2-8% of the total tablet weight, among them F9 formulation containing 8% CCS shows maximum drug release at 40 minutes.

Among all the formulations (F1 to F9), F9 formulation containing 8% CCS shows maximum drug release within short period of time i.e., 40 minutes. Increase in the concentration of superdisintegrants shows decrease in drug release time. Therefore F9 formulation shows improved dissolution studies so it is selected as optimized formulation.

So, the drug release kinetics were performed for F9 formulation.

Drug release kinetics studies: Best formulation F9

In vitro drug release data of all the Liquisolid compacts formulations of Vilazodone was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetics and according to equations of drug release. The results of linear regression analysis including regression coefficients from the above data it is evident that the optimized formulation (F9) follows zero-order release kinetics.

Zero Order Release Kinetics

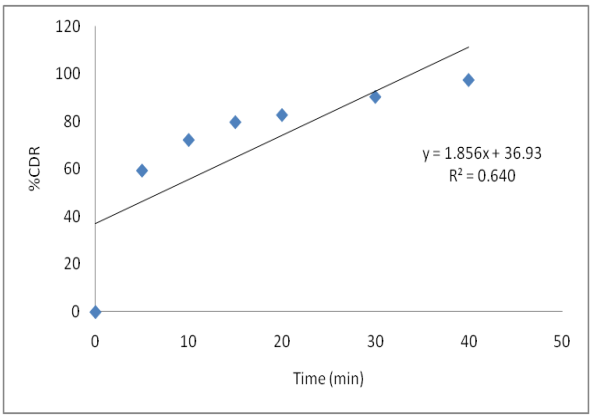

Fig No 11: Zero order release profile of formulation F9.

First Order Release Kinetics

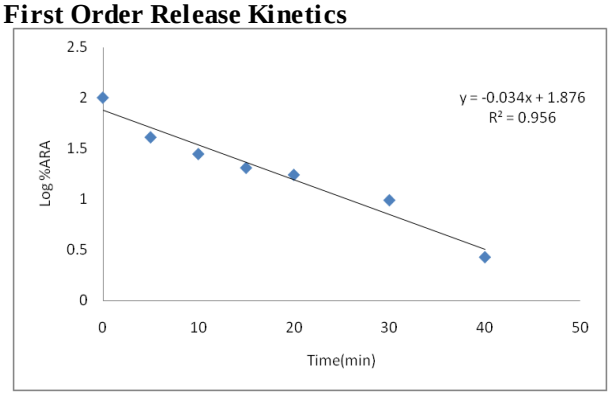

Fig No 12: First order release profile of formulation F9.

Table No 7: Kinetic data of the formulation F9.

Orde of kinetics	Zero Order	First order
REGRESSION (R)	0.640	0.956

DISCUSSION

The drug release from the Liqui-solid compacts was explained by using mathematical model equations such as zero order, first order, and equation methods. Based on the regression values it was concluded that the optimized formulation F9 follows First order kinetics.

CONCLUSION

From the present study, the following conclusions can be drawn:

- Liquisolid compacts of Vilazodone were prepared using PEG 400 by taking R:2 ratio.
- All the prepared formulations were found to be having drug content within acceptable limits in the range of 95.35 to 99.89% respectively.
- As the super disintegrant concentration increases, the drug release time decreases.
- IR spectroscopic studies indicated that there are no drug-excepient interactions.
- When compared to other all the formulations F9 is the best formulation which showed 97.32% of drug released respectively with in 40 mins containg CCS.
- Optimized formulations of Liquisolid compacts displayed First order release kinetics.

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