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FORMULATION AND EVALUATION OF SINTERED MATRIX TABLET OF VENLAFAXINE HYDROCHLORIDE

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ABTRACT

Venlafaxine HCl has short half-life 4-5hrs, therefore it need to be frequently administered during therapy which gives patient incompliance A Sintered matrix Tablet reduce Dosing Frequency and Improve the patient Compliance. Therefore, in this Study attempt has been done to design and evaluate the effect of processing method, sintering condition and subsequent drug release of Venlafaxine HCl Sintered Matrix Tablet. Were Prepared using combination of Eudragit RL100(10-50%w/w)by direct compression Method .The Prepared Tablet were using 75^0 c temperatures Thermal Treatment(Hot air Oven) for time period The Sintered Tablet Chartered by Hardness friability and in vitro dissolution tests. It was evident that different Processing method, time sintering for identical formulation significantly impact the release profile of drug. From prepared matrices, it was noticed that the Venlafaxine HCl release rate was inversely related to time of Sintering.

KEYWORDS: Venlafaxine HCl Unsintered matrix tablet, in vitro drug Release, diffusion, Sustained release sintered matrix tablet.

INTRODUCTION

The oral rout of drug delivery is considered the most convenient and it widely used for the drug product development purposes. The oral route is the one widely used for administration of drugs. The most popular oral formulations available in the market are tablets and preferred by physicians and patients alike.[1-3]

In recent years, considerable attention has been focused on the development of new delivery systems.[4]

Sustained release (SR) technology has rapidly emerged over the past three decades as a new interdisciplinary science that offers novel approaches to the delivery of bioactive agents into systemic circulation at a predetermined rate[4]. Sustained release formulations have been demonstrated to improve therapeutic efficiency by maintenance of a steady drug plasma concentration. Sustained release dosage forms are formulated in such a manner as to make the drug available over a long period following its administration. A typical sustained release system with reduced fluctuations via slow release over an extended period of time is designed to provide constant or nearly constant drug levels in plasma. In practically, an oral sustained release should allow a reduction in dosing frequency as compared to conventional dosage form when the same drug is present.[1,2]

To prepare sustained release formulation matrix system is widely used. It is the release system in which drug is dissolved or dispersed in rate controlling polymer, which prolongs and controls the release of the drug. When developing an oral controlled release system Matrix type drug delivery systems are an interesting and promising option. In fact a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. release rate controlling polymer (hydrophilic and hydrophobic) polymers.[1-3]

Sintering is defined as the bonding of adjacent particle surfaces in a mass of powder, or in a compact, by the application of heat. Conventional sintering involves the heating of a compact at a temperature below the melting point of the solid constituents in a controlled environment under atmospheric pressure. The changes in the hardness and disintegration time of tablets stored at elevated temperatures were described as a result of sintering. The sintering process has been used for the fabrication of sustained release matrix tablets for the stabilization and retardation of the drug release.[13-15]

The aim of the present investigation is, therefore, to Eudragit RL100 and evaluate it for sustained release carrier, using Venlafaxine HCL is a Antidepressant Drug with activity. It readily absorbed from the gastrointestinal track with oral bioavailability of about

45% and a plasma elimination half-life ranging from 4-5 hr. administration of Venlafaxine HCL in sustained release dosage would be more desirable for therapeutic concentration. Hence, there is need to reduce the dosing frequency which can be done with use of sustained release dosage form.

MATERIALS AND METHODS

Materials

Venlafaxine HCl was obtained as a gift sample from Wochartt Pharmaceutical Ltd., Aurangabad. Eudragit RL100were obtained as a gift sample Research Lab, Fine Chem Industry, Mumbai, All the reagents were used are laboratory grade.

Methods for preparation Tablet

Direct compression[17-18]

The materials required were first sifted through stainless steel sieve no. 40# mesh. The powders were then dry mixed by spatulation. Tablets were prepared by direct compression method with 8mm stainless steel punch using rotary press (Karnavati Minitab, India). Compression force for all the tablets was adjusted to get tablets of hardness 4 kg/cm^2. Hardness was measured by Monsanto type hardness tester (Cadmach, Ahmadabad, India). Weight of were adjusted to 300mg of all compress tablets.

Sintering Method

Thermal Treatment[18]

Thermal sintering is a method of heating a polymer in a sintering furnace below its melting point (solid state sintering) until its particles adhere to each other. In this process, polymer particles will undergo fusion or formation of welded bonds between each particle. The thermal sintering method involves the exposure of the formulation to a polymer glass transition temperature in which the polymer forming the matrix slowly softens and welded bonds are formed. The drug particles will be entrapped in the formed matrix, resulting in the controlled release of the active ingredient. However, this method may be applied to only those drugs that are resistant to the temperature of exposure and this may be the limiting factor for many drugs that get degraded at elevated temperatures. Thermal treatment the prepared tablet were placed on aluminum foil and subjected to heating at temperature75^0 C for 1,4, 8,hrs in hot air oven.

A) Drug identification and drug-excipients compatibility study[16-26]

1) Melting Point

Melting point of were Venlafaxine HCl determined by taking a small amount of sample in a capillary tube closed at one end and placed in melting point apparatus(Analab Scientific).The capillary containing drug was dipped in liquid paraffin inside the melting point apparatus and the melting point was noted in triplicate.

2) UV Spectrum and Calibration curve of Venlafaxine HCl[17]

The UV spectrum of Venlafaxine HCl was obtained using UV Shimadzu V1800 Accurately weighed 100 mg of the drug was dissolved in sufficient quantity of Distilled water and volume made up to 100 ml. The stock solution was diluted to obtain a concentration of 100 µg/ml. 1 ml of aliquot was withdrawn and volume was made up to 10 ml using respective solvent to obtain the concentration of 10 µg/ml. The resultant solution was scanned from 400 to 200 nm and the spectrum was recorded to obtain the value of maximum Wavelength in respective solvents. To gives 5-25ug/ml.

3) Fourier Transform Infra-Red Spectra (FTIR)[18]

The drug sample was placed in FTIR cuvette. The drug sample was scanned over the range of 4000-400 cm-1on an FTIR (Bruker). The FTIR spectra of drug sample were recorded. Similarly, the procedure repeated by dispersing a sample {drug, drug and polymer (1:1) as well as mixture of drug and polymers (1:1:1:1)} in FTIR cuvette

4) Differential scanning colorimetry[18]

DSC was used to study the physical and chemical interaction between drug and excipient used. DSC thermo gram of pure drug and drug excipient mixture were recorded by Differential scanning calorimeter (DSC-60) under nitrogen flow (50ml/min) at scanning rate 10^{o}C/min from 100^{o}C to 400^{o}C.

5) Compatibility Study[25}

Compatibility study was carried out by using Fourier transform infrared spectrophotometer (Brukar). FTIR study was carried on pure drugs. Physical mixture of drugs and polymers were prepared. The infrared absorption spectrums of and physical mixture of Venlafaxine HCl drugs and polymers was recorded using the wave number 4000 to 400 cm^{-1}.

B) Formulation And Evalution[18-25]

factors 3 levels full factorial design was employed to design sustained release matrix tablet of Venlafaxine HCl This design was suitable for exploring quadratic response surfaces and constructing second order polynomial models. The two independent formulation variables analyzed during the study were total polymer concentration in the sustained release matrix tablet that is Eudragit RL 100 (X1) and Time (X2). The selected factors with the actual and coded levels as per design are represented in table (7.3). The higher, lower and intermediate of each factor are coded as +1, -1 and 0, respectively. The dependent variable investigated was percentage drug release (Y1).

Factor levels

Independent variables

X1 –Eudragit RL100 Polymer
X2 – Sintering Time

Dependent variables
Y1 – In-vitro drug release (%)

Table 1: Formulation of Venlafaxine HCL Unsintered Matrix Tablet.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Venlafaxin	75	75	75	75	75	75	75	75	75
e HCL Eudragit RL-100	30	90	150	30	90	150	30	90	150
Mg. Stearate	1.5	1.5	1,5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
MCC	192	132	72	192	132	72	192	132	72
Total	300	300	300	300	300	300	300	300	300

(All quantities are in mg).

C) Evaluation of Venlafaxine HCl Unsintered and Sintered Matrix Tablet (Before and after sintering):[18,25]

1. Tablet Characteristics
The compressed matrix tablets were evaluated for thickness, weight variation, hardness, friability and drug content.

2. Thickness: The thicknesses of tablet were determined using micrometer screw gauge. Three tablets from each batch of formulation were used and mean thickness value and Standard Deviation (SD) calculated for each formulation.

3. Hardness: For each formulation, the hardness of three tablets was measured using the Monsanto hardness tester (Coslab) and mean value and SD calculated.

4. Friability: For each formulation the friability of 20 tablets was determined using Roche Friabilator (Roche, Model 902).

5. Drug content: Three tablets were selected from each formulation. Each tablet finely powdered and taken in 100 ml volumetric flask 50 ml of phosphate buffer (pH 6.8) was added, sonicated for 30 min, made up to 100 ml with phosphate buffer (pH 6.8), and filtered. After suitable dilution with phosphate buffer (pH 6.8), the concentration was determined at 250 nm by using UV spectrophotometer.

6. Dissolution Study[18-20]
In vitro drug release studies of the prepared matrix tablets were conducted for a period of 12 hours by using an USP Type II (Paddle) Dissolution apparatus (Electrolab TDT 08L, India) at 37± 0.5°C. The agitation speed was 50 rpm. The dissolution study was carried out in 900 ml0.1 N hydrochloric acid at 37±0.5 ºC for first 2 hours and then in 900 ml of phosphate buffer (pH 6.8) up to 10hours. 5 ml of the sample was withdrawn at regular intervals and the same volume of fresh dissolution medium was replaced to maintain the volume constant. The samples withdrawn were filtered through a whatmam filter no.1 and the drug content in each sample was analysed with UV spectrophotometer. The amount of drug present in the samples were calculated with the help of calibration curve constructed from reference standard

7. Differential scanning colorimetry[24-25]
DSC was used to study the tablet should be used in the sintered matrix tablet of Optimized Batch physical and chemical interaction between drug and excipient used. DSC thermo gram of pure drug and drug excipient mixture were recorded by Differential scanning calorimeter (DSC-60) under nitrogen flow (50ml/min) at scanning rate 10°C/min from 100°C to 400°C

Data Analysis[26] Various mathematical models like; Zero-order model, First-order model, Higuchi (Matrix) model, Hixson and Crowell cube-root equation and Korsmeyer-Peppas Model were evaluated with respect to the dissolution profiles of the formulations. PCP disso software was used to fit models to dissolution profiles.In order to investigate the mode of release from the formulation the release data were analyzed with the PCB Disso Software.

E) Stability Study[25-26]
The optimized formulation was wrapped in aluminium foil and stored at 40°C±2°C and 75% RH ± 5% for Three month. Tablet was analyzed for the hardness, drug content, % CDR.

RESULT AND DISCUSSION

1) Melting Point: The melting point of Venlafaxine HCl was determined on Digital melting point apparatus was found to be 216º-218ºC which is in good agreement with reported melting point

2) UV Spectrum and Calibration curve of Venlafaxine HCl : The UV spectrum of Venlafaxine HCl solution (10µg/ml) exhibited wavelength of absorbance maximum at 224 nm which complies with the reported and calibration curve shows r2=0.9984 fig.1,2

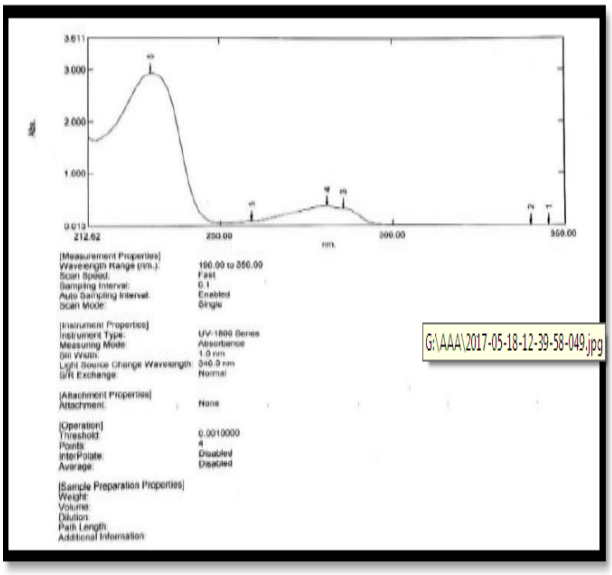

Fig. 1: UV-Visible spectrum of Venlafaxine HCl in Distilled Water.

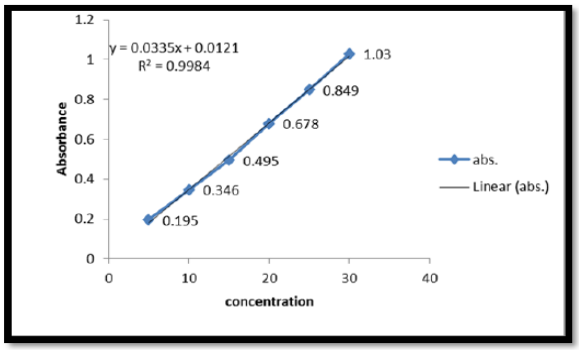

Fig. 2: Calibration curve of Venlafaxine HCl in Distilled Water at 224nm.

3) Fourier Transform Infra-Red Spectrophotometer (FTIR)

In all physical mixtures of drug and polymer, there was neither masking of single characteristic peak nor existence of additional peak in the spectra. (Fig. 3 and Table 2) so we can conclude that drug and polymers are compatible with each

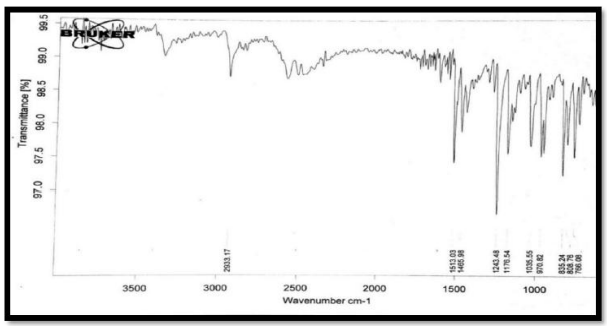

Fig. 3: FT-IR spectrum of Venlafaxine HCl.

Table 2: Major Peaks observed in IR spectrum of Venlafaxine HCl.

Sr. No.	Functional Group	Standard frequency (cm-1)	Observed IR frequency (cm-1)
1	C-O-C	1260-1220	1243
2	Aliphatic C-H	3000-2850	2933
3	Aromatic	3100-3045	3045
4	O-H Stretch	3500-3200	3300

4) Differential scanning calorimeter (DSC)

The endothermic peak at 210.7ºC of blend can be attributed as that of Venlafaxine HCl. (214.3 ºC) Thus the thermogram showed thatthe Venlafaxine HCl, physical mixture of Optimized batch. Shown that fig.

No. 4, 5 Table 3:

Identification Test	Observed Result	Observed Result Optimized Batch	Reported Standards
DSC Analysis	Endothermic peak at 214.3^{0}C	Endothermic peak at 210.7	Endothermic peak at 217^{0}C

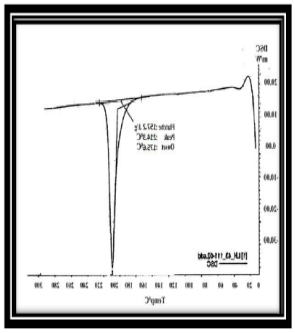

Fig. 4: pure drug

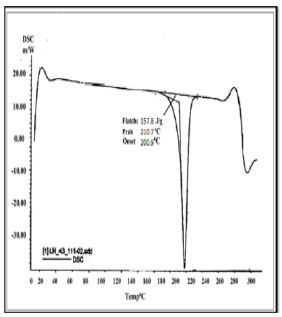

Fig. 5: optimized batch 9.

5) Compatibility Study

A) Venlafaxine HCl and Eudragit RL100:

Infra-red spectra of physical mixture showed matching peaks with the drug spectra. The characteristic peaks of drug were also present in the spectra of physical mixture. A spectrum of physical mixture is shown in Figure 6. Interpretation of Infra-red Spectra of Venlafaxine HCl and Eudragit RL100 is shown in Table No.4/

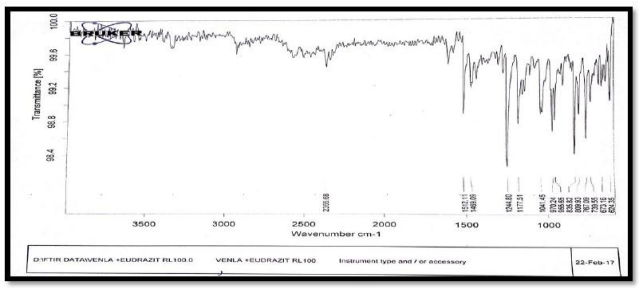

Fig. 6: FT-IR spectrum of Venlafaxine HCl and Eudragit RL100.

Table 4: Interpretation of FTIR spectra of Venlafaxine HCl and EudragitRL100.

Sr. No.	Functional Group	Standard frequency (cm-1)	Pure Drug	Pure Drug+ Eudragit RL100
1	C-O-C	1260-1220	Present	Present
2	Aliphatic C-H	3000-2850	Present	Present
3	Aromatic	3100-3045	Present	Present
4	O-H Stretch	3500-3200	Present	Present

6) Evalution Of Tablet

Table 5: Evaluation of Unsintered Matrix Tablet for F1 to F9.

Formulation code	Weight variation (mg)	Hardness (kg/cm$^{2)}$	Thickness (mm)	Friability (%)	Drug content (%)
	Mean ± S.D	Mean± S.D	Mean± S.D	Mean± S.D	Mean± S.D
F1	299±1.2	4.06±0.07	4.54±0.010	0.67±0.014	98.60±0.662
F2	299±0.80	4.06±0.07	4.54±0.078	0.50±0.014	96.64±0.281
F3	299±0.81	4.06±0.07	4.54±0.010	0.85±0.070	97.76±0.662
F4	299±0.87	4.08±0.02	4.52±0.010	0.84±0.070	97.76±0.571
F5	299±0.87	4.0.6±0.05	4.54±0.010	0.94±0.014	97.66±0.662
F6	299±1.24	4.06±0.05	4.52±0.028	0.84±0.070	98.66±0.571
F7	299±0.87	4.08±0.04	4.5±0.070	0.90±0.014	96.57±0.492
F8	299±0.87	4.04±0.04	4.54±0.010	0.83±0.014	98.40±0.916
F9	300±0.45	4.08±0.04	4.54±0.010	0.76±0.012	98.82±0.306

6.1) Evaluation of Sintered Matrix of Tablet for F1 to F9

Table 6: Evaluation of Sintered Matrix of Tablet.

Formulation code	Weight Variation (mg) Mean ± S.D	Hardness (kg/cm$^{2)}$ Mean± S.D	Thickness (mm) Mean± S.D	Friability (%) Mean± S.D	Drug content (%) Mean± S.D
F1	299±1.2	4.46±0.16	4.56±0.010	0.15±0.014	99.06±0.692
F2	299±0.80	4.64±0.17	4.54±0.037	0.32±0.014	97.28±0.238
F3	299±0.81	4.76±0.17	4.54±0.010	0.33±0.070	97.03±0.638
F4	299±0.87	4.54±0.17	4.54±0.010	0.43±0.014	97.91±0.790
F5	299±0.87	4.84±0.05	4.46±0.037	0.60±0.014	98.41±0.724
F6	299±1.24	5.6±0.54	4.54±0.010	0.42±0.014	98.87±0.219
F7	299±0.87	4.86±0.4	4.46±0.037	0.32±0.012	98.37±0.213
F8	299±0.87	5.6±0.12	4.54±0.010	0.22±0.014	98.78±0.144
F9	300±0.42	6.4±0.12	4.54±0.010	0.22±0.07	99.95±0.531

7) In Vitro Dissolution study

7.1) Unsintered Matrix Tablets containing

In Vitro drug release from study of Formulations.

Venlafaxine HCl tablet with Eudragit RL100 was prepared by direct compression method as polymer forms matrix with the drug so as to sustain the drug release. The drug release .Dissolution study was performed in 0.1 N HCl for 1st 2 hr and for remaining 10 hr in Phosphate buffer pH 6.8, obtained result summarized in is shown in the Table 7.

Table 7: In-vitro drug release from formulations F1to F9 (Unsintered -Matrix Tablet).

Time (hr)	Cumulative Drug Release (%) (Mean± S.D)								
	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
1	20.07±0.6	17.42±0.031	17.54±0.2	18.33±0.2	20.11±0.72	16.88±0.10	16.08±0.7	23.07±0.17	15.47±0.2
2	26.97±1.11	27.34±084	35.84±0.29	30.2±±0.19	30.29±0.60	29.27±0.8	33.0.9±0.31	34.17±0.28	35.16±0.17
3	35.2±0.5	44.49±0.360	41.52±0.29	38.8±0.10	43.3±0.24	38.08±0.10	41.75±0.32	39.48±0.29	44.8±0.54
4	40.33±0.21	66.30±0.29	68.4±0.38	46.03±0.10	54.3±0.43	59.9±0.17	58.0.3±0.58	58.21±0.21	64.04±0.2
5	57.07±2.10	80.2±0.2	81.66±0.77	60.3±0.10	71.72±0.46	77.9±0.2	67.17±0.17	67.1±0.77	76.5±0.43
6	70.1±0.41	102.24±0.24	101.92±0.7	95.2±0.19	87.02±0.27	96.9±0.7	78.02±0.31	92.4±0.45	86.15±0.29
7	102.24±1.13			101.9±0.4	103.9±0.7	100.40±0.21	101.45±0.7	102.9±0.18	101.3±0.31

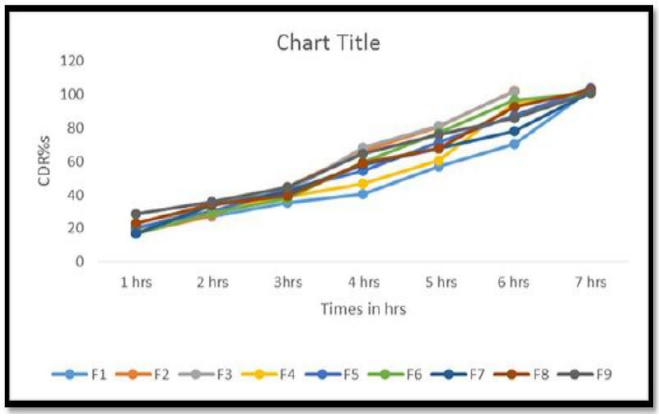

Fig 7: **Dissolution profile of Formulation F1 to F9 (Unsintered Matrix Tablet).**

7.2) Sintered Matrix Tablets containing

Table 8: In Vit*ro* drug release from study of Formulations (F1-F9) Sintered Matrix Tablets containing.

Time (hr.)	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
1	19.30± 0.17	20.76± 0.32	17.27± 0.17	16.07± 0.17	22.93± 0.12	14.2± 0.12	25.5± 0.29	19.04± 0.7	10.05± 0.10
2	22.5± 0.5	27.8± 0.12	26.4± 0.3	22.06± ±0.30	31.72± 0.07	27.05± 0.12	27.03± 0.21	26.07± 0.2	28.30± 0.21
3	30.6± 0.2	35.5± 0.28	35.50± 0.60	34.04± 0.79	38.6± 0.1	34.02± 0.12	34.17± 0.07	35.07± 0.7	35.53± 0.33
4	38.8± 0.5	42.3±0.2 1	41.57± 0.24	50.3± 0.19	48.08± 0.92	42.06± 0.12	45.03± 0.17	41.2± 0.21	46.03± 0.27
5	45.9± 0.23	57.7± 0.20	61.38± 0.29	55.04± 0.19	59.9± 0.29	56.12± 0.17	51.8± 0.12	52.1± 0.21	51.25± 0.1
6	48.85± 0.3	68.3± 0.21	67.69± 0.24	58.02± 0.3	68.04± 0.12	68.22± 0.17	57.07± 0.21±	58.04± 0.12	59.01± 0.21
7	53.01± 0.7	82.08± 0.21	77.9± 0.23	64.18± 0.20	76.04± 0.1	74.72± 0.17	63.07± 0.21	6403± 0.13	64.08± 0.12
8	68.03± 0.69	97.88 0.21	81.53± 0.092	71.22± .17	86.68± 0.19	79.22± 0.21	76.16± 0.18	76.05± 0.17	69.2± 0.29
9	86.5± 0.7	103.45± 0.31	90.6± 0.9	89.50± 0.081	99.84± 0.3	84.66± 0.33	86.07± 0.33	85.4± 0.17	76.09±0.2 1
10	103.67±0 .8		101.75 ±0.17	102.72± 0.17	102.50 ±0.18	93.56± 0.07	92.06± 0.7	92.20± 0.21	86.03± 0.21
11						102.±0.2 3	100.5±0.3 2	95.23±0.2 3	92.20±0.1 0
12								98.±0.52	95.53±0.5 0

Drug release from matrix tablet is determined by drug characteristics, delivery system and destination (site of drug release). Drug content of each tablet was 75 mg and 900 ml of dissolution medium phosphate buffer pH6.8 was used for dissolution studies. Maintaining sink condition is important during the dissolution experiment for consistent and accurate measurement of the dissolution rate. Sink conditions could be maintained throughout the dissolution study and drug solubility could not be a factor responsible for retardation of drug release from the formulations studied because high solubility of drug. Hence retardation of drug release from the formulations could be attributed to obtained result.

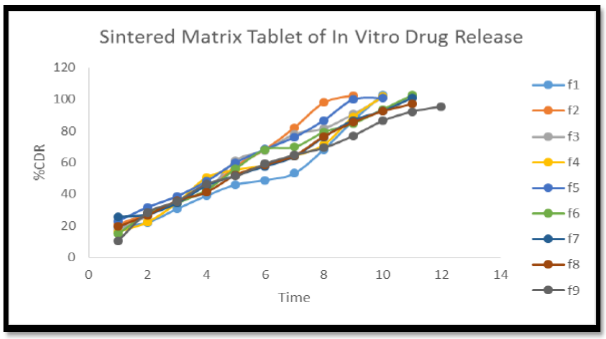

Fig. 8: Dissolution profile of Formulation F1to F9 (Sintered Matrix Tablet).

8. Model assessment for the dependent variables

After putting the data in Design Expert software (version 7.1.5), Fit summary applied to data in that, quadratic model had been suggested by the software so as per this model the equation is as follows: Model equation in coded term

Y1= +100.94-1.19* A-2.64* B

3DSurface Plot

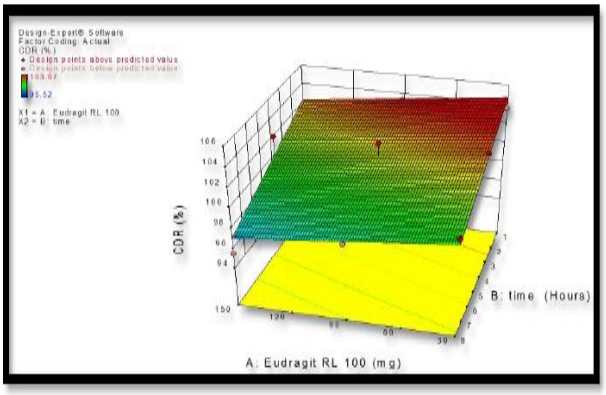

Fig: 9 Surface Plot Response 3D surface plot Showing Effect of Eudragit RL l00 and sintering time on release

Contour plot for Y1

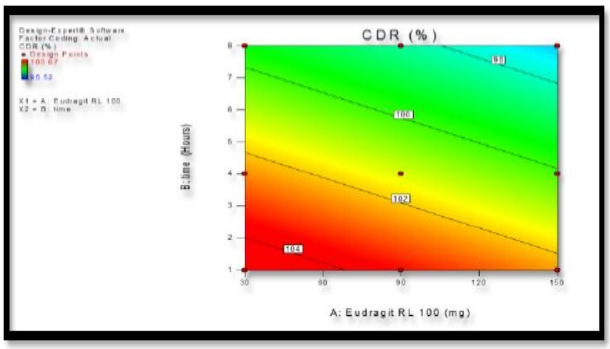

Fig. 10: Contour plot showing effect of Eudragit RL100 and Sintering Time on release.

Table 9: Drug release kinetics formulations.

Formulation Code	Zero order R^2	First order R^2	Higuchi R^2	Korsemayer-Peppas R^2	Korsemayer-Peppas n
F1	0.984	0.958	0.6749	0.9205	0.7172
F2	0.9849	0.958	0.6746	0.9545	0.685
F3	0.9844	0.956	0.6749	0.9355	0.702
F4	0.9705	0.958	0.6749	0.9761	0.702
F5	0.9954	0.956	0.6749	0.9835	0.672
F6	0.9890	0.958	0.6749	0.9747	0.698
F7	0.9896	0.956	0.6749	0.9370	0.675
F8	0.9824	0.986	0.8722	0.9831	0.433
F9	0.9815	0.980	0.8942	0.9915	0.385

DISCUSSION

In the present study, the drug release was analyzed to study the kinetics of drug release mechanism. The results showed that the factorial design batches followed korsmeyer peppas model kinetics. The R^2 values of all batches (F1 and F9) of Zero order model was found close to one and The R^2 value of F1-F9 of korsmeyer peppas model was found close to one. The value of n > 0.5 (except F8 and F9) of korsmeyer peppas indicates that it follows polymer swelling and diffusion type of release mechanism and F8, F9 follows the diffusion as mechanism of drug release as . F9 follow Korsmeyer-peepas order kinetics r^2=0.9915 and n=0.385.

Table 10: Composition of optimized formulationby Design Expert Software.

Optimized formulation Venlafaxine HCl	Quantity (mg) 75
Eudragit RL100	150
Magnesium Stearate	1.5
Talc	1.5
Microcrystalline Cellulose	72
Total	300

Table 11: Determination of powder characteristics Optimized Formulation.

Bulk density (gm/ml)	Tapped density (gm/ml)	Compressibility (Carr's index)	Hausner ratio	Angle of repose(^{0})
0.3010±0.018	0.03588±0.029	15.86±1.22	1.18±0.05	29.35±0.83

Table 12: Evaluation of optimize batch tablets characteristic.

Thickness mm	Hardness kg/cm^2	Friability %	Content uniformity
4.54±0.010	6.4±0.12	0.22±0.07	99.95±0.531

Table 13: Predicted and experimental values of optimised formulation.

Respones	Preticated	Exiperimental Values
Repones12hrs	95.52	95.53±050

9. Stability study

The result of the stability study of the optimized batch for IPQC and poder characteristics was shown in Table and comparison of in-vitro drug release was shown in fig 6. The accelerated stability studies indicate that the developed SR tablets are unaffected after 3 months storage under accelerated conditions as no changes are observed in the hardness, no signs of visually distinguishable changes are observed in the appearance, texture and color of the formulation. The data of drug content before the study and after the study shows the changes but are within the limit. On the basis of these results, it may be concluded that the optimized formulation developed is stable under accelerated conditions for 3 months.

Table 14: Comparison of % CDR for stability study

Time (hrs)	% CDR			
	Before Stability Study	After 1 Month	After 2 Month	After 3 Month
1	9.63	8.92	8.97	8.96
2	24.30	23.89	22.76	23.8
3	35.55	33.14	33.15	33.14
4	46.16	45.56	45.55	45.54
5	51.45	51.12	51.28	51.26
6	59.23	59.33	59.56	59.50
7	64.48	64.45	64.40	64.45
8	69.27	69.25	69.26	69.24
9	76.13	76.15	76.18	76.17
10	86.86	86.26	86.26	86.28
11	92.06	92.46	92.47	92.24
12	95.53	94.50	94.45	94.40

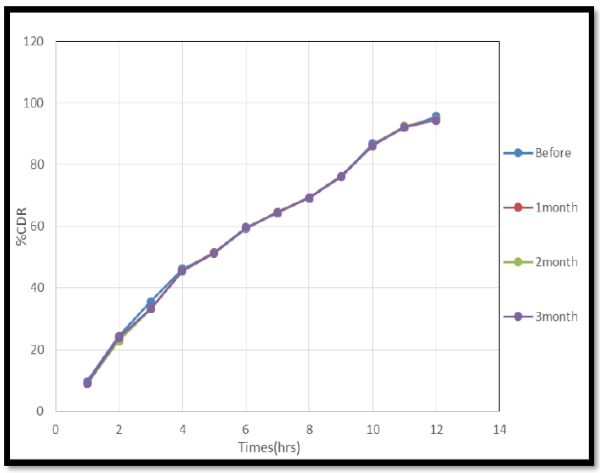

Fig. 11: Comparison of dissolution profile of optimize batch during stability study.

DISCUSSION

In this work we studied the mechanism of effect of Sintering, sintering time Sintering method and polymer concentration on release of Venlafaxine HCl as model drug form tablet. Unsintered tablet Shown Higher drug release in12hrs where present drug release was found to be inversely proportional to sintering time and polymer concentration on sintering time 75^0 c for 1to8 hrs. After observing the values Of correlation Coefficient and release rate constant for Unsintered and Sintered tablet the R values indicated that F9 batch show matrix as a best fit model and n values show that formulation follow diffusion Mechanism.

CONCLUSION

Sustained release matrix tablet of venlafaxine HCl were prepared by different Sintering Method. From the result it is concluded that the release rate drug inversely proportional to Sintering time Polymer Concentration. When effect of polymer concentration.is considered, among one polymer results initial release was further drug release retardation is confirmed due to Eudragit RL100.When effect Sintering is considered then bond formation between drug and polymer is responsible for retardation in drug release. Sintering due to heat treatment favor sustained drug release in more proportion as compare to Unsintered matrix tablet. Thus, on the basis of result obtained sintering technique proved to be effective than unsintering technique by further retarding release profile drug. By Using Sintering technique friability of Tablet was found to decrease with increasing sintering time and hardness was increased with increasing sintering time.

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