CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.18329252

Available online at: http://www.iajps.com *Research Article*

DEVELOPMENT AND CHARACTERIZATION OF VENLAFAXINE EXTENDED-RELEASE BILAYER TABLET

Dr. Alladi Saritha[1*], Sravanthi[2]

[1] Professor and HOD, Department of Pharmaceutics, SSJ College of Pharmacy, Vattinagulapally, Gandipet, Rangareddy District

[2]Student, Department of Pharmaceutics, SSJ College of Pharmacy, Vattinagulapally, Gandipet, Rangareddy District

Abstract

The present study aimed to develop and evaluate venlafaxine extended-release bilayer tablets capable of providing an initial loading dose followed by a sustained drug release for up to 12 hours. The bilayer system consisted of an immediate-release layer to achieve rapid onset of action and a sustained-release layer to maintain therapeutic plasma concentration. Tablets were prepared by direct compression using suitable polymers and excipients, and were subjected to standard pre- and post-compression evaluations including weight variation, thickness, hardness, friability and drug content. All formulations showed acceptable physical properties: hardness 5.2–5.6 kg/cm², friability <0.4 % and weight variation within pharmacopeial limits, confirming good mechanical strength and uniformity. In-vitro dissolution studies revealed an initial release of approximately 23–29 % of venlafaxine within the first hour, followed by a controlled and nearly linear release pattern. By 12 hours, cumulative drug release ranged from 93 % to 98 %, indicating successful extended-release characteristics. Among the eight formulations (F1–F8), F7 exhibited the most desirable profile with adequate burst release and highest cumulative release at 12 hours. The study demonstrates that a bilayer tablet approach is an effective oral drug delivery system for venlafaxine, providing both rapid onset and prolonged therapeutic action, and may improve patient compliance in the management of depressive disorders.

Keywords: *Venlafaxine, Polymers, Extended release, Direct compression parameters, Bilayer tablets, In vitro drug release*

Corresponding author:

Alladi Saritha,

Professor and HOD, Department of Pharmaceutics,
SSJ College of Pharmacy, Vattinagulapally,
Gandipet, Rangareddy District

QR CODE

Please cite this article in press ***Alladi Saritha et al., Development And Characterization Of Venlafaxine Extended-Release Bilayer Tablet,*** *Indo Am. J. P. Sci, 2026; 13(01).*

INTRODUCTION:

Extended-release (ER) drug delivery systems have been widely explored to overcome the limitations of conventional immediate-release (IR) dosage forms. Among them, bilayer tablet technology offers a unique advantage by combining two distinct layers in a single dosage unit.[1] one layer designed for immediate release to provide rapid onset of action, and the second engineered for controlled or extended release to maintain prolonged therapeutic effect. Such a dual-release profile is particularly beneficial for drugs like venlafaxine, where a swift onset of antidepressant efficacy coupled with steady-state plasma concentration is desired.[2] Venlafaxine, a serotonin norepinephrine reuptake inhibitor (SNRI), is widely used in the treatment of depression, generalized anxiety disorder, and panic disorder due to its dual mechanism of action and favorable therapeutic profile.[3] However, the short biological half-life of venlafaxine (approximately 4–5 hours) necessitates frequent dosing, which may lead to fluctuating plasma concentrations, reduced medication adherence, and increased incidence of side effects such as nausea, hypertension, and insomnia.[4] Therefore, designing an extended-release oral formulation is essential to achieve sustained therapeutic action, maintain consistent plasma drug levels, and improve patient compliance.[5] The present research aims to design, formulate, and characterize a venlafaxine extended-release bilayer tablet using suitable polymers and excipients to achieve the desired dual release profile. The study evaluates physical parameters, dissolution behavior, and release kinetics to optimize the formulation and ensure its suitability for clinical use.[6]

MATERIALS

Venlafaxine was procured from Hetero Labs, HYD. Sodium alginate, Tragacanth, Croscaramellose were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY:

Drug and excipient compatibility studies

Drug excipients compatibility studies were performed to know the compatibility of excipient with drug at accelerated conditions. The study was conducted by preparing homogenous mixture of excipients with drug and filled in HDPE bags and LDPE bags. Glass vials were exposed to 600 C and 400C/75 %RH for 4 weeks and LDPE bags were exposed to 400C±75 %RH for 4 weeks. Samples were observed periodically for any physical change.[7,14]

Preparation of Venlafaxine tablets

Formulation Table

Table-1: Preparation of Immediate release layer of Venlafaxine

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8
Venlafaxine	25	25	25	25	25	25	25	25
Croscaramellose sodium	10	20	30	40	-	-	-	-
SSG	-	-	-	-	10	20	30	40
Microcrystalline cellulose	60	50	40	30	60	50	40	30
Talc	2	2	2	2	2	2	2	2
Magnesium Stearate	3	3	3	3	3	3	3	3
Total wt.	100	100	100	100	100	100	100	100

Preparation of Immediate Layer of Venlafaxine by Direct Compression Method[8]

1. Step1: Weigh all the ingredients in required quantity
2. Step2: Transfer all ingredients into a mortar, triturate for 10minutes until to get fine powder and sieve the material. (#60)
3. Step3: then transfer the material into blender for proper distribution of drug in blend for 10minutes.
4. Step 4: then addition of lubricant, mix well.
5. Step5: Perform the micromeritic properties (Precompression studies).
6. Step6: Compression.

Table-2: Preparation of Sustained release layer of Venlafaxine

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8
Venlafaxine	50	50	50	50	50	50	50	50
HPMC	50	100	150	200	-	-	-	-
Sodium alginate	-	-	-	-	50	100	150	200
Microcrystalline cellulose	195	145	95	45	195	145	95	45
Talc	2	2	2	2	2	2	2	2
Magnesium Stearate	3	3	3	3	3	3	3	3
Total wt.	300	300	300	300	300	300	300	300

Preparation of Sustain release Layer of Venlafaxine by Direct compression Method:[9]

1. Step1: Weigh all the ingredients in required quantity
2. Step2: Transfer all ingredients into a mortar, triturate for 10minutes until to get fine powder and sieve the material. (#40)
3. Step3: then transfer the material into blender for proper distribution of drug in blend for 10minutes.
4. Step 4: then addition of lubricant, mix well.
5. Step5: Perform the micromeritic properties (Precompression studies).
6. Step6: Compression.

FINAL TABLET COMPRESSION: The bilayer tablet compression was made using 8 mm punch in a 27 station rotary tablet machine with double feed. In this, optimized sustained release Venlafaxine blend were introduced first in to the die cavity and a slight precompression was made so that the layer was uniformly distributed. After that optimized immediate release of Venlafaxine blend were added through the other feed and a final compression was made.[10]

Evaluation studies[11,12,13]

Weight variation:

Weight variation test was done on a batch of 20 tablets. The tablets were weighed individually and average weight of all the tablets was determined. The difference in the weight of all the tablets from the average weighed was calculated. Then the mean deviation of each tablet from the average weight was determined

Thickness:

Twenty tablets were randomly selected form each batch and there thickness was measured by using vernier caliper. Thickness of three tablets from each batch was measured and mean was calculated.

Hardness:

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets were determined.50

Friability:

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Twenty tablets were weighed and placed in the Roche friabilator, which was then operated for 25 rpm for 4 min. After revolution Tablets were dedusted and reweighed. Compressed tablets should not loose more than 1% of their weight.

The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100$$

Where,

% F = friability in percentage

Wo = Initial weight of tablet

W = weight of tablets after revolution

Drug Content

Weigh each tablet individually and record identy. Powder each tablet separately (if uncoated, you may weigh intact and apply content estimation method. Keep identity for each unit. For each tablet accurately transfer an amount of powder equivalent to the labelled dose (or dissolve the entire tablet) into a volumetric flask. Use a suitable solvent that fully dissolves API and excipients. Sonicate if needed and make to volume. Filter (0.45 / 0.22 µm) or centrifuge if required to remove insoluble excipients, then dilute aliquots to the working concentration for assay. Assay each individual unit solution by UV against a calibrated standard prepared on the same day. Report each unit result as % of label claim**.**

In- Vitro Release study:

The dissolution test in compendial media was carried out using USP apparatus 2 (paddle) (TDT-08, Electrolab, Mumbai, India). The dissolution medium was 750 mL of filtered and degassed

0.1 M HCl for 2 h, followed by the addition of 250 mL phosphate buffer at a final pH of 6.8, maintained at 100 rpm and 37.0 ± 0.5°C. Samples were collected at specified time points (from 0 h for up to 8 h), filtered through a 0.45 µm filter, and analysed for drug content with a Uv spectroscopy.

Drug release kinetics

Zero-order equation is followed when the drug dissolution from FNM matrix layer is without disaggregate of the polymer and drug is released slowly in controlled manner. The following equation is adopted:

Q=Q0+k0t

Where Q represents the amount of drug dissolved in time t, Q0 is the initial amount of the drug in the solution and k0 is the zero order release constant expressed in units of concentration/time.

First-order equation is followed for the release of the drug from the matric and can be expressed by the first order release kinetics equation:

In Q=InQ0+k1t

where k1 is the first order rate constant and t is the time.

Higuchi equation is followed when matrix is swelling and drug release is affected by change in the surface area. Higuchi equation defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time and can be expressed as

Q=kHt1/2

Where Q is the amount of drug release at time t and kH is the Higuchi release constant.

Stability studies:

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile. The prepared Matrix tablets of Venlafaxine were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2oc and refrigerator 2-8oc for a period of 90 days.

RESULTS AND DISCUSSION:

Drug - excipient compatibility studies (FT-IR)

The compatibility between the drug and other excipients was evaluated using FTIR peak matching method. There was no appearance or disappearance of peaks in the drug-lipid mixture, which confirmed the absence of any chemical interaction between the drug and other chemicals.

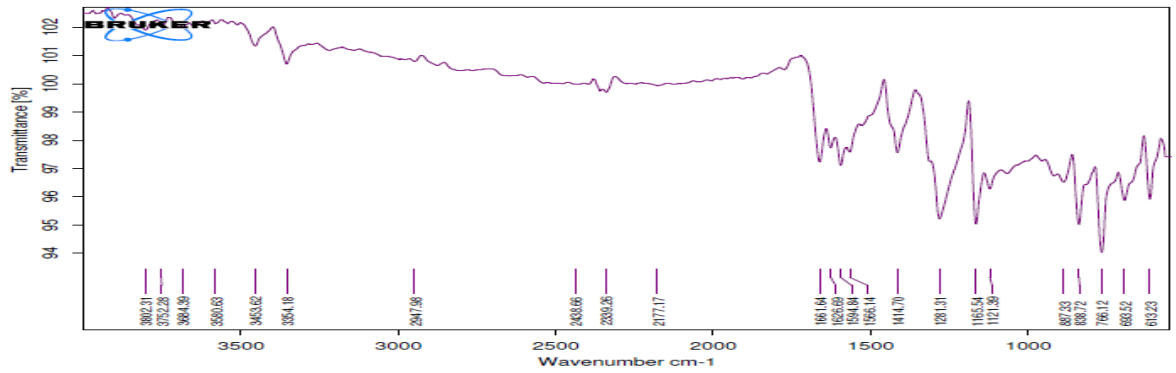

Fig-1: FT-IR Sample for Venlafaxine

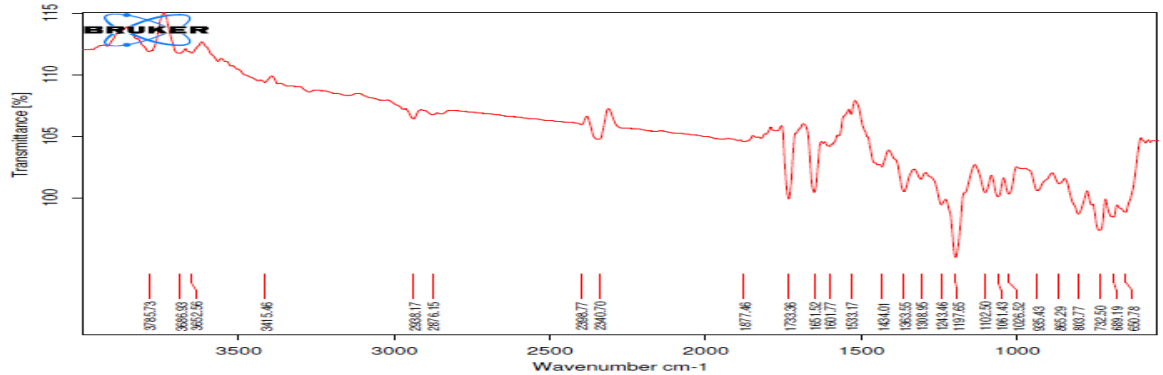

Fig-2: FTIR Studies of Optimized formulation

Evaluation studies

Table-3: Physical parameters of tablets of each batch

S. No.	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	400	3.87	5.31	0.35	85.63
F2	399	3.59	5.20	0.30	84.23
F3	401	3.60	5.60	0.27	82.46
F4	398	3.48	5.28	0.31	86.92
F5	400	3.27	5.43	0.34	80.16
F6	400	3.19	5.25	0.28	88.25
F7	401	3.26	5.46	0.36	90.12
F8	399	3.22	5.55	0.40	89.51

Weight variation The tablet weights ranged between 399–401 mg**,** which is well within the USP/BP acceptance limit of ±5% for tablets of this weight range. This narrow range indicates uniform die fill and good flow properties of the granules during compression.

Thickness: Thickness varied slightly from 3.19 to 3.87 mm**.** Such minor variation can be attributed to normal compression force adjustments and is acceptable provided it does not affect packaging or dosing. The slightly higher thickness of batch F1 (3.87 mm) may reflect a marginally lower compression force compared to the other batches.

Hardness: Tablet hardness was in the range of 5.20–5.60 kg/cm^2**,** which is within the typical range (4–8 kg/cm^2) required to withstand mechanical stress during handling and transportation. This also ensures the tablets maintain their integrity while still allowing proper disintegration and dissolution.

Friability: Friability values were 0.27–0.40 %**,** well below the pharmacopeial limit of <1 %**.** This confirms that the tablets have adequate mechanical strength and are resistant to abrasion and breakage.

Drug content uniformity: The drug content ranged from 80.16 % (F5) to 90.12 % (F7)**.** Most batches fall within the USP acceptance criteria of 85–115 % of the label claim. However, F3 (82.46 %) and F5 (80.16 %) are slightly below the lower limit, indicating possible inhomogeneous drug distribution or minor losses during granulation. Formulations F6–F8 showed comparatively higher and more consistent drug content (≈88–90 %), suggesting better blend uniformity.

In-vitro Dissolution Study : All the 8 formulation of prepared extended matrix tablets of Venlafaxine were subjected to in-vitro release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for the 12 hrs.

Table-4: Dissolution Profile of F1 to F8

Time (hrs.)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
0	0	0	0	0	0	0	0	0
1	23.56	25.67	26.32	28.81	27.42	25.19	28.91	26.84
2	35.79	35.46	34.78	35.69	34.91	35.10	37.48	38.49
3	45.10	44.18	45.96	44.72	45.20	44.69	46.89	45.12
4	58.16	57.98	58.42	59.83	55.38	57.44	58.76	55.24
6	65.25	64.57	65.74	66.49	67.19	66.28	69.82	68.72
8	72.39	75.15	76.98	77.52	78.16	79.25	77.58	75.60
10	88.91	82.35	83.46	82.46	83.25	85.12	86.13	85.10
12	93.26	92.68	93.34	95.82	94.58	94.35	97.82	95.55

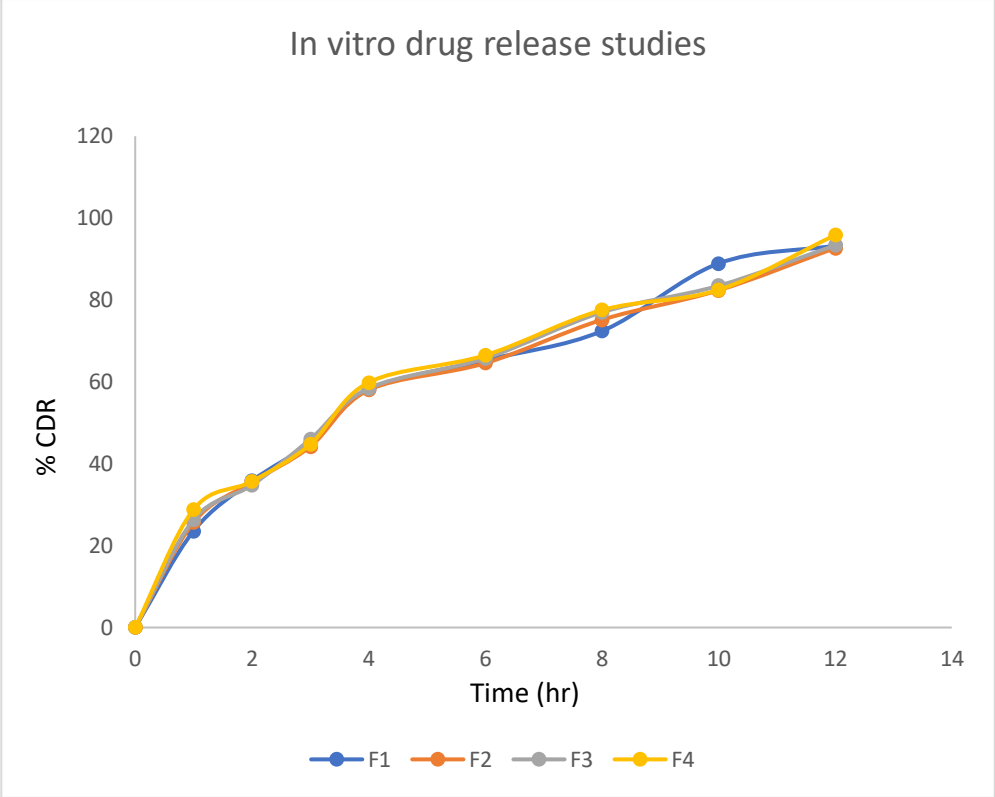

Fig-3: Dissolution profile of F1-F4 Formulation

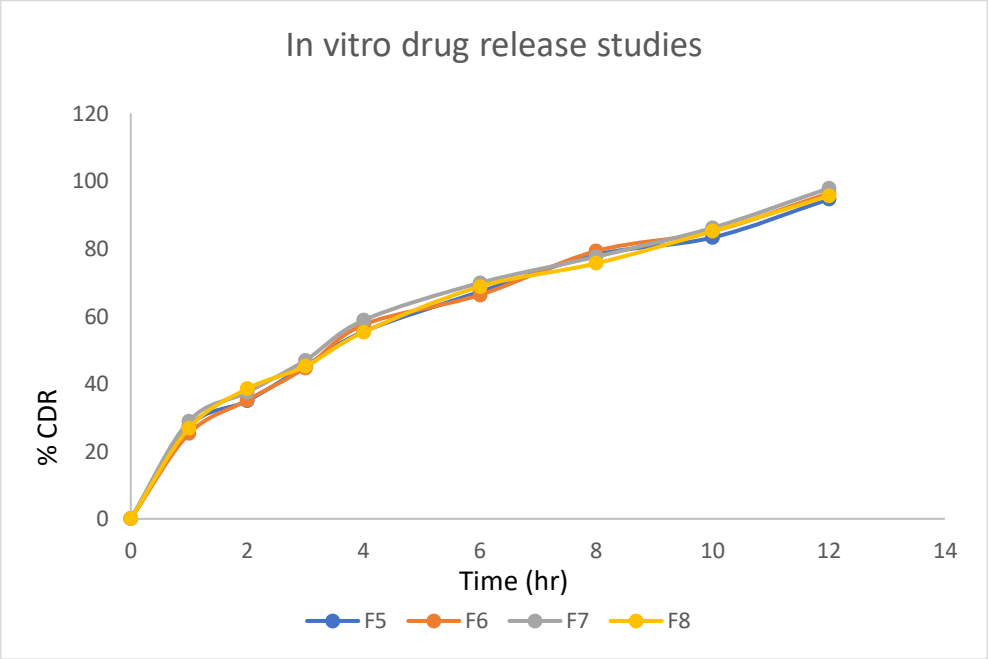

Fig-4: Dissolution profile of F5-F8 Formulation

The dissolution data confirm that all bilayer tablet formulations achieved a sustained and nearly complete drug release over 12 hours, consistent with the design of an extended-release dosage form. Among them, F7 demonstrated slightly superior performance, combining good early release with complete drug liberation at 12 h. These findings indicate that the polymeric matrix successfully maintained controlled release and that F7 may be the most promising candidates for further scale-up and stability studies

Release order kinetics:

Zero order kinetics:

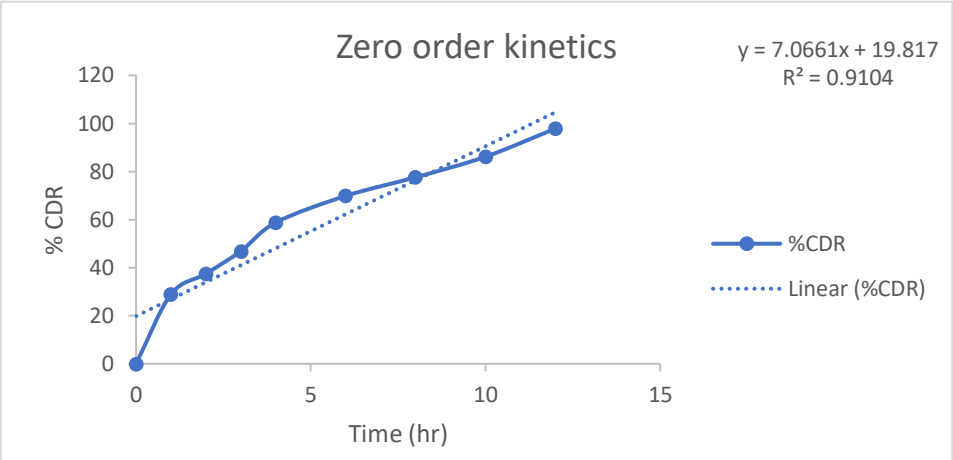

Fig-5: Drug release kinetics of zero order kinetics

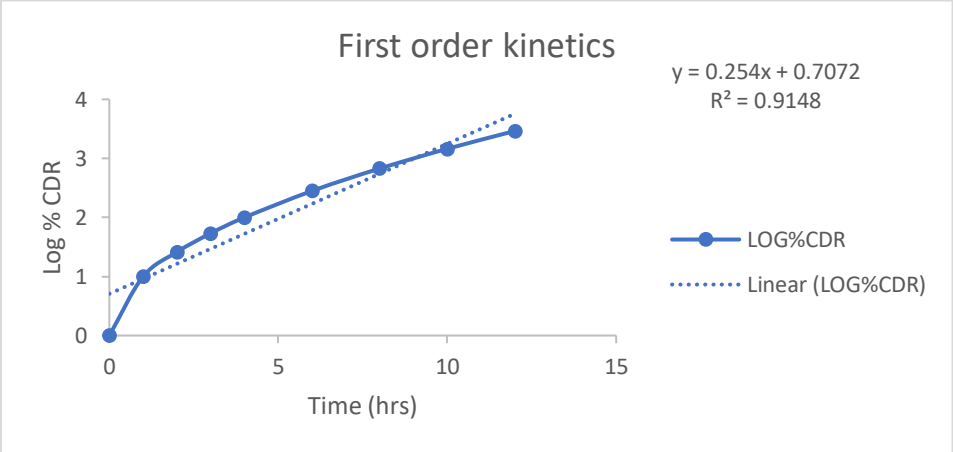

Fig-6: Drug release kinetics of First order kinetics

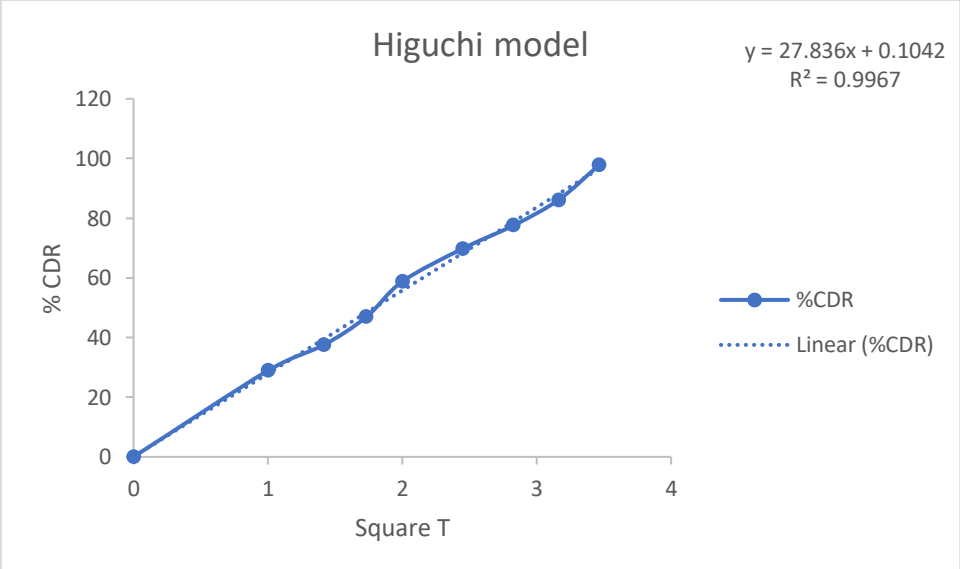

Fig-7: Drug release kinetics of Higuchi model

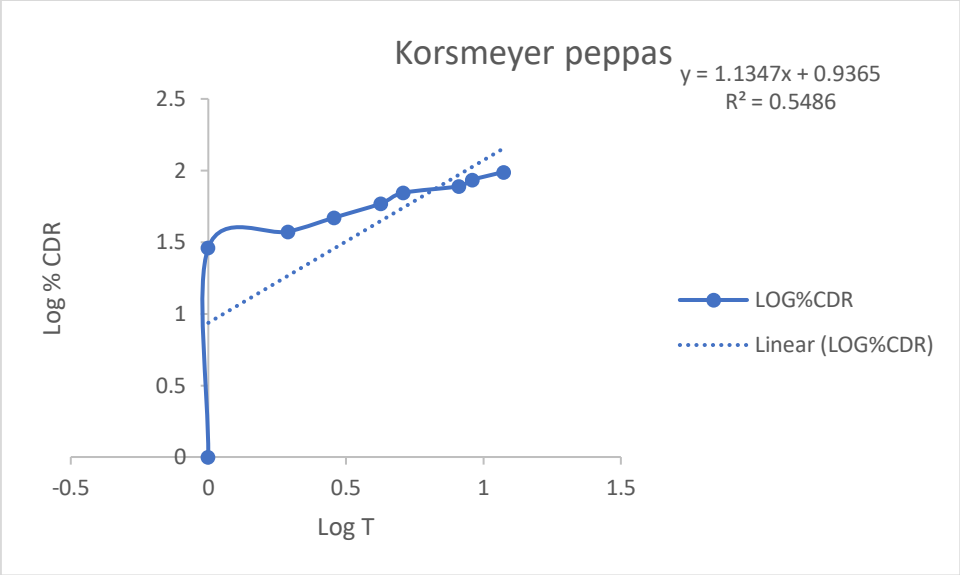

Fig-8: Drug release kinetics of Korsmeyer peppas

Stability studies

Extended release matrix tablets of Venlafaxine formulated in the present study were subjected to accelerated stability studies. Stability studies of the prepared formulations were performed at ambient humidity conditions, at room temperature, at 40°c and 2-8°c for a period up to 90 days. The samples were withdrawn after periods of 90 days and were analyzed for its appearance, hardness, friability, drug content and in vitro release. The results revealed that no significant changes in appearance, drug content, hardness, friability, and in vitro release for F7 formulation. When it was stored at the three storage conditions. However, there was slight variation in invitro release when it is stored at various temperature, there was no change when it is stored at 40°c and room temperature.

Table-5: Results of stability studies of optimized formulation F7

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd	Limits as per Specifications
F-7	**25^{0}C/60%RH**	97.82	96.85	95.36	94.65	**Not less than**
F-7	**30^{0}C/75% RH**	97.82	96.28	95.48	94.67	**Not less than**
F-7	**40^{0}C/75% RH**	97.82	96.75	95.35	94.78	**Not less than**

CONCLUSION:

Bilayer tablets of venlafaxine were successfully formulated to deliver an initial loading dose followed by sustained drug release for up to 12 h, thereby fulfilling the design objective of an extended-release oral dosage form. The findings confirm that the bilayer approach can enhance patient compliance by reducing dosing frequency while maintaining therapeutic levels. Formulations F7, in particular, showed optimal physicochemical characteristics and dissolution behaviour and are recommended for further scale-up, stability testing, and in-vivo evaluation to establish their clinical performance.

REFERENCES:

1. Deshpande RD, Gowda DV, Mahammed N, Maramwar DN. Bi-layer tablets-An emerging trend: a review. International journal of pharmaceutical sciences and research. 2011 Oct 1; 2(10):2534-2544.
2. Reddy KR, Mutalik S, Reddy S. Once-daily sustained-release matrix tablets of nicorandil: formulation and in vitro evaluation. AAPS pharm SciTech. 2003 Dec 1; 4(4):480-488.
3. Kanvinde SA, Kulkarni MS. Stability of oral solid dosage forms–A global perspective. Pharma times. 2005 May; 37(5):9-16.
4. Gohel MC, Bariya SH. Fabrication of triple-layer matrix tablets of Venlafaxine using xanthan gum. AAPS Pharmscitech. 2009 ;10(2):624-630.
5. Momin MM, Kane S, Abhang P. Formulation and evaluation of bilayer tablet for bimodal release of Venlafaxine . Front Pharmacol. 2015 Jul 9;6:144.

6. Reddy RK and SrinivasN. Formulation and evaluation of bilayered tablets of losartan potassium. IP. 2014;2(1):312-320. 14. Prakash VK and Shankar UB. Formulations and evaluation of ibuprofen floating tablets. IJPCBS. 2012;2(4):47-481.
7. Sandeep N and GuptaMM. Immediate drug release dosage form a review. JDDT. 2013;3(2):155-161.
8. Pateriya A, Bhowmick M, Pandey GK, Joshi A and Dubey BR. Formulation and evaluation of player tablets of candesartan and hydrochlorothiazide for the treatment of hypertension. JDDT. 2013;3(6):21-35.
9. Kumar HG, Jaganathan K, Kumar SR and Peruma lP. Formulation and invitroevaluation of bilayer floating tablets of metformin hydrochloride and sitagliptin phosphate. Intern J Pharma Resea. 2013;5(1):53-59.
10. Kumar HA, Kavitha K,Kumar SA,Kumar RM and Singh JSD. Novel approach of bilayer tablet technology are view. IJPCBS. 2013;3(3):887-893.
11. Sahota R, Singh G, Mankoo P, Kaur R, Singh S, Nagpal M, Upendra K and JainUK, Shelly KS and Sharma M. Development and characterization of bilayer tablets containing metformin hydrochloride sustained release layer and atorvastatin calcium in the immediate release layer. IPP. 2013;1(3):220-229.
12. Chaudhari S, Bawaskar M and Shirsat A. Formulation and evaluation of player floating tablet of carvedilol phosphate. JDDT. 2012;2(5):9-19. 21. Indian Pharmacopoeia. The Controller of Publication, Delhi. 1996; 2: 735.
13. Siepmann J, Peppas NA. HPMC matrices for controlled drug delivery: new model combining diffusion, swelling and dissolution mechanisms and predicting the release kinetics, Pharm Research, 2000; 16: 1748-1756.
14. Bhargav Bhongiri*, Vadivelan Ramachandran, and Raman Suresh Kumar. "Preformulation Studies of S-Equol." Journal of Pharmaceutical Negative Results, 2022, 1020-1029.IF-0.654.