Original Article

INTERNATIONAL JOURNAL OF EXPERIMENTAL AND BIOMEDICAL RESEARCH

Published by Pharma Springs Publication Journal Home Page: https://pharmasprings.com/ijebr

Formulation and evaluation of Nevirapine sustained release tablets using various polymers by liquid-solid compact method

Swathi Krishna K V*[1], Sai Priyanka

Department of Pharmaceutics, Saastra College of Pharmaceutical Education & Research, Near Varigonda Jwalamukhi Temple, Muthukur Raod, Kakupalli, Nellore-524 311 Andhra Pradesh, India.

Article History:

Received on: 21 Aug 2024
Revised on: 26 Sep 2024
Accepted on: 29 Sep 2024

Keywords:

Nevirapine,
sustained release,
polymers,
liquid-solid compact method

Abstract

This present research aims to formulate and evaluate the Nevirapine sustained release tablets using various polymers using a liquid-solid compact method. The current study's methodology involved comparing the two polymers, argum, and xanthumgum, and evaluating the impact of the active components' physicochemical makeup on the drug release profile utilizing the liquid solid compact method using Tween 80 and propylene glycol.The formulation is appropriate for wet granulation, according to the sieve analysis results, compressibility index, and angle of repose.According to this study, Nevirapine can be administered via an extended-release drug delivery system because its formulation prolongs its duration of action within the therapeutic range without causing toxicity as with conventional dose forms. These dosage forms provide the capacity to increase and decrease the frequency of doses.

*Corresponding Author

Name: Dr. K.V. Swathi Krishna
Phone: +91 8309013961
Email: swathikrishna004@gmail.com

eISSN: 2583-5254
DOI: https://doi.org/10.26452/ijebr.v3i4.668

Production and hosted by
Pharmasprings.com

INTRODUCTION

The idealized goal highlights the two factors, spatial location and temporal drug delivery, crucial to drug delivery. Targeting a drug to a particular organ or tissue is known as spatial placement, whereas regulating the pace at which the Drug is delivered to the intended tissue is known as temporal delivery. To address these two issues, a well-thought-out, sustained-release drug delivery system can be a significant step forward. Although most research has focused on oral dose forms that meet the temporal requirement for drug delivery, many of the more recent strategies being investigated may also allow for spatial placement [1]. Significant "Valleys" and "Peaks" may exist in the Drug's blood level if the dosage is not adjusted for the Drug's biological half-life. For

instance, regular dosage is necessary to maintain consistent therapeutic levels in medications with short half-lives. A crucial factor to take into account for some disease states is the possibility that the Drug's blood level may not be within the therapeutic range at an appropriate early stage. This technique may fail if the patient does not follow the multiple-dosing protocol. Many times, these issues are severe enough to make sustained-release drugs preferable to drug therapy using traditional dosage forms. This characteristic and the inherent incapacity of traditional dosage forms to accomplish spatial placement make research on sustained-release drug delivery methods beautiful [2].

METHODOLOGY:

Analytical Method Development

Preparation of 6.8 phosphate buffer

Monobasic potassium phosphate was weighed at 27.22g and diluted to a volume of 1000 ml to create a stock solution. To get a solution of 0.2M sodium hydroxide, 8g of sodium hydroxide was weighed and diluted to 1000ml. The stock solution transferred 50 ml of the monobasic potassium phosphate solution into a 200 mL volumetric flask. Water made up the remaining capacity after 22.4 ml of the stock solution for the 0.2M sodium hydroxide solution was added [3].

Determination of λ_{max} of Nevirapine 6.8 phosphate buffer

Procedure

Working standard: A 1000µg/ml ppm concentrated stock solution was obtained by weighing and dissolving 50 mg of Nevirapine in 50 ml of 6.8 phosphate buffer and then adding more 6.8 phosphate buffer to reach a volume of 50 ml [4].

Dilution 1: 10µg/ml concentrated solution was obtained by diluting 10 ml of the working standard solution with 6.8 ml phosphate buffer.

Dilution 2: 10µg/ml concentrated solution was obtained by diluting 10 ml of the working standard solution with 6.8 ml phosphate buffer.

This solution's corresponding scan spectrum curve was noticed when scanned at 200 and 400 nm wavelengths. λmax is the wavelength that corresponds to the maximal absorption [5].

Formulation of Nevirapine SR tablets by liquid, solid compact method

The Liqui Solid Compact Method's processing phases:

The following General Methodology was used to prepare the Nevirapine SR tablets:
1. Every component and drug, Aerosil and Mg. stearate, were precisely weighed. They were then co-sifted through a #60 sieve and combined with a solvent.

2.#40 Sieve passed Magnesium Stearate, Aerosil, was used to lubricate the abovementioned mixture.

3. The resultant blend, which had an average hardness of 4.0 kg/cm2, was subsequently

Table 1 Nevirapine SR formulation using the liquid-solid compact technique

Ingredients	Formulation code											
	NF1	NF2	NF3	NF4	NF5	NF6	NF7	NF8	NF9	NF10	NF11	NF12
Nevirapine	100	100	100	100	100	100	100	100	100	100	100	100
PG	50	50	100	100	150	150						
Tween 80							50	50	50	100	100	100
Guargum	100		100		100		100		100		100	
Xanthumgum		100		100		100		100		100		100
Mcc pH 102	200	200	200	200	200	200	200	200	200	200	200	200
Aerosil	5	5	5	5	5	5	5	5	5	5	5	5
Mg.stearate	5	5	5	5	5	5	5	5	5	5	5	5
Total wt. (mg)	460	460	510	510	560	560	460	460	510	510	560	560

compressed into tablets using a 16-station tablet compression machine employing 8mm to 12mm dies[6].

A) Pre-Compression studies

Bulk density: Using a bulk density apparatus, the bulk density was ascertained by precisely weighing a quantity of powder in a measuring cylinder and recording the volume and weight of the entire powder [7]. The formula for bulk density, which is measured in gm/ml, is

$$\mathbf{BD} = \frac{\mathbf{W}}{\mathbf{V_o}}$$

Tapped density:

A precisely weighed quantity of powder was placed in a measuring cylinder, and after 30 tappings, the volume of powder and the weight of the entire powder were recorded. This method was used to calculate the taped density.

$$\mathbf{TD} = \frac{\mathbf{W}}{\mathbf{V_F}}$$

Carr's index: One significant metric that may be derived from the bulk and tap densities is the compressibility index. Based on the apparent bulk density and tapped density, a material with values between 20 and 30 percent is considered free-flowing. The following method was used to calculate the bulk Drug's percentage compressibility.

$$\textbf{Compressibility index} = \frac{(\mathbf{TD} - \mathbf{BD})}{\mathbf{100}}$$

Hausner's ratio: It shows the powder's flow characteristics. Hausner's ratio is the powder's bulk density ratio to its tapped density.

The angle of repose: The angle of repose is the maximum angle formed by the surface of the powder pile and the horizontal plane. These studies were carried out before and after adding lubricant or glideant. The angle of repose (ɵ) was then calculated.

$$\theta = \mathbf{tan}^{-1}\frac{\boldsymbol{h}}{\boldsymbol{r}}$$

B) Post-compression studies [9-10]

Weight variation: For each tablet to have the right amount of drugs, the weight of the manufactured tablet was measured. We calculated the tablets' average weight. We compared the average weight fluctuation with the weight of each tablet individually.

Thickness: A vernier caliper that was calibrated was used to measure thickness. It was decided to measure the tablet's thickness. Each formulation's twelve tablets were chosen randomly, and each tablet's thickness was measured separately.

Friability: The friability of the produced tablets was assessed using a Roche friability device. Twelve pills are weighed initially and then transferred into a friability to calculate the friability percentage. After that, % friability was determined using a formula.

Drug content uniformity: The Drug was precisely weighed out of the manufactured tablets and ground up with a pestle and mortar. The UV-visible spectrophotometer was used to analyze the samples and determine the drug concentration.

Hardness: The Monsanto tester was used to determine the hardness of twelve tablets. The kg/cm2 unit of measurement for hardness was used. A ran~~dom sample~~ of twelve tablets was used to measure their hardness. Twelve tablets' average hardness was noted. [9]

Data analysis [11-12]:

Examine the release mechanism and rate of release of the Higuchi matrix, zero order, first order, and Peppa's model. The model with the best fit was chosen based on the r-value.

Zero-order kinetics:

Examine the release mechanism and rate of release of the Higuchi matrix, zero order, first order, and Peppa's model. The model with the best fit was chosen based on the r-value.

$$\mathbf{Qt} = \mathbf{Q_o} + \mathbf{K_o t}$$

First order kinetics

The release rate data were fitted to the following equation to investigate the first-order release rate kinetics.

$$\mathbf{Log\ Qt} = \frac{\mathbf{Log\ Q_o K_1 t}}{\mathbf{2.303}}$$

Higuchi's model It was possible to derive mathematical expressions for drug particles distributed as diffusion media within a homogeneous matrix. Additionally, the formula is

$$\frac{Mt}{M\infty} = KH\frac{t1}{2}$$

Korsmeyer- Peppas Model:

As shown in the following equation, the power law effectively characterizes the fractional drug release that is exponentially related to the release period and comes from slabs, cylinders, and spheres[11].

$$\frac{Mt}{M\infty} = Ktn$$

$$Log(\frac{Mt}{M\infty}) = \log K + n \log t$$

RESULTS AND DISCUSSION

FT-IR spectroscopy

Pure Nevirapine's unique absorption peaks were found in the FTIR spectra at 3087.56, 2994.16, 1707.56, 1460.7, 13620.10, and 705.5 cm-1, which correspond to O-H, C-H, C=O C-C, C-O stretching, and OH-bending (**Figure 1**). According to the spectrum data, all physical combinations of pharmaceuticals and polymers showed no appreciable changes in the infrared peaks, which are the primary peaks for medications and are acquired as nearer values. The fact that pharmaceuticals were molecularly distributed throughout the polymers or drug-loaded formulations suggests no interactions.

Evaluation of Tablets

A) Pre-Compression studies

Inference:

The flow characteristics of the Nevirapine SR tablets were assessed, and Table 10 displays the results for the compression tablet mixtures. It was discovered that for every formulation, the tapped and bulk densities were nearly identical. The blends showed satisfactory flow and compressibility, with Carr's index and Hausner's ratio in the range of < 18 and 1.0 to 1.56, respectively. All of the formulations' angles of repose were determined to be within the range of 11.03–18.23˚, suggesting passable flow (adding a glidant will improve the flow).

B) Post compression studies:

Inference:

The weight variation stayed within the parameters. The tablets were found to range in thickness from 3.03 to 5.26 mm. The hardness values for several formulations ranged from 4.39 to 5.98 kg/cm2, signifying adequate mechanical strength. All the formulations had friabilities of less than 1.0% W/W, indicating mechanical solid resistance in the tablet. According to the findings, the drug content was between 98 and 102%.

INVITRO DISSOLUTION STUDIES OF NEVIRAPINE ER TABLETS

Dissolution profile

Out of all the formulations, F2 demonstrated the most favorable outcomes. Diffusion exponent n for the F2 formulation is between 0.45 and 0.89, indicating that non-fiction anomalous diffusion is being followed.

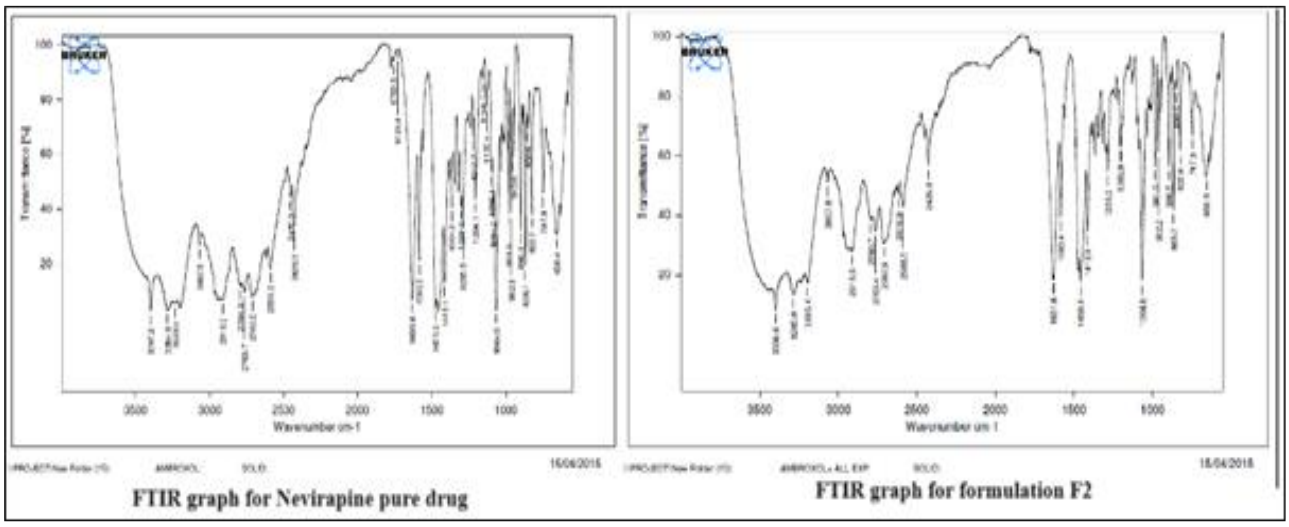

Figure 1 FTIR graph for pure Drug and formulation F2

Table 2 Nevirapine ER tablet pre-compression studies *n=3

Formulation Code	Bulk density (Kg/cm^3)	Tapped density (Kg/cm^3)	Cars index	Hausner ratio	Angle of repose (˚)
NF1	0.42	0.53	16.4	1.42	13.63
NF2	0.41	0.47	12.2	1.6	13.28
NF3	0.52	0.59	14	1.17	12.59
NF4	0.45	0.52	12.8	1.24	8.28
NF5	0.38	0.48	16.2	1.58	17.24
NF6	0.43	0.53	18.3	1.46	12.25
NF7	0.35	0.38	8.7	1.34	12.04
NF8	0.42	0.51	17	1.52	16.34
NF9	0.38	0.49	17	1.24	12.95
NF10	0.42	0.52	18.5	1.54	13.25
NF11	0.43	0.53	14.4	1.41	14.61
NF12	0.40	0.46	8.7	1.2	12.84

Table 3 Studies on Nevirapine SR tablets after compression

Formulation Code	% weight variation	Thickness	% Friability	%Drug Content	Hardness (Kg/cm^2)
NF1	Pass	3.17±0.12	0.23	103.0 ±1.1	4.67 ±0.16
NF2	Pass	3.52±0.16	0.16	102.2 ±1.4	5.14 ±0.14
NF3	Pass	4.05±0.058	0.13	99.7±1.2	5.57 ±0.12
NF4	Pass	5.2±0.13	0.44	102.6 ±0.7	5.97 ±0.03
NF5	Pass	3.04±0.04	0.33	100.7±1.3	4.62 ±0.04
NF6	Pass	3.84±0.16	0.15	99.8 ±2.2	5.3 ±0.03
NF7	Pass	4.94±0.06	0.21	98.3 ± 1.6	5.6 ±0.11
NF8	Pass	5.27±0.12	0.34	99.4 ± 1.3	5.92 ±0.04
NF9	Pass	3.03±0.3	0.19	99.3 ±1.4	4.38 ±0.03
NF10	Pass	3.48±0.14	0.21	100.3 ±1.4	4.86 ±0.03
NF11	Pass	4.91±0.18	0.32	101.2± 1.6	5.72 ±0.12
NF12	Pass	5.14±0.12	0.16	100.3 ±1.8	5.89 ±0.13

Table 4 In-vitro Dissolution results of Formulation trails

Time (hrs)	% Drug Released											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
1	43	15	21	15	52	44	24	21	19	12	11	6
2	54	24	31	21	63	48	39	33	24	18	14	12
3	65	36	43	36	74	57	53	42	28	24	18	19
4	78	49	51	44	82	64	58	48	39	34	21	27
6	88	71	65	56	92	77	66	57	44	42	27	35
8	97	84	77	67	100	87	74	61	53	48	35	41
10	100	98	84	73	100	95	82	68	67	52	45	48
12	100	100	91	82	100	100	92	75	77	64	54	55

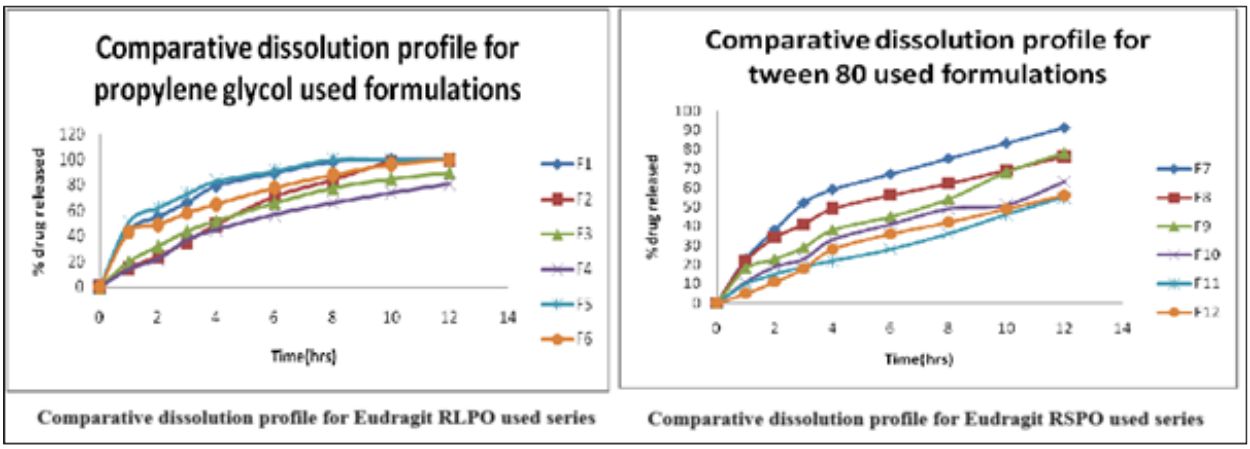

Figure 2 Comparative dissolution profiles of the utilized series of Eudragit RLPO and Eudragit RSPO

Table 5 R2 value and n result table

Formulation Code	R square value				n value
	Zero-order	First order	Higuchi plot	Peppas plot	
NF1	0.867	0.994	0.973	0.972	0.355
NF2	0.980	0.984	0.980	0.988	0.814
NF3	0.961	0.999	0.996	0.990	0.613
NF4	0.970	0.996	0.990	0.979	0.718
NF5	0.825	0.991	0.953	0.967	0.289
NF6	0.915	0.976	0.991	0.984	0.366
NF7	0.935	0.990	0.994	0.970	0.526
NF8	0.936	0.987	0.997	0.988	0.479
NF9	0.986	0.985	0.986	0.981	0.600
NF10	0.976	0.990	0.988	0.988	0.687
NF11	0.992	0.990	0.974	0.983	0.670
NF12	0.985	0.996	0.976	0.975	0.965

Good correlation values in the model Higuchi plots for the F2 formulation indicate that the Drug is released through a diffusion mechanism.

SUMMARY AND CONCLUSION

The current study's methodology involved comparing the two polymers, argum, and xanthumgum, and evaluating the impact of the active components' physicochemical makeup on the drug release profile utilizing the liquid solid compact method using Tween 80 and propylene glycol.

The formulation is appropriate for wet granulation, according to the sieve analysis results, compressibility index, and angle of repose.

According to this study, the Nevirapine can be administered via an extended-release drug delivery system because its formulation prolongs its duration of action within the therapeutic range without causing toxicity as with conventional dose forms. These dosage forms provide the capacity to increase and decrease the frequency of doses.

From an industry perspective, the method used to prepare the matrix system—wet granulation—is efficient and cost-effective.

Based on the findings, we can verify that the drug release mechanism from sustained release matrix tablets follows the Higuchi model and that the drug release order is first.

The product should be studied in vivo further if the in vitro drug release trials prove successful, as this could increase patient compliance.

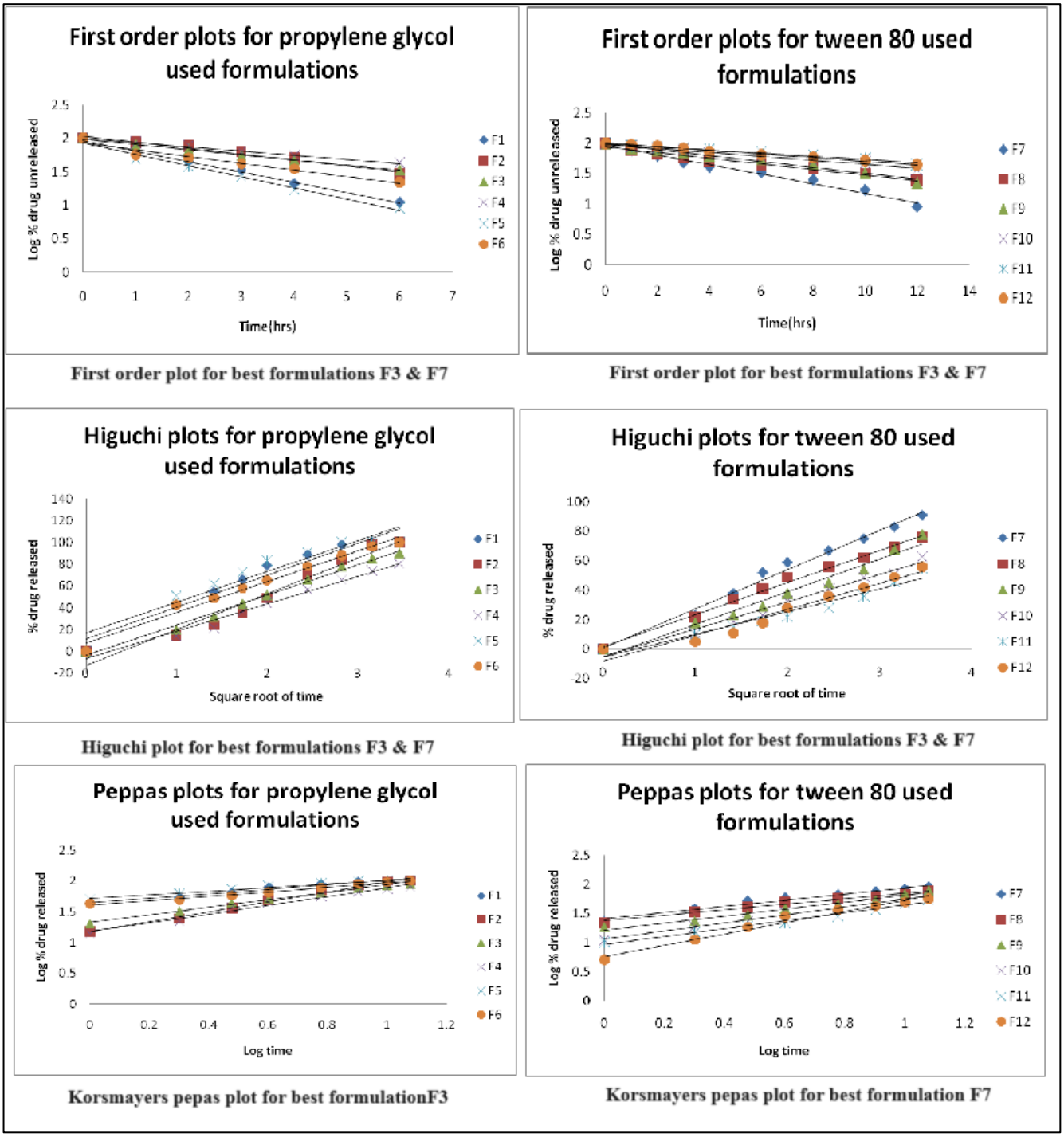

Figure 3 Release order Kinetics plots for best formulations

ACKNOWLEDGEMENT:

The corresponding author desires to express gratitude to the management of Saastra College of Pharmaceutical Education & Research, Jwalamukhi temple, Varigonda, Nellore, India, for their constant support in completing this research work.

Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

Funding Support

The authors declare that they have no funding for this study.

REFERENCES

[1] Mandal U, Gowda V, Ghosh A, Selvan S, Solomon S, Kumar Pal T, et al. Bioequivalence Study of Two Formulations Containing 400 mg Dexibuprofen in Healthy Indian Subjects. Arzneimittel-Forschung/Drug Research. 2008;58(7):342-347.

[2] Hussain Shah SN, Asghar S, Akram Choudhry Md, Sajid Hamid Akash Md, Rehman NU, Baksh S, et al. Formulation and evaluation of natural gum-based sustained-release matrix tablets of flurbiprofen using response surface methodology. Drug Development and Industrial Pharmacy. 2009;35(12):1470-1478.

[3] Dhopeshwarkar V, O'Keeffe JC, Zatz JL, Deete R, Horton M, et al. Development of An Oral Sustained-Release Antibiotic Matrix Tablet Using In-Vitro/In-Vivo Correlations, Drug Development and Industrial Pharmacy. 1994; 20(11):1851-1867.

[4] Skoug JW, Mikelsons MV, Vigneron CN, Stemm NL, et al. Qualitative evaluation of the mechanism of release of matrix sustained release dosage forms by measurement of polymer release. Journal of Controlled Release. 1993;27:227-245.

[5] Zaara Majeed, Faheem Unnisa Begum, Asfia Kauser, Sumaiya Sultana, Humera Sultana, Fareeha Mirza, Husna Fatima, Najma Shaheen, et al. Formulation and In-Vitro Evaluation of Lamivudine Sustained. IOSR Journal of Pharmacy and Biological Sciences. 2018;13(2):01-15.

[6] Yeole PG, Galgatte UC, Babla IB, Nakhat PD, et al. Design and evaluate xanthan gum-based sustained-release matrix tablets of diclofenac sodium. Indian Journal of Pharmaceutical Sciences. 2006;68(2):185-189.

[7] Morkhade DM, Fulzele SV, Satturwar PM, Joshi SB, et al. Gum Copal and Gum Damar: Novel Matrix forming Materials for Sustained Drug delivery. Indian Journal of Pharmaceutical Sciences. 2006; 53-58.

[8] Gonullu U, Uner M, Yener G, et al. Introduction of sustained release Opipramol Di hydrochloride matrix tablets as a new approach in the treatment of depressive disorders. International Journal of Biomedical Science. 2006; 2(4):337-343.

[9] Srivastava AK, Wadhwa S, Mishra B, et al. Oral sustained delivery of Atenolol from floating matrix tablets - formulation and in vitro evaluation. Drug development and industrial pharmacy. 2005;31(4-5):367-374.

[10] Dindigala, A. K., Reddy, C. S., & Makineni, A. Enhancement of Solubility and Dissolution Rate of Simvastatin Tablets by Liquisolid Compact Approach. Journal of Drug Delivery and Therapeutics, 2024; *14*(8), 64-72. https://doi.org/10.22270/jddt.v14i8.6733

[11] Reza Siahi Md, Barzegar-Jalali Md, Monajjemzadeh F, et al. Design and Evaluation of 1- and 3-layer Matrices of Verapamil Hydrochloride for Sustaining Its Release. AAPS PharmSciTech. 2005;6(4): E626-E632.

[12] Corti G, Cirri M, Maestrelli F, Mennini N, et al. Sustained-release matrix tablets of metformin hydrochloride in combination with triacetyl-β-cyclodextrin. European Journal of pharmaceutics and biopharmaceutics. 2008;68(2):303-309.