ORIGINAL ARTICLE

Effect of Diluents on the Drug Release of Controlled-Release Matrix Tablets of BCS Class I Drugs

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Abstract

Objectives: This study aimed to assess the influence of soluble and insoluble diluents on drug release from the controlled-release (CR) matrix tablets of Biopharmaceutics Classification System (BCS) Class I drugs prepared with hydrophilic polymers. **Methods:** Tramadol hydrochloride (TDL HCl) and venlafaxine hydrochloride (VFX HCl)-CR matrix tablets (CR) were prepared with polymers of hydrophilic nature (Kollidon SR and xanthan gum) with and without diluents (insoluble and soluble, such as dicalcium phosphate, microcrystalline cellulose, lactose monohydrate, and mannitol). Pre-compression and post-compression parameters were evaluated for these CR tablets. *In vitro* drug release kinetics were evaluated using zero-order, first-order, and the mechanism was evaluated employing Higuchi, Peppas, and Hixson–Crowell. Model-independent parameters such as T_{50}, T_{75}, mean dissolution time $(MDT)_{50}$, MDT_{75}, f_1, and f_2 comparison were also performed. These model-dependent and model-independent methods were used to compare *in vitro* drug release between the formulations prepared with and without diluents. **Results and Conclusion:** The first order release was followed by all the formulations. The drug release in many cases followed an erosion mechanism in addition to the Higuchi diffusion mechanism from these tablets. The correlation coefficient values of these mechanisms are close to each other. The primary observation was that the presence of insoluble diluents (dicalcium phosphate and microcrystalline cellulose) in the hydrophilic matrix of VFX HCl tablets retarded the drug release significantly. However, water-soluble diluents (lactose monohydrate and mannitol) enhanced the drug release when incorporated in the hydrophilic matrix of VFX HCl with synthetic polymer (Kollidon SR) only, and did not affect the release when the natural polymer (xanthan gum) was used. Diluents did not influence drug release in the case of the TDL HCl formulation prepared with hydrophilic polymers.

Key words: Controlled release, diluents, drug release kinetics, hydrophilic polymers, tramadol hydrochloride, venlafaxine hydrochloride

INTRODUCTION

Controlled release (CR) formulations using various polymers effectively modulate drug release. While many studies have examined polymer influence, little is known about the impact of diluents on CR formulations.[1] This study investigates how diluents affect drug release from CR matrix tablets of tramadol hydrochloride (TDL HCl) and venlafaxine hydrochloride (VFX HCl), which are Biopharmaceutics Classification System (BCS) Class I drugs with similar solubility, molecular weight, and dose (100 mg). Their comparable physicochemical and pharmacokinetic properties make them ideal for evaluating diluent effects on drug release.[2,3]

METHODS

Drug-excipient compatibility studies

Compatibility between drug and excipients was done by subjecting the drug-excipient physical mixtures at 40 ± 2°C, 75 ± 5% RH for 1 month, and then analyzing the interaction through physical evaluation, differential scanning calorimetric

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Received: 22-01-2026
Revised: 06-03-2026
Accepted: 16-03-2026

(DSC), and Fourier transmission infrared spectrophotometric (FTIR) evaluation.[4-8]

In vitro estimation of TDL HCl and VFX HCl

TDL HCl and VFX HCl showed maximum absorbance at 271 nm and 275 nm, respectively. Drug estimation in 1:3 drug-polymer (Kollidon SR and xanthan gum) mixtures was done in 0.1N HCl using regression equations from absorbance-concentration plots, and triplicate experiments were averaged for accuracy.[9-12]

Solubility studies

A solubility study of both drugs was quantified in 0.1N HCl (pH 1.2) by the equilibrium method, shake-flask technique in an orbital shaking incubator (Geiotech, SI 600R).[13,14]

Preparation of matrix tablets of TDL HCL and VFX HCL

The different matrix formulations of TDL HCl and VFX HCl were prepared using the selected polymers and diluents using the direct compression technique.

Evaluation of pre-compression blend

All the formulations of TDL HCl and VFX HCl pre-compression blend were subjected to evaluation of micromeritic properties. Using the bulk density and tapped density values, Hausner's ratios and Carr's index were determined.[15-17]

Evaluation of tablets

Evaluation tests for appearance, hardness, thickness, uniformity of weight, friability, drug content,[18] and *in vitro* dissolution were performed for the compressed tablets.[18-21]

Drug content estimation

100 mg of drug equivalent powder was weighed and dissolved in 50 mL of 0.1N HCl. After suitable dilution, drug content was measured at 271 nm for TDL HCl and at 275 nm for VFX HCl using a calibration curve. Each drug content estimation was done in triplicate.

In vitro dissolution studies

Based on the recommendation given by OGD for TDL HCl extended release tablets, the media was selected as 0.1N HCl. Considering that both drugs have similar saturated solubility in 0.1N HCl, as shown in Table 1, the same medium was considered for both drugs.[22]

Evaluation of drug release

Model-dependent approaches and model-independent approaches were used for drug release evaluation. In model-dependent methods, zero-order and first-order were used for release kinetics. Higuchi, Erosion, and Peppa's equations were used for establishing the mechanism of release.

Under model-independent approaches, ratio test procedures, mean dissolution time (MDT), difference factor (f_1), and similarity factor (f_2) were used.[23-32]

Evaluation of apparent intrinsic dissolution[33]

The intrinsic dissolution was carried out using 500 mL 0.1N HCl as media with a stirring speed of 50 rpm and at 37 ± 0.5°C.

Evaluation of solubility parameters

The solubility parameters of the drugs and polymers were evaluated following Hoy's solubility parameter method.[34,35]

$$\delta(tot)^2 = \delta D^2+\delta P^2+\delta H^2$$

Table 1: Concentration versus absorbance for TDL HCl and VFX HCl in 0.1 N HCl

Concentration versus absorbance for TDL HCl		Concentration versus absorbance for VFX HCl	
Concentration (µg/mL)	**Absorbance (Mean±SD, *n*=3)**	**Concentration (µg/mL)**	**Absorbance (Mean±SD, *n*=3)**
20	0.171±0.005	10	0.046±0.007
40	0.280±0.007	20	0.087±0.002
60	0.388±0.003	40	0.175±0.004
80	0.514±0.002	60	0.257±0.006
100	0.627±0.005	80	0.348±0.003
120	0.806±0.004	100	0.422±0.005
Regression equation	y=0.00646x+0.0161	Regression equation	y=0.0042x+0.0027
Correlation coefficient (r)	0.9970	Correlation coefficient (r)	0.9997

TDL HCl: Tramadol hydrochloride, VFX HCl: Venlafaxine hydrochloride, SD: Standard deviation

Stability study

The trial formulations of the same batch were kept under stability conditions, at accelerated conditions (40 ± 2°C, 75 ± 5% RH) for 6 months in a stability chamber (Thermolab, GMP model). Samples were withdrawn at 3- and 6-month time intervals and were evaluated for physical appearance, hardness, drug content, and drug release studies. Visual observation was used for physical appearance.[36]

RESULTS AND DISCUSSION

Compatibility studies

DSC thermograms showed endothermic peaks for TDL HCl and VFX HCl at 181.98°C and 210.8°C, respectively, closely matching reported melting points.[5,6,37] The added excipients also exhibited the respective melting peaks as reported.

FTIR analysis of individual drugs, pure excipients, stored at ambient temperature, and drug-excipient mixtures stored at 40 ± 2°C, 75 ± 5% RH for 4 weeks showed no new or missing peaks, confirming no drug–excipient interactions and good compatibility of both drugs with the excipients.

In vitro estimation of TDL HCl and VFX HCl

A good linear correlation was observed for both the drugs in the studied concentration range of 20–120 µg/mL and 10–100 µg/mL for TDL HCl and VFX HCl, respectively, in 0.1N HCl. The corresponding regression equations and slopes are shown in Table 1, Figures 1 and 2.[38-42]

In all the interference studies, more than 99.0% of the drug was estimated.

Solubility studies

Both the drugs showed similar solubility in 0.1N HCl media. TDL HCl shows 621.14 ± 0.75, and VFX HCl shows 625.04 ± 0.82 mg/mL. It is also reported in the literature that TDL HCl and VFX HCl show high pH-independent solubility across the physiological pH at 37°C.

Formulation of TDL HCl and VFX HCl matrix tablets

Matrix tablets were optimized using Kollidon SR and xanthan gum without a diluent, with a 1:3 drug-polymer ratio providing sustained 12-h release; hence, both TDL HCl and VFX HCl tablets were prepared using this ratio and evaluated for all formulation parameters. All the formulations were evaluated for pre-compression and post-compression parameters.

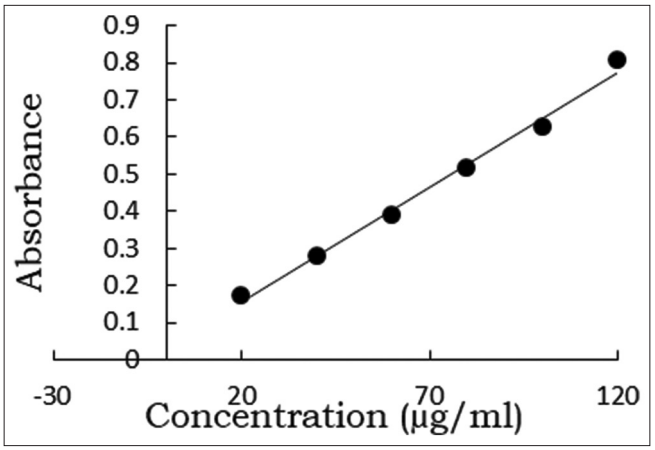

Figure 1: Standard graph for tramadol hydrochloride in 0.1 N HCl

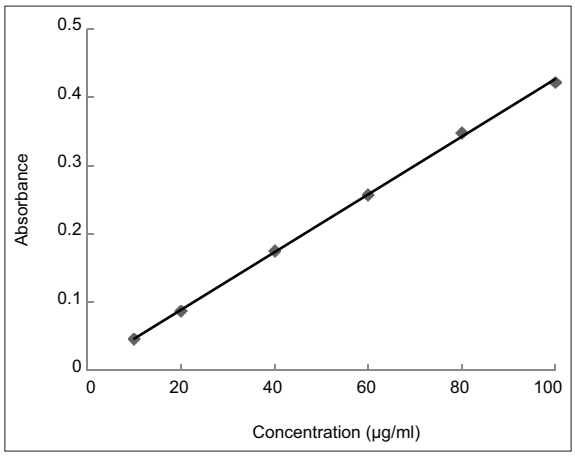

Figure 2: Standard graph for venlafaxine hydrochloride in 0.1N HCl

Pre-compression blend evaluation

The micromeritic properties of the different formulation blends of TDL HCl and VFX HCl indicated that all the pre-compression powder blends showed free-flowing properties with a good compressibility index. This also indicated that the polymers have low interparticle friction.

Evaluation of tablets

The different tablet characteristics were found to be acceptable as described in Table 2. The uniformity of weight, hardness, and friability was within the range of acceptable criteria, indicating good mechanical strength of the tablets. The percentage drug content varied between 98% and 102% in different formulations, indicating content uniformity in the prepared batches, which falls within the pharmacopeial limits.

In vitro dissolution studies

TDL HCl showed consistent 12-h release with a 1:3 drug-polymer ratio, unaffected by diluent type, whereas VFX HCl

Table 2: Properties of TDL HCl and VFX HCl matrix tablets

Formulation	Hardness[a] (kp)	Thickness[a] (mm)	Uniformity of weight[b] (mg)	Friability[c] (%)	% drug content[d]
TDL HCl matrix tablets					
TK	7.2±0.16	5.1±0.08	405±1.68	0.09	99.74±0.42
TKD	8.2±0.62	5.3±0.15	505±1.38	0.11	100.12±0.63
TKC	9.1±0.78	5.6±0.23	505±2.62	0.16	98.37±0.51
TKL	8.5±0.52	5.2±0.22	505±2.28	0.13	99.21±0.23
TKM	7.7±0.16	5.1±0.02	505±1.18	0.08	100.28±0.36
TX	7.4±0.62	5.3±0.13	405±1.58	0.21	99.37±0.45
TXD	9.1±0.78	5.0±0.18	505±2.61	0.16	101.83±0.82
TXC	8.7±0.52	5.2±0.25	505±1.69	0.25	99.02±0.77
TXL	8.1±0.78	5.6±0.12	505±2.38	0.19	100.55±0.56
TXM	8.9±0.52	5.4±0.26	505±2.28	0.22	99.91±0.63
VFX HCl matrix tablets					
VK	7.2±0.16	5.3±0.18	405±1.21	0.29	100.21±0.32
VKD	8.2±0.62	5.6±0.05	505±1.78	0.18	99.23±0.21
VKC	9.1±0.78	5.1±0.13	505±2.12	0.22	98.87±0.74
VKL	8.5±0.52	5.5±0.21	505±1.58	0.27	99.65±0.12
VKM	7.7±0.16	5.7±0.12	505±2.18	0.18	100.23±0.56
VX	7.4±0.62	5.9±0.23	405±1.88	0.25	100.12±0.51
VXD	9.1±0.78	5.1±0.11	505±1.69	0.36	99.74±0.85
VXC	8.7±0.52	5.2±0.15	505±2.65	0.29	99.23±0.13
VXL	8.1±0.78	5.5±0.22	505±2.38	0.16	100.11±0.68
VXM	8.9±0.52	5.4±0.26	505±1.28	0.24	98.61±0.91

[a]Mean±standard deviation, *n*=6, [b]Mean±%deviation, *n*=20, [c]*n*=16 (405 mg)/12 (505 mg), [d]Mean±standard deviation, *n*=3.
TDL HCl: Tramadol hydrochloride, VFX HCl: Venlafaxine hydrochloride

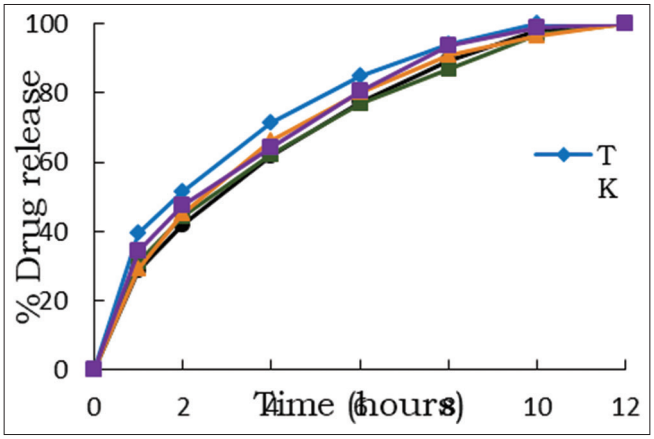

Figure 3: Tramadol hydrochloride – Kollidon SR matrix tablets dissolution profiles

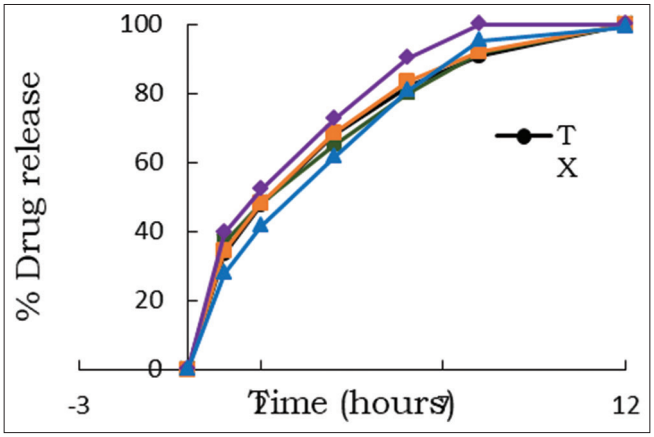

Figure 4: Tramadol hydrochloride – Xanthan gum matrix tablets dissolution profiles

release varied with water-soluble diluents, accelerated and insoluble diluents retarded release, especially with Kollidon SR.

The dissolution results are compiled in Tables 3 and 4, depicted in Figures 3-6.

The influence of diluents on the *in vitro* drug release of matrix tablets of TDL HCl and VFX HCl prepared with hydrophilic polymers was evaluated with model-independent parameters and summarized in Table 5.

Drug release kinetics showed that all TDL HCl and VFX HCl formulations followed first-order release; six TDL HCl formulations (TK, TKD, TKC, TKL, TXD, and TXL) followed the Higuchi diffusion mechanism, while others followed erosion-based release.

Table 3: Drug release data of TDL HCl-Kollidon SR matrix tablets and TDL HCl-xanthan gum matrix tablets (mean±standard deviation, *n*=6)

Time (Hours)	Drug release data of TDL HCl-Kollidon SR matrix tablets					Drug release data of TDL HCl-xanthan gum matrix tablets				
	TK	TKD	TKC	TKL	TX	TXD	TXC	TXL	TXM	TKM
1	39.5±0.39	28.7±0.43	31.2±0.56	29.2±0.62	33.7±0.53	36.8±0.41	34.5±0.59	39.4±0.62	27.8±0.70	34.4±0.59
2	51.4±0.41	41.9±0.44	44.1±0.48	44.9±0.51	47.7±0.41	48.0±0.48	48.0±0.48	51.9±0.58	41.6±0.48	47.3±0.48
4	71.5±0.53	61.8±0.52	62.0±0.44	66.0±0.48	68.2±0.48	64.9±0.53	68.7±0.53	72.4±0.52	61.4±0.55	64.2±0.51
6	85.0±0.43	77.3±0.61	76.9±0.52	80.3±0.56	81.7±0.58	80.0±0.59	83.4±0.44	90.2±0.48	80.7±0.67	80.4±0.64
8	94.0±0.59	89.3±0.48	87.1±0.61	90.8±0.70	97.7±0.66	96.8±0.69	96.9±0.68	99.1±0.67	98.1±0.43	93.9±0.68
12	100.0±0.49	100.0±0.53	100.0±0.71	100.0±0.58	100.0±0.70	100.0±0.66	100.0±0.71	100.0±0.43	100.0±0.61	100.0±0.39

TDL HCl: Tramadol hydrochloride, VFX HCl: Venlafaxine hydrochloride

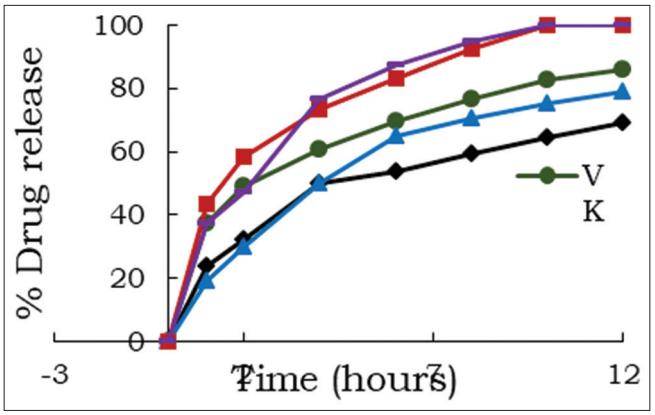

Figure 5: Venlafaxine hydrochloride – Kollidon SR matrix tablets dissolution profiles

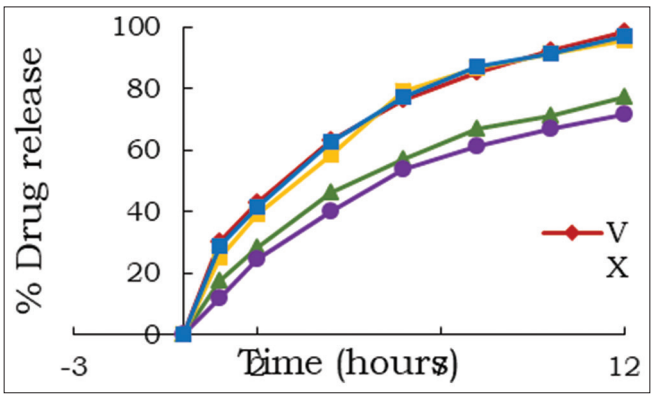

Figure 6: Venlafaxine hydrochloride – Xanthan gum matrix tablets dissolution profiles

TDL HCl formulations TK, TKM, TXD, and TXL followed Fickian diffusion, whereas others showed non-Fickian release; in VFX HCl, most (VK, VKD, VKC, VKL, VXD, and VXC) followed Higuchi diffusion, and VKM, VXL, and VXM followed erosion, with model-independent parameters (T_{50}, T_{75}, MDT_{50}, and MDT_{75}, f_1, f_2).

Evaluation of apparent intrinsic dissolution

The intrinsic dissolution rate of the two drugs was compared in 0.1N HCl and found to be 12.982 and 13.641 mg/0.5 cm^2 for TDL HCl and VFX HCl, respectively. No significant difference in the intrinsic dissolution rate of both drugs was observed.

Evaluation of solubility parameters

Although TDL HCl and VFX HCl have similar solubility and intrinsic dissolution rates, their release was differently influenced by polymers and diluents, prompting calculation of partial and total solubility parameters to assess these effects.

Both drugs have similar partial and total solubility parameters, suggesting similar solubility behavior; however,

Table 4: Drug release data of VFX HCl-Kollidon SR matrix tablets and VFX HCl-xanthan gum matrix tablets (mean±standard deviation, *n*=6)

Time (Hours)	Drug release data of VFX HCl-Kollidon SR matrix tablets					Drug release data of VFX HCl-xanthan gum matrix tablets				
	VK	VKD	VKC	VKL	VX	VXD	VXC	VXL	VXM	VKM
1	37.1±0.43	23.8±0.51	19.2±0.59	43.6±0.43	30.3±0.68	17.5±0.39	11.8±0.45	25.1±0.69	28.6±0.41	37.1±0.71
2	48.8±0.51	32.4±0.53	30.0±0.62	58.4±0.49	42.8±0.61	28.3±0.47	24.5±0.53	39.3±0.51	41.7±0.58	47.3±0.59
4	60.8±0.56	49.8±0.46	49.9±0.66	73.3±0.55	63.2±0.57	46.3±0.51	40.1±0.49	58.4±0.48	62.7±0.44	76.6±0.44
6	69.4±0.69	53.6±0.63	65.0±0.53	83.2±0.71	76.6±0.43	57.2±0.63	53.9±0.63	79.5±0.41	77.5±0.51	87.5±0.49
8	76.4±0.70	59.1±0.71	70.4±0.41	92.7±0.63	85.6±0.39	67.2±0.59	61.4±0.67	86.8±0.58	87.3±0.62	95.0±0.53
10	82.9±0.47	64.3±0.67	75.3±0.48	100.1±0.60	92.5±0.71	71.3±0.60	67.2±0.61	91.3±0.61	91.5±0.71	98.6±0.67
12	85.9±0.39	69.2±0.41	79.0±0.70	100.2±0.57	98.4±0.63	77.3±0.71	71.7±0.40	95.7±0.70	97.4±0.39	100±0.39

TDL HCl: Tramadol hydrochloride, VFX HCl: Venlafaxine hydrochloride

Table 5: Effect of diluents on drug release from Kollidon SR and Xanthan gum

Drug	Hydrophilic polymer	Effect of water-soluble diluent	Effect of water-insoluble diluent
TDL HCl	Kollidon SR	Non-significant	No Significant effect observed
	Xanthan gum	Non-significant	Non-significant
VFX HCl	Kollidon SR	Accelerated the release ↑	Drug release was retarded ↓
	Xanthan gum	Non-significant effect observed	Drug release was retarded ↓

TDL HCl: Tramadol hydrochloride, VFX HCl: Venlafaxine hydrochloride

TDL HCl release was unaffected by polymers or diluents, whereas VFX HCl release was slowed by insoluble diluents and slightly faster with soluble diluents, highlighting diluent impact on drug release.

The higher molecular weight of VFX (277.42) compared to TDL (263.39) results in a lower diffusion coefficient, explaining its slower diffusion-based release relative to TDL.[43]

Stability study

Stability studies showed that after 6 months at accelerated conditions (40 ± 2°C, 75 ± 5% RH), TDL HCl and VFX HCl matrix tablets retained appearance, hardness, drug content, and dissolution profiles, with f_2 values >50 confirming similarity to initial samples, indicating good stability.

CONCLUSION

The study concluded that water-insoluble diluents, when incorporated into the hydrophilic matrix of VFX HCl, retarded drug dissolution. In contrast, water-soluble diluents accelerated drug release when incorporated into the hydrophilic matrix of VFX HCl with the synthetic polymer only, and did not influence the release when a natural polymer was used. Moreover, none of the diluents influenced drug release in the case of the TDL HCl formulations. This difference was further investigated through a detailed evaluation of various properties, including saturated solubility, apparent intrinsic dissolution, and the solubility parameters of both the drugs and polymers. Based on this evaluation, the observed variation could be attributed to differences in the molecular weights of the two drugs, which may have resulted in variations in their diffusion coefficients and consequently led to differences in their release behavior. All formulations were found to be stable under accelerated storage conditions (40 ± 2°C/75 ± 5% RH) for 6 months, with no significant changes in tableting characteristics, drug content, or drug release behavior. The saturated solubility and intrinsic dissolution rates of both drugs were found to be very similar.

ACKNOWLEDGMENT

The authors are thankful to Mylan Laboratories for providing all the materials used in the study.

REFERENCES

1. Bruschi M. Strategies to modify the drug release from pharmaceutical systems. In: Bruschi M, editor. Strategies to Modify the Drug Release from Pharmaceutical Systems. United Kingdom: Woodhead Publishing; 2015. p. 87-194.
2. U.S. Food and Drug Administration. Drug Label Information;2008.Availablefrom:https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021692s005s007lbl.pdf [Last accessed on 2019 Apr 25].
3. U.S. Food and Drug Administration. Drug Label

Information;2008.Availablefrom:https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/020699s081lbl.pdf [Last accessed on 2019 Aug 25].
4. U.S. Food and Drug Administration. Quality by Design for ANDAs. Available from: https://www.fda.gov [Last accessed on 2025 Dec 17].
5. DrugBank. Drug Information DB00193. Available from: https://www.drugbank.ca/drugs/db00193 [Last accessed on 2017 Oct 10].
6. Sigma-Aldrich. Safety Data Sheet: Sigma 42965. Version 3.10. United States: Sigma-Aldrich; 2017.
7. O'Neil MJ, editor. The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals. 12th ed. Whitehouse Station, NJ: Merck & Co.; 1996. p. 1695.
8. Gavaskar B, Vijaya Kumar S, Dodda D. Effect of tablet formulation variables on tramadol HCl elementary osmotic pump tablet. Int J Contemp Res Rev 2010;1:1-4.
9. Swain S, Behera A, Dinda SC, Patra CN, Jammula S, Beg S, *et al*. Formulation design, optimization and pharmacodynamic evaluation of sustained release mucoadhesive microcapsules of venlafaxine HCl. Indian J Pharm Sci 2014;76:354-63.
10. Pharmacopeia US. National Formulary (USP 36-NF 31). Rockville, MD: United States Pharmacopeial Convention; 2013. p. 5438-9.
11. Kucuk A, Kadioglu Y. Determination of tramadol hydrochloride in ampoule dosage forms by using UV spectrophotometric and HPLC-DAD methods in methanol and water media. Farmaco 2005;60:163-9.
12. United States Pharmacopeial Convention. Committee of Revision. United States Pharmacopeia, the National Formulary. United States Pharmacopeial Convention, Incorporated. Rockville, MD: United States Pharmacopeial Convention; 2013. p. 5554-5.
13. Rathore GS, Basniwal PK, Suthar M, Gupta RN. Spectrophotometric estimation of venlafaxine hydrochloride. Asian J Chem 2009;21:5908-12.
14. Higuchi T, Connors KA. Phase solubility studies. Adv Anal Chem Instrum 1965;4:117-212.
15. Dezani AB, Pereira TM, Caffaro AM, Reis JM, Serra CH. Equilibrium solubility versus intrinsic dissolution: Characterization of lamivudine, stavudine and zidovudine for BCS classification. Braz J Pharm Sci 2013;49:853-63.
16. Rockville MD. United States Pharmacopeia and National Formulary (USP 35-NF 30). Rockville, MD: United States Pharmacopeial Convention; 2012. p. 801-2.
17. Pharmacopoeia I. Ghaziabad: Indian Pharmacopoeia 2014. Ghaziabad: Indian Pharmacopoeia Commission; 2014. p. 256-8.
18. Lazarus J, Cooper J. Absorption, testing, and clinical evaluation of oral prolonged-action drugs. J Pharm Sci 1961;50:715-32.
19. Pharmacopoeia I. Ghaziabad: Indian Pharmacopoeia 2014. Vol 2. Ghaziabad: Indian Pharmacopoeia Commission; 2014. p. 1553-4.
20. U.S. Food and Drug Administration. Dissolution Database. Available from: https://www.accessdata.fda.gov/scripts/cder/dissolution [Last accessed on 2012 Feb 20].
21. Wagner JG. Interpretation of percent dissolved-time plots derived from *in vitro* testing of conventional tablets and capsules. J Pharm Sci 1969;58:1253-7.
22. Higuchi T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci 1963;52:1145-9.
23. Hixson AW, Crowell JH. Dependence of reaction velocity upon surface and agitation. Ind Eng Chem 1931;23:923-31.
24. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. Int J Pharm 1983;15:25-35.
25. Peppas NA. Analysis of Fickian and non-Fickian drug release from polymers. Pharm Acta Helv 1985;60:110-1.
26. Costa P, Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci 2001;13:123-33.
27. Qiu Y. *In vitro-in vivo* correlations: Fundamentals, development considerations, and applications. In: Qiu Y, Chen Y, Zhang GGZ, Liu L, editors. Developing Solid Oral Dosage Forms: Pharmaceutical Theory and Practice. New York: Academic Press; 2009. p. 379-406.
28. Podczeck F. Comparison of *in vitro* dissolution profiles by calculating mean dissolution time (MDT) or mean residence time (MRT). Int J Pharm 1993;97:93-100.
29. Rinaki E, Dokoumetzidis A, Macheras P. The mean dissolution time depends on the dose/solubility ratio. Pharm Res 2003;20:406-8.
30. European Medicines Agency. Guideline on the Investigation of Bioequivalence. Available from: https://www.ema.europa.eu [Last accessed on 2012 Aug 18].
31. Rockville MD. United States Pharmacopeia and National Formulary (USP 35-NF 30). Rockville, MD: United States Pharmacopeial Convention; 2012. p. 660-3.
32. Hoy KL. Solubility parameter as a design parameter for water borne polymers and coatings. J Coated Fabrics 1989;19:53-67.
33. International Council for Harmonisation (ICH). Stability Testing of New Drug Substance and Products Q1A(R2). Available from: https://www.ich.org/page/quality-guidelines [Last accessed on 2012 Jun 12].
34. Miyazaki T, Sivaprakasam K, Tantry J, Suryanarayanan R. Physical characterization of dibasic calcium phosphate dihydrate and anhydrate. J Pharm Sci 2009;98:905-16.
35. Sahoo J, Murthy PN, Biswal S, Manik. Formulation of sustained-release dosage form of verapamil hydrochloride by solid dispersion technique using Eudragit RLPO or Kollidon®SR. AAPS PharmSciTech 2009;10:27-33.
36. Kumaresan G, Velraj R, Iniyan S. Thermal analysis of D-mannitol for use as phase change material for latent heat storage. J Appl Sci 2011;11:3044-8.
37. Ciolacu D, Ciolacu F, Popa VI. Amorphous cellulose - structure and characterization. Cellul Chem Technol 2011;45:13-21.

38. Zohurian MJ, Shokrolahi F. Thermal studies on natural and modified gums. Polym Test 2004;23:575-9.
39. Coates J. Interpretation of infrared spectra, a practical approach. In: Meyers RA, editor. Encyclopedia of Analytical Chemistry. Chichester: John Wiley and Sons; 2000. p. 10815-37.
40. Brittain HG, editor. Profiles of Drug Substances, Excipients and Related Methodology. Vol. 45. United States: Academic Press; 2020. p. 466.
41. Mandic CZ, editor. Physico Chemical Methods in Drug Discovery and Development. Vol. 1. New Delhi: IAPC Publishing; 2012. p. 48-9.
42. Mircioiu C, Voicu V, Anuta V, Tudose A, Celia C, Paolino D, *et al*. Mathematical modeling of release kinetics from supramolecular drug delivery system. Pharmaceutics 2019;11:140.
43. Hishikawa Y, Kakino Y, Tsukamoto H, Tahara K, Onodera R, Takeuchi H. Control of drug diffusion behavior of xanthan and locust bean gum gel by agar gel. Chem Pharm Bull (Tokyo) 2016;64:1450-7.

Source of Support: Nil. **Conflicts of Interest:** The authors declare no conflict of interest. One of the authors (Santanu Chakrabortty) is an employee of Mylan Laboratories Ltd.