IAR Journal of Medicine and Surgery Research
ISSN Print : In Process | **ISSN Online :** In Process
Frequency : Bi-Monthly
Language : English
Origin : KENYA
Website : https://www.iarconsortium.org/journal-info/IARJMSR

OPEN ACCESS JOURNALS

Research Article

Release Kinetic Study of Matrix Type Transdermal Patch Using an Analgesic Drug

Article History

Received: 05.07.2020
Accepted: 22.07.2020
Revision: 29.07.2020
Published: 05.08.2020

Author Details

Mohit Saini*[1] Sneha Singh[1], Amit Kumar[2] Lalit Parihar[3] and Mukesh Kumar[4]

Authors Affiliations

[1]Aroma College Roorkee, Haridwar (UK), India

[2]Smt. Manjira Devi Shikshan and Prashikshan Institute Hitanu Dhanari, Uttarkashi, India

[3]R.V.Northland Institute, G.T.road Dadri Greater Noida, Gautam Budh Nagar, (UP), India

[4]Dr. K. N. Modi Institute of Pharmaceutical Education and Research, Modinagar, (UP), India

Corresponding Author*
Gladys Modupe Kayode

How to Cite the Article:
Mohit Saini *et al.*, (2020) Release Kinetic Study of Matrix Type Transdermal Patch Using an Analgesic Drug. *IAR J. Med & Surg Res. 1(1)*1-8.

Copyright @ 2020: This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

Abstract: Transdermal therapeutic systems are defined as a self-contained, distinct dosage forms which, when applied to the intact skin, deliver the drug, through the skin at control rate to the systemic circulation. TDDS characterizes one of the most quickly advancing areas of novel drug delivery. TDDS are designed for controlled liberate of drug through the skin into systemic circulation maintaining consistent efficacy and reducing dose of the drug and its related side effects. Present study was conducted to prepare transdermal patch of Tramadol HCL with permeation enhancer to diminish extra side effects and to provide sustain drug delivery. Various kinetics models were examined for optimized formulation. The drug release data of all the formulation were fitted to different kinetic models to find out the kinetics of drug release from transdermal patch. The drug release data was also fitted to zero order (cumulative amount of drug release vs. time) power equation to find out the drug release mechanism.

Keywords: Release Kinetics, TDDS patch & Tramadol HCL.

INTRODUCTION

Transdermal drug delivery systems (TDDS), also called as "transdermal patches," are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. In order to transport therapeutic agents through the human skin for systemic effects, the comprehensive morphological, biophysical and physicochemical properties of the skin are to be considered. Transdermal delivery provides a foremost edge over injectable and oral routes by increasing patient compliance and avoiding first pass metabolism respectively (Jain, N. K. (Ed.). 2008).There are many advantages associated with Transdermal drug delivery systems (Prabhakar, D. *et al.*,2013):

- Drugs avoid the hepatic and pre systemic metabolism thereby increasing bioavailability (Budavari, S., Eds. 2001).
- Risks and inconveniences of IV therapy are avoided (Kathleen, P. 1999).
- Dose frequency reduced and predictable sustained and extended duration of action (Soni, H. *et al.*,2020).
- Easy termination of drug therapy.
- It gives superior patient compliance due to elimination of multiple dosing intervals (Ramkanth, S. *et al.*,2010).
- Enhanced therapeutic efficiency by avoiding the peaks and troughs in systemic drug levels associated with conventional delivery (Kumar, D., & Kumar, A. 2020).
- Self –administration.

Tramadol belongs to the anisole group containing a methoxybenzene or a derivative. Tramadol hydrochloride, (±) cis-2-[(dimethylamino) methyl]-1-(3- methoxyphenyl) cyclohexanol Hydrochloride (Budavari, S., Eds. 2001). Tramadol Hydrochloride is a narcotic like analgesic used in severe pain. Tramadol has inhibitory action on 5-HT2C receptor and even though the parent and M1 metabolite of Tramadol binds to μ opioid receptors and results in weak inhibition and reuptake of norepinephrine and serotonin. In several animal tests Tramadol-induced analgesia is only partially antagonized by the opiate antagonist naloxone (Kumar, D. *et al.*,2019; Kumar, A. *et al.*,2019; Tiwari, D. 2017; Kumari, P. 2017; & Singh, S. *et al.*,2015). Present study was conducted to prepare transdermal patch of Tramadol HCL and release kinetic studies with the help of different models.

MATERIAL AND METHOD

Drug: Tramadol hydrochloride was obtained as gift sample from JubilantChemsys Ltd., Noida.
Polymers: HPMC E15was obtained fromJegchem Universal, Mumbai and Eudragit RS100, Eudragit RL100 and Eudragit RE 100 were obtained from TriownChemie, Ahmedabad.
Plasticizer: PEG 400 was used.
Solvents: Acetone, phosphate buffer.
Other reagents: Di sodium hydrogen phosphate, sodium hydroxide, potassium di hydrogen orthophosphate

Formulation Development

The tramadol hydrochloride transdermal patches were prepared by solvent casting technique. The polymeric solution was prepared by dissolving Eudragit RS 100, RL100 and Hydroxypropyl methyl cellulose E15 (Eudragit RS100: HPMC E15), (Eudragit RL100: HPMC E15) and (Eudragit RS100: Eudragit RL100) in different ratios, along with drug, in acetone (Dan, S. *et al.*,2011). The solution was poured into a glass ring placed on the surface of backing membrane and aluminum foil kept in a Petri dish. Backing membrane was prepared by the Eudragit E. The patches were kept at room temperature to evaporate the solvent overnight (Soni, H. *et al.*,2020; Soni, S. 2019; & Tiwari, P., & Malik, J. K. 2020). The patches were cut to desire size and stored in desiccator until use.

***In Vitro* Drug Released Studies**

The in-vitro drug released studies of the patches was carried using modified KesharyChienFranz diffusion cell. The cylinder consists of two chambers, the donor and the receptor compartment. The donor compartment was unfasten at the top and was exposed to atmosphere. The temperature was maintained at 37 ± 0.5̊C and receptor compartment was provided with sampling port. The diffusion medium used was phosphate buffer (pH 7.4). The diffusion was carried out for 10 hours at an interval one hour for 10 hours (1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 hour). 5 ml sample was withdrawn from the same volume of phosphate buffer pH 7.4 was added to receptor compartment to maintain sink conditions and the samples were analyzed at 271nm in UV spectrophotometer (Ramkanth, S. *et al.*,2010).To the study mechanism of drug release from these formulations, the data were treated according to zero order (cumulative amount of drug release vs. time), first order (log cumulative release amount of drug vs. time) and Higuchi's (cumulative amount of drug released vs. square root time) pattern.

Modified kesharychien diffusion cell

Release kinetic evaluation

A release data were settled to different mathematical model to reveal the release mechanism. Zero order, first order and higuchi release model were used for this purpose.All curve sitting and plotting was performed using MS-Excel solver.

RESULT AND DISCUSSION

In the present study Tramadol hydrochloride loaded transdermal patches were formulated using Eudragit RS 100, Eudragit RL 100 and HPMC E15 in different combination as matrix forming agent and polyethylene glycol 400 (PEG 400) is used as plasticizer. The patches were prepared by varying the ratio of two polymers in each group and also by varying the quantity of plasticizer to understand their impact on the responses (table.1-3). The *in-vitro* drug

release result showed in fig 1-9 for different models. The correlation of coefficient of group1 to3 was tabulated in table 4-6 respectively. The drug release data of all the formulations were fitted to different kinetic models to find out the kinetics of drug release from transdermal patch. The drug release data was also fitted to zero order (cumulative amount of drug release vs. time) power equation to find out the drug release mechanism. The drug release data was also fitted to zero order (cumulative amount of drug release vs. time) power equation to find out the drug release mechanism. The data obtained from the current work suggest the possibility of developing the drug into transdermal patch. The release of drug in all group of formulation was found to be similar and slow (release after 10 hours 54.35%).

CONCLUSION

The result of present works showed that release the drug in planned, predictable and slower than normal approach. Therefore, transdermal patch can be used a suitable device for long term management of pain. The TDDS for analgesic drug had been suggested in many articles. The present study confirms that the TD patch can improve the therapeutic efficacy of poorly water soluble drugs like Tramadol. The slow releases of the tramadol revealed that drug remains localized for a longer period of time and attain prolong therapeutic action.

Table 1: Different formulation of group - 1

S.NO.	FORMULATION CODE	RATIO OF POLYMER	EUDRAGIT RS100 (mg)	HPMC E15 (mg)	DRUG (mg)	PLASTICIZER (ml)
1.	F1	2:1	240	120	360	0.2
2.	F2	1:1	180	180	360	0.2
3.	F3	1:2	120	240	360	0.2
4.	F4	2:1	320	160	240	0.2
5.	F5	1:1	240	240	240	0.2
6.	F6	1:2	160	320	240	0.2

Table2: Different formulation of group - 2

S.NO.	FORMULATION CODE	RATIO OF POLYMER	EUDRAGIT RL100 (mg)	HPMC E15 (mg)	DRUG (mg)	PLASTICIZER (ml)
1.	F1	2:1	240	120	360	0.2
2.	F2	1:1	180	180	360	0.2
3.	F3	1:2	120	240	360	0.2
4.	F4	2:1	320	160	240	0.2
5.	F5	1:1	240	240	240	0.2
6.	F6	1:2	160	320	240	0.2

Table 3: Different formulation of group- 3

S.NO.	FORMULATION CODE	RATIO OF POLYMER	EUDRAGIT RS100 (mg)	EUDRAGIT RL100 (mg)	DRUG (mg)	PLASTICIZER (ml)
1.	F1	2:1	240	120	360	0.5
2.	F22	1:1	180	180	360	0.5
3.	F3	1:2	120	240	360	0.5
4.	F4	2:1	320	160	240	0.5
5.	F5	1:1	240	240	240	0.5
6.	F6	1:2	160	320	240	0.5

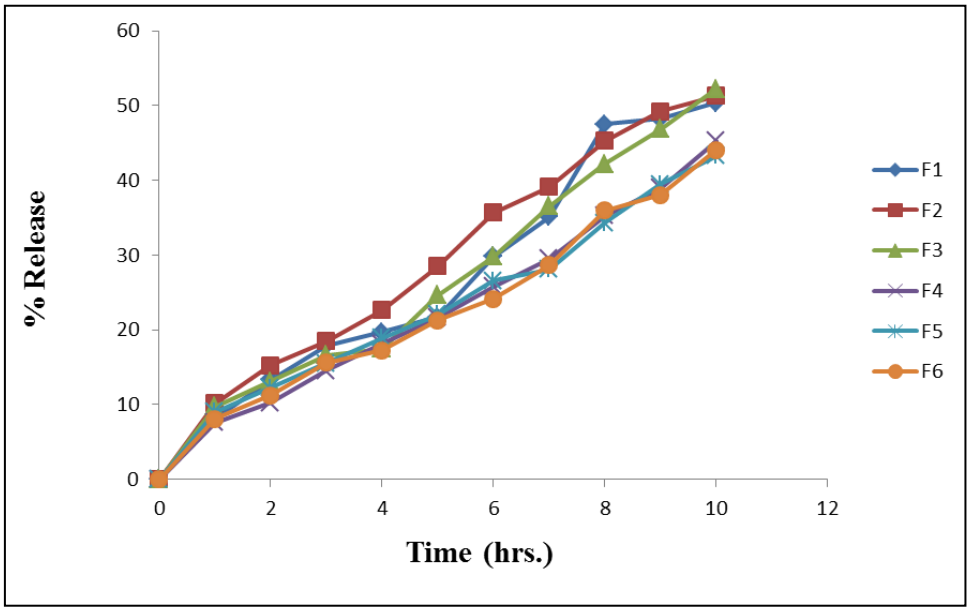

Figure 1: Zero order release curve of group-1

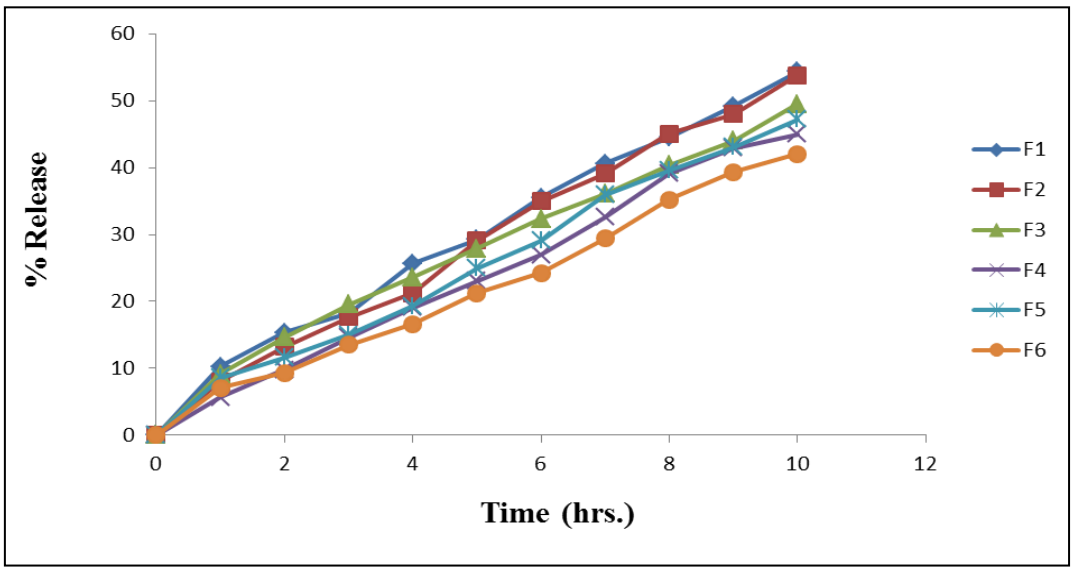

Figure 2: Zero order release curve of group-2

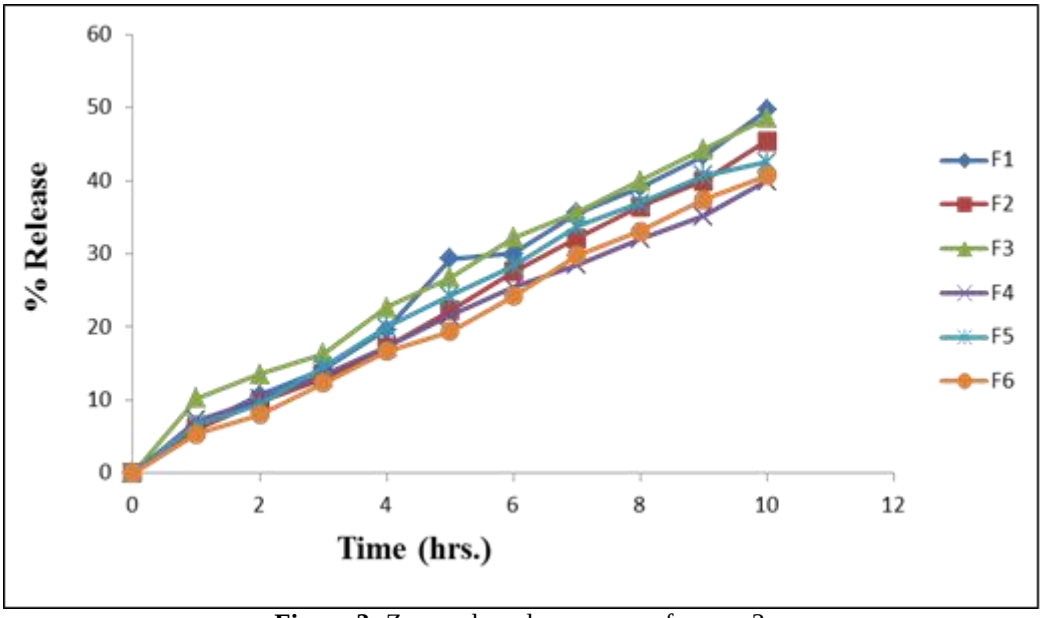

Figure 3: Zero order release curve of group-3

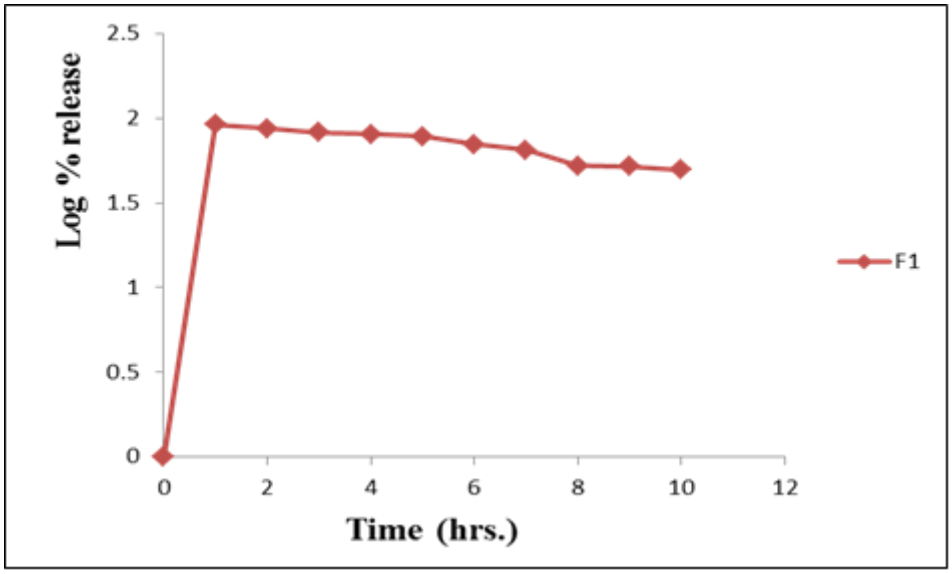

Figure 4: First order release curve group-1 (Formulation code F1)

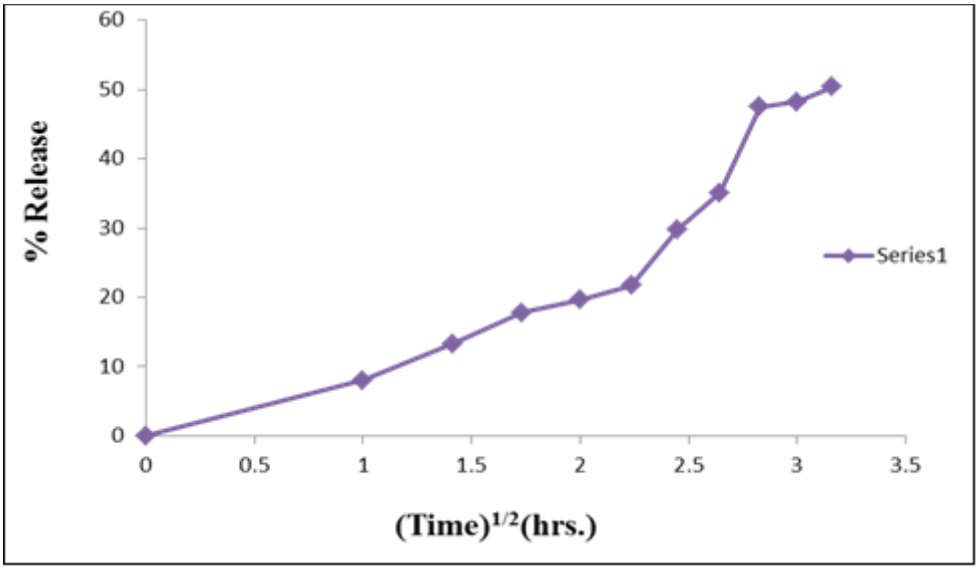

Figure 5: Higuchi release curve of group-1 (Formulation code F1)

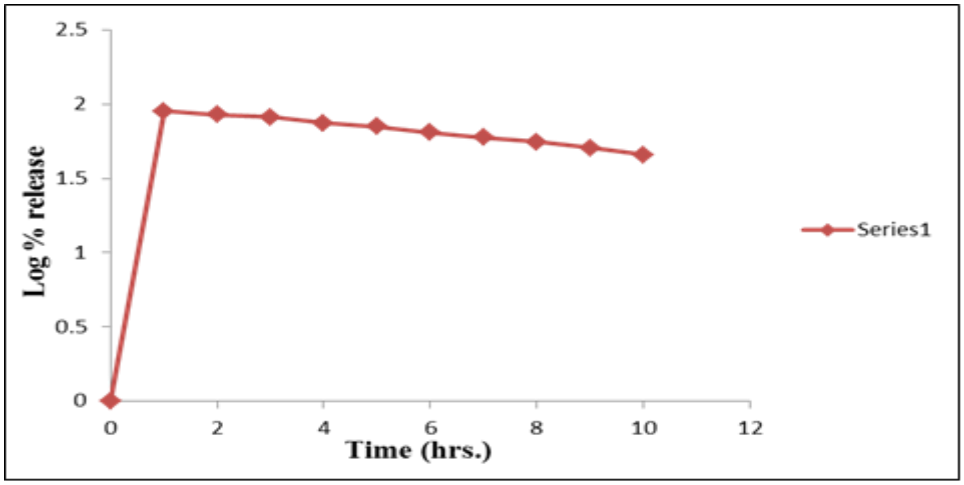

Figure 6: First order release curve of group-2 (Formulation code F1)

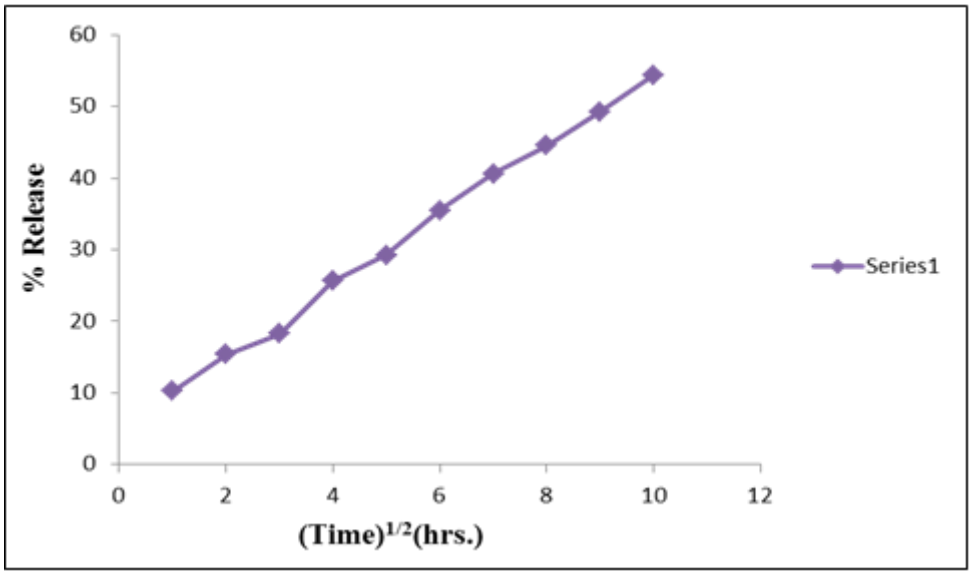

Figure 7: Higuchi release curve of group-2 (Formulation code F1)

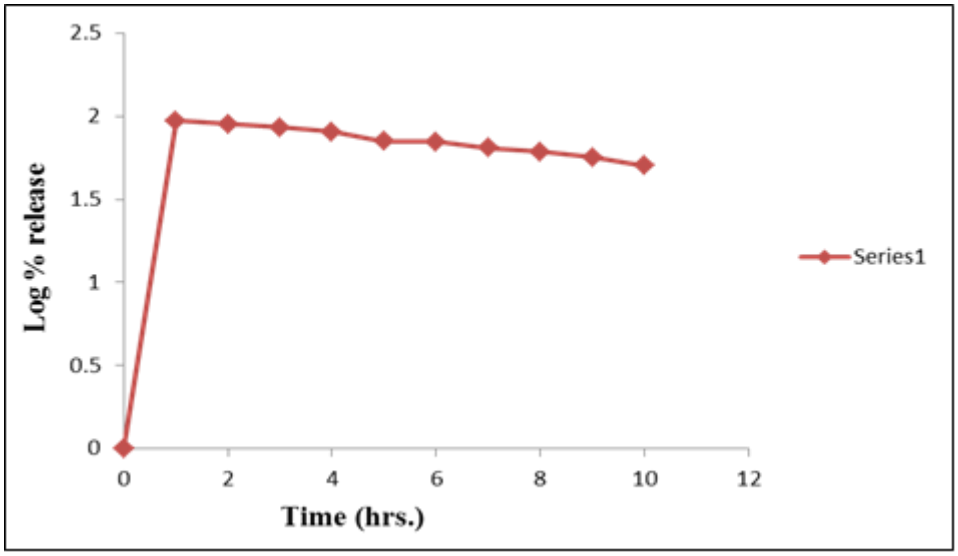

Figure 8: First order release curve of group-3 (Formulation code F1)

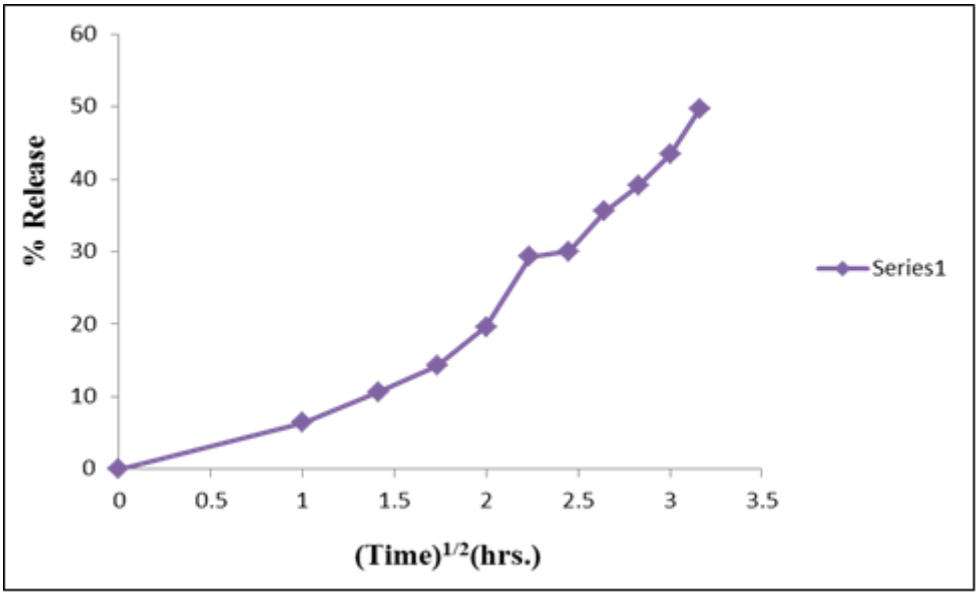

Figure 9: Higuchi release curve of group-3 (Formulation code F1)

Table 4: Correlation coefficient of group-1

Formulation Code	Correlation coefficient (R^2)		
	Zero Order Kinetics	First Order Kinetics	Higuchi Kinetics
F1	0.9726	0.9536	0.9054
F2	0.9889	0.9915	0.9083
F3	0.9863	0.9701	0.9033
F4	0.9935	0.9808	0.9042
F5	0.9865	0.9807	0.8995
F6	0.9859	0.9740	0.9002

Table 5: Correlation coefficient of group-2

Formulation Code	Correlation coefficient (R^2)		
	Zero Order Kinetics	First Order Kinetics	Higuchi Kinetics
F1	0.9922	0.9932	0.9082
F2	0.9954	0.9917	0.9131
F3	0.9887	0.9950	0.9082
F4	0.9961	0.9895	0.9150
F5	0.9939	0.9908	0.9093
F6	0.9942	0.9857	0.9080

Table 6: Correlation coefficient of group-3

Formulation Code	Correlation coefficient (R^2)		
	Zero Order Kinetics	First Order Kinetics	Higuchi Kinetics
F1	0.9982	0.9899	0.9148
F2	0.9982	0.9896	0.9137
F3	0.9721	0.9778	0.9100
F4	0.9949	0.9952	0.9081
F5	0.9928	0.9966	0.9175
F6	0.9975	0.9914	0.9150

REFERENCE

1. Budavari, S., Eds. (2001). In; The Merck Index, 13th Edn., Merck & Co., Inc., Whitehouse Station, NJ pp. 958,1163,1809.
2. Dan, S., Malik, J. K., Singh, N., Bharati, D., & Bose, A. (2011). Development and Optimization of Fixed Dose Antihypertensive Combination Drugs using Double Layer Sustained Release Microsphere Technology. *Asian Journal of Chemistry*, *23*(9), 3883-3886.
3. Jain, N. K. (Ed.). (2008). *Advances in controlled and novel drug delivery*. CBS Publishers & Distributors. 108-110.
4. Kathleen, P. (1999). Eds., In; Martindale The Complete Drug Reference 32nd Edn., Pharmaceutical Press, London, 1999, pp. 622,623,630.
5. Kumar, A., Kumar, A., & Malik, J. K. (2019). Preformulation studies of Drotaverine HCl: An integral part of formulation design. *European Journal of Biomedical and Pharmaceutical Sciences*, *6*(13), 304-307.
6. Kumar, D., & Kumar, A. (2020). Formulation and evaluation of fast dissolving uncoated tablets of Drotaverine HCl, *World Journal of Pharmaceutical Research*, *9*(1), 1716-1727.
7. Kumar, D., Kumar, A., Malik, J. K., & Semwal, P. (2019). Process Evaluation and In-vitro Drug Release Study of Fast Dissolving Uncoated Tablets of Drotaverine HCl. *European Journal of Scientific Exploration*, *2*(6),1-8.
8. Kumari, P. (2017). Overview on: - characteristic of isoflavones & its biological activity *International Journal of Biology, Pharmacy and Allied Science*, *6*(3), 447-467.
9. Malik, J. K., Sharma, A., Singh, S., & Jain, S. (2013). RETRACTED: Nanosuspension of vasicine from Adhatoda vasica: Isolation and characterization. *Drug invention today*, *5*(1), 32-38.
10. Prabhakar, D., Sreekanth, J., & Jayaveera, K. N. (2013). Transdermal drug delivery patches: a review. *Journal of Drug Delivery and Therapeutics*, *3*(4), 231-221.
11. Ramkanth, S., Alagusundaram, M., Gnanaprakash, K., Rao, M., Saleem, M., Paneer, K., & Chetty, C. M. (2010). Design and characterization of matrix type transdermal drug delivery system using metoprololtartarate. *Int J Adv Pharm Res*, *1*(1), 1-5.
12. Singh, S., Chandel, H. S., Kushwaha, S., & Malik, J. (2015). Evaluation of Antidiabetic Activity of Combination of Trace Elements. *Chemical Science International Journal*, 25-37.
13. Soni, H. *etal*. (2020). Preformulation Studies of Tramadol HCl: Vital Part of Formulation Design. *EJBPS. 7* (1), 369-373.
14. Soni, H., Sharma, S., Malik, J. K., & Sarankar, S. K. (2020). Role of healthy food in prevention of neural tube defects: A Review. *Saudi J Med Pharm Sci*, *6*(1), 20.
15. Soni, S. (2019). Recent Updates On Phytoceuticals Used In Pancreatitis. *Asian Journal of Medical and Health Research*, *4*(7), 1-13.
16. Tiwari, D. (2017). Cosmetotextiles used as a medicine *International Journal of Pharma and Chemical Research*, *3*(4), 814-828.
17. Tiwari, P., & Malik, J. K. (2020). A comprehensive review on botanical as anti-ulcer therapeutics: prospective avenues of biocompatible drug discovery. *Scholars International Journal of Tradicinal and Complementary Medicine, Published by Scholars Middle East Publishers, Dubai, United Arab Emirates*, *3*(2), 27-32.