

# 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

DOI: 10.47310/iarjmsr.2020.V01i01.01

## Author Details

Mohit Saini<sup>\*1</sup> Sneha Singh<sup>1</sup>, Amit Kumar<sup>2</sup>  
Lalit Parihar<sup>3</sup> and Mukesh Kumar<sup>4</sup>

## Authors Affiliations

<sup>1</sup>Aroma College Roorkee, Haridwar (UK), India

<sup>2</sup>Smt. Manjira Devi Shikshan and Prashikshan Institute Hitanu Dhanari, Uttarkashi, India

<sup>3</sup>R.V.Northland Institute, G.T.road Dadri Greater Noida, Gautam Budh Nagar, (UP), India

<sup>4</sup>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, ( $\pm$ ) 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-HT<sub>2C</sub> receptor and even though the parent and M1 metabolite of Tramadol binds to  $\mu$  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 E15 was obtained from Jegchem 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 desired size and stored in desiccator until use.

### In Vitro Drug Released Studies

The in-vitro drug release studies of the patches were carried out using modified KesharyChienFranz diffusion cell. The cylinder consists of two chambers, the donor and the receptor compartment. The donor compartment was unfastened at the top and was exposed to atmosphere. The temperature was maintained at  $37 \pm 0.5^\circ\text{C}$  and the receptor compartment was provided with a sampling port. The diffusion medium used was phosphate buffer (pH 7.4). The diffusion was carried out for 10 hours at an interval of one hour for 10 hours (1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 hours). 5 ml sample was withdrawn from the same volume of phosphate buffer pH 7.4 was added to the receptor compartment to maintain sink conditions and the samples were analyzed at 271 nm in a UV spectrophotometer (Ramkanth, S. *et al.*, 2010). To study the 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

Release data were fitted to different mathematical models to reveal the release mechanism. Zero order, first order and Higuchi release models were used for this purpose. All curve fitting and plotting were 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

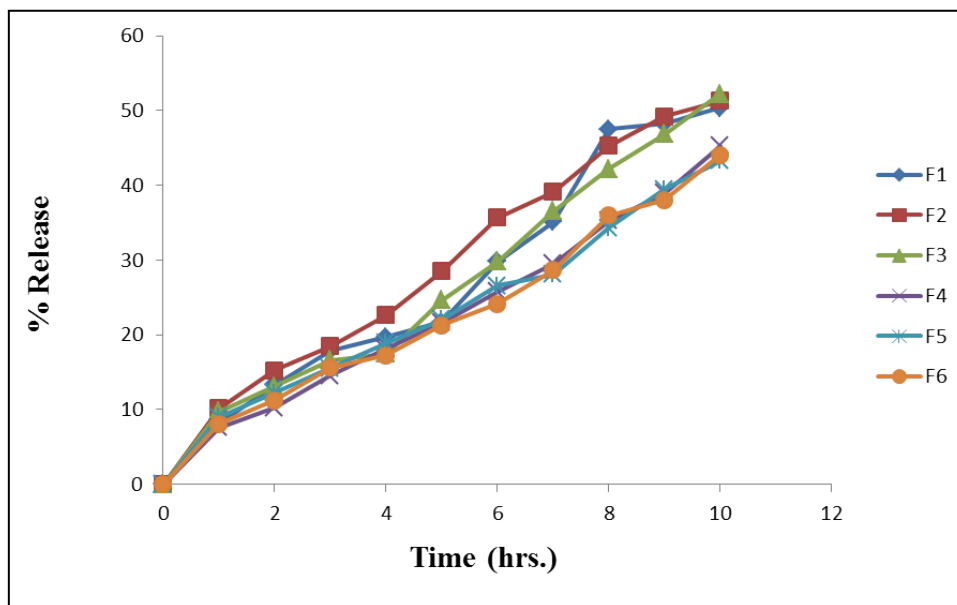


Figure 1: Zero order release curve of group-1

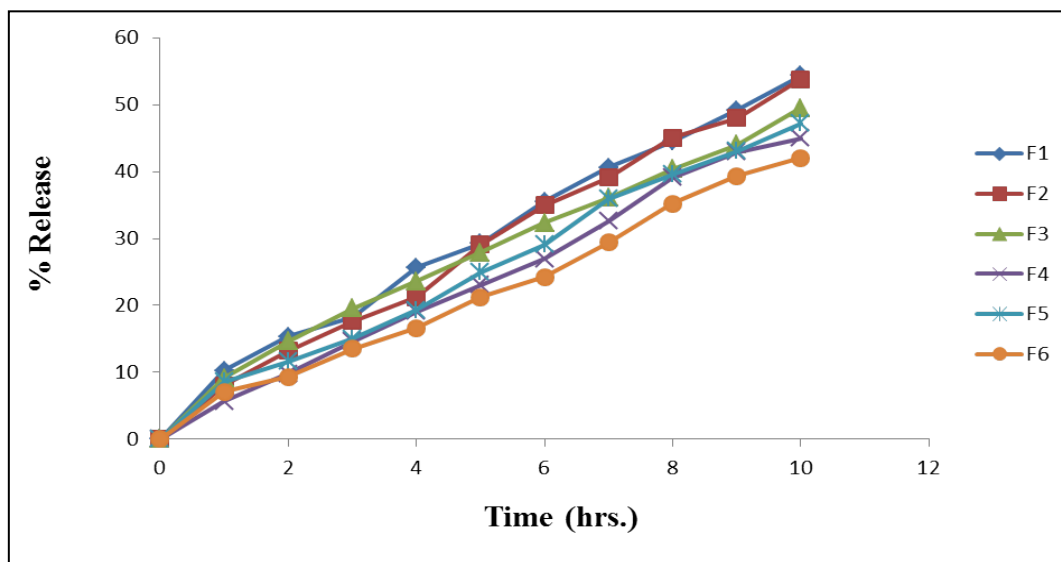


Figure 2: Zero order release curve of group-2

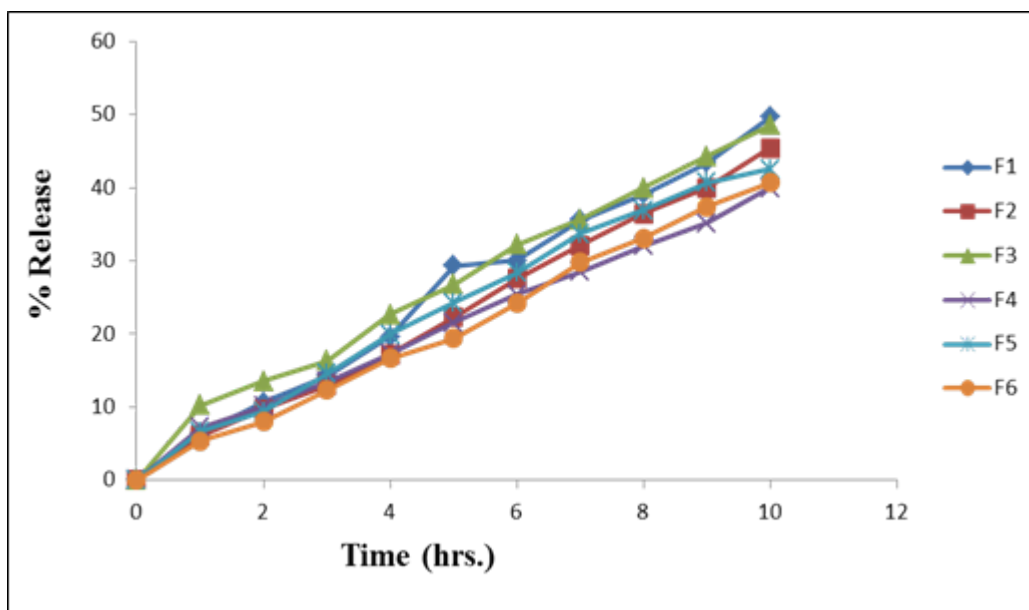


Figure 3: Zero order release curve of group-3

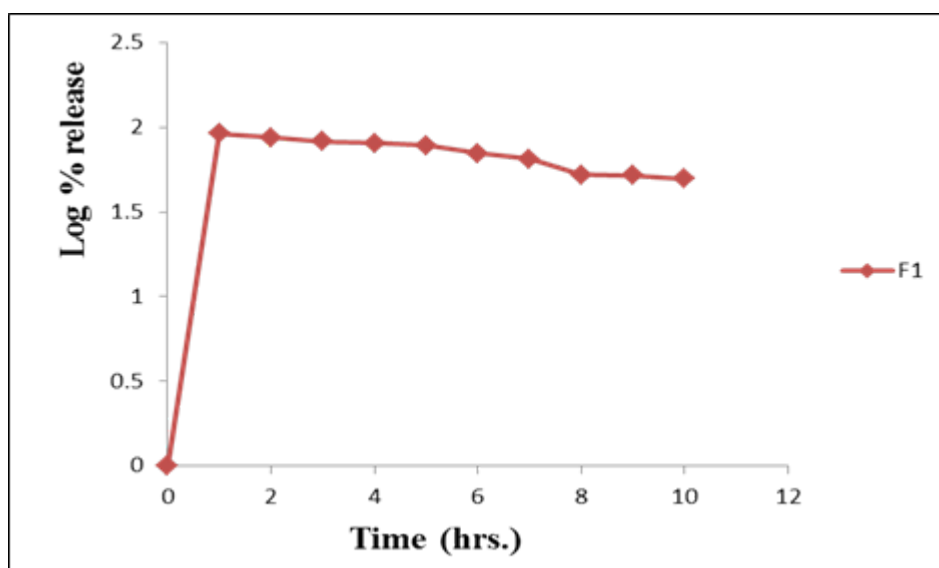
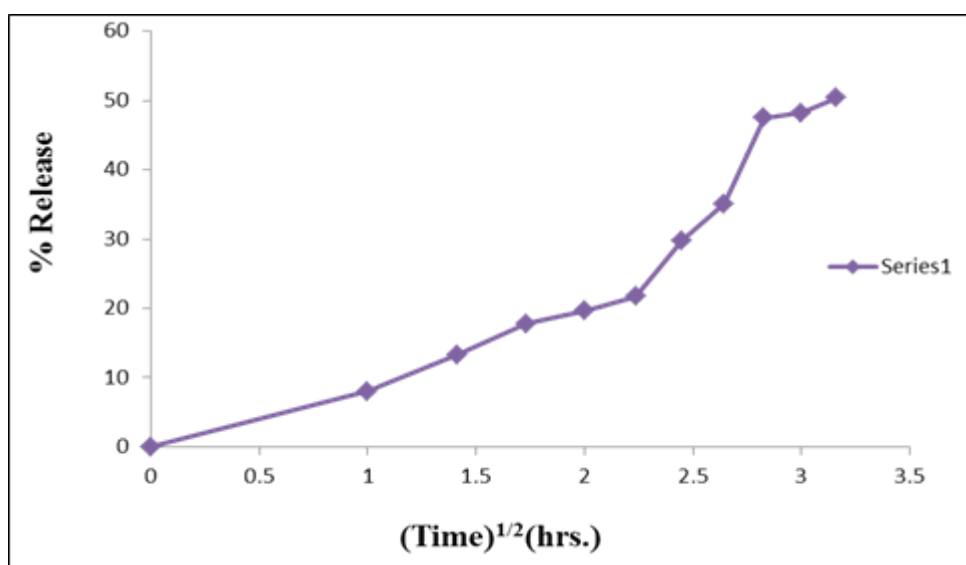
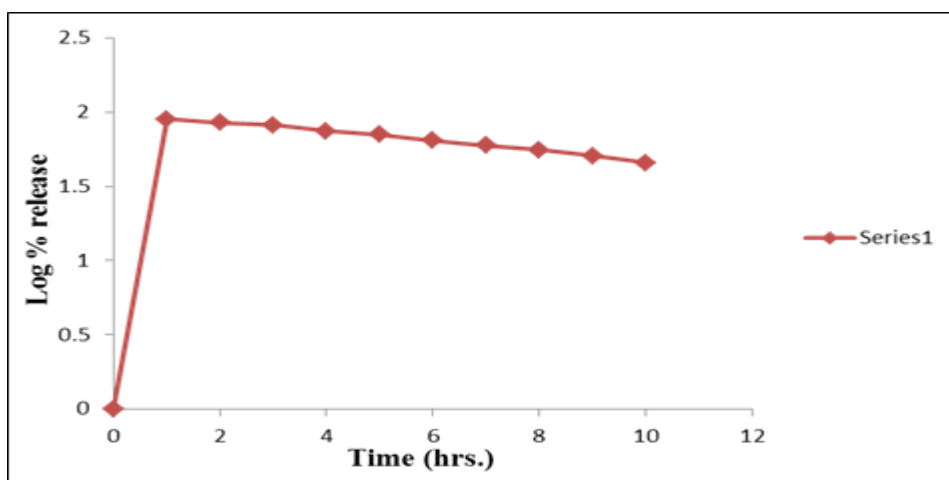


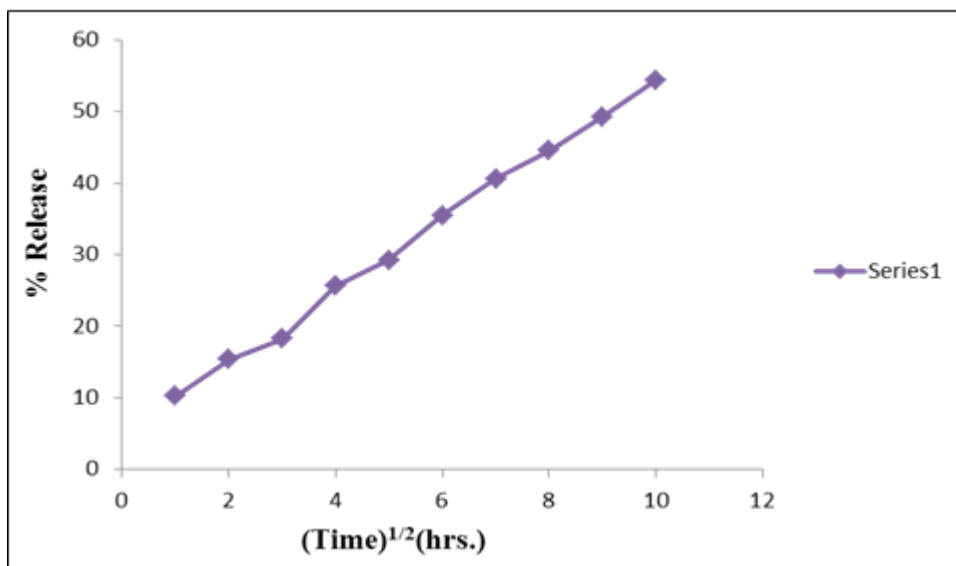
Figure 4: First order release curve group-1 (Formulation code F1)



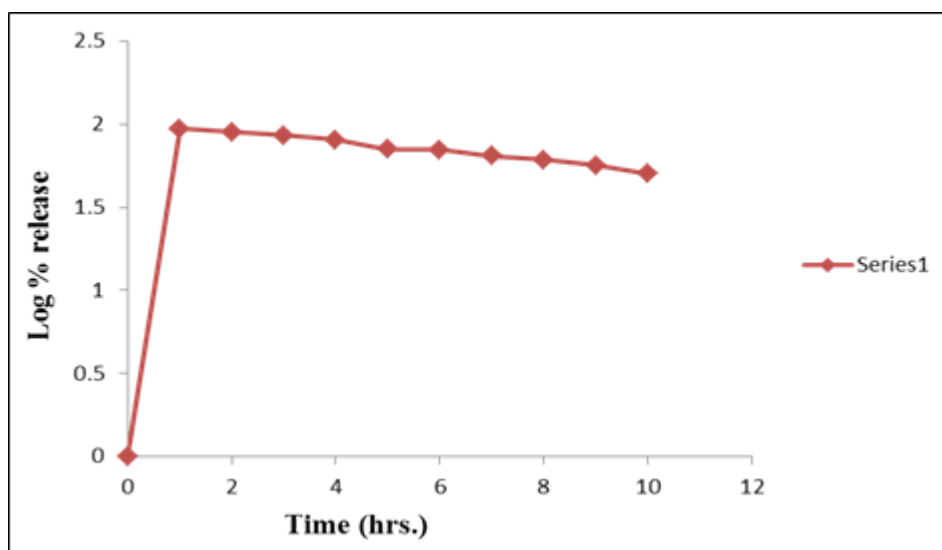
**Figure 5:** Higuchi release curve of group-1 (Formulation code F1)



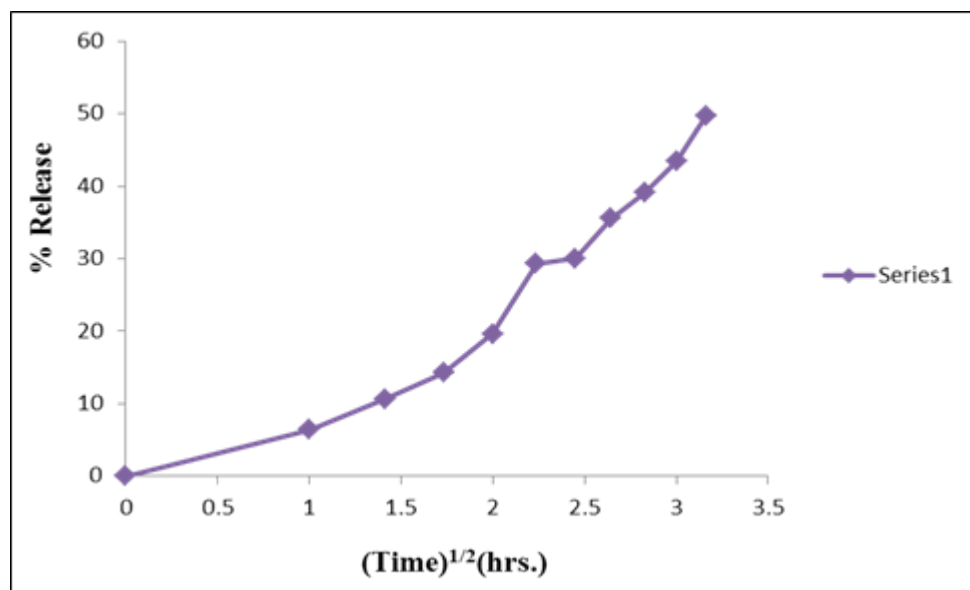
**Figure 6:** First order release curve of group-2 (Formulation code F1)



**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

Correlation coefficient ( $R^2$ )			
Formulation Code	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

Correlation coefficient ( $R^2$ )			
Formulation Code	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

Correlation coefficient ( $R^2$ )			
Formulation Code	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 32<sup>nd</sup> 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. et al. (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.