World Journal of Current Medical and Pharmaceutical Research
Content available at www.wjcmpr.com ISSN: 2582-0222

FORMULATION AND *INVITRO* EVALUATION OF EFFERVESCENT FLOATING TABLETS OF HYDROPHILIC POLYMERS USING PROPRANOLOL HYDROCHLORIDE AS A MODEL DRUG

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Article History

Received on: 05-02-2025
Revised on: 28-02-2025
Accepted on: 31-03-2025

Abstract

Objective: The main aim of this project is to formulate and *in vitro* evaluation of effervescent drug delivery using Propanolol HCl as a model drug.

Methodology: The effervescent floating drug delivery was prepared using hydrophilic polymer in two different grades, HPMC K4M and HPMC K200M. Sodium carbonate is used as a gas-generating agent in floating tablets. The tablets were prepared by the wet granulation method. The ratio of HPMC to ethyl cellulose was kept constant at 2:1. The formulated tablets were evaluated for physicochemical properties, *in vitro* buoyancy, floating properties, swelling studies, *in vitro* dissolution studies, and drug release kinetics.

Results: The result of *in vitro* dissolution showed that the sustained release can be achieved using HPMC and increasing the concentration of hydrophilic polymers like HPMC K4M and HPMC K200M increases the capacity of holding the drug within the polymer for a longer time. However, changing the viscosity of the HPMC had no significant difference in the drug release profile. The floating lag time for all the formulations was found to be less than 2 minutes with a floating time of more than 24 hours which showed the adequate buoyancy of the tablets.

Conclusion: The present studies showed that using hydrophilic polymers like HPMC K4M and HPMC K200M along with ethyl cellulose and sodium carbonate as gas generating agents can be used for developing sustained released effervescent floating tablets.

Keywords: Propranolol Hydrochloride;gastro retentive drug delivery system;floating drug delivery, HPMC.

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DOI: https://doi.org/10.37022/wjcmpr.v7i1.354

Introduction

The oral drug delivery system is one of the oldest and most extensively used routes of drug administration due to its ease of administration, flexibility in formulation, and patient compliance [1]. However, most orally administered drugs show poor bioavailability when administered in their conventional dosage form for several reasons [2]. Such problems encountered within the conventional dosage form can be overcome by a modified-release drug delivery system with prolonged Gastro Retention Time. Gastro retentive drug delivery system (GRDDS) is one of the approaches that have been proposed to retain the drug in the stomach for achieving a prolonged and predictive drug delivery profile. GRDDS can be broadly classified into a floating System and a Non-floating System [3]. A floating drug delivery system (FDDS) is a low-density approach where the dosage form has a bulk density less than the gastric fluids such that the dosage form floats in and over the gastric contents. Thus, it remains buoyant and releases the drug slowly at the desired rate for a prolonged period [4]. The floating drug delivery system is further divided into; an effervescent system and a non-effervescent system. An effervescent floating drug delivery system is the matrix type of system that is prepared with the help of swellable polymers like xanthan gum, chitosan, methylcellulose, etc., and effervescent agents like sodium bicarbonate, citric acid /tartaric acid [5–7]. The main mechanism involved in this system is the liberation of carbon dioxide gas as it comes in contact with the gastric content and gets entrapped in the swollen hydrocolloid of the system resulting in the buoyancy to dosage form [8]. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves the solubility of drugs that are less soluble in a high pH environment [9].

In the present study, propranolol HCl was selected as a model drug for an Effervescent floating drug delivery system using a

matrix. Propranolol is a well-known beta-blocker used in the management of high blood pressure, angina pectoris, cardiac arrhythmia, prevention of migraine headache, hereditary tremors, hypertrophic subaortic stenosis, and tumors of the adrenal gland [10]. These are easily absorbed from the GIT, have a short half-life of 3-4 hours, are eliminated quickly from the blood circulation, and require frequent dosing [9]. Due to the short half-life and to overcome the frequent dosing Propanolol HCl has been selected for the developing effervescent floating drug delivery system using a matrix system.

Methodology

Drugs and chemical

Propanolol Hydrochloride and Hydroxypropyl Methylcellulose (HPMC) K4M were obtained as gifts from Deurali Janata Pharmaceuticals Pvt. Ltd. Nepal. Hydroxypropyl Methylcellulose (HPMC) K200M was obtained as a gift from CTL Pharmaceutical Pvt.Ltd, Nepal. Other chemical reagents and excipients were purchased from Sigma Aldrich, Inc. (St. Louis, MO, USA).

Instruments

12 station Rotary tablet press (Acura fluid pack industries), Analytical Balance (AR 3130, Capacity - 310 gm. Readability - 0.1 mg Ohaus Corp, Pine Brook, USA), UV Visible Spectrophotometer UV-1601 (Shimadzu Corporation, Kyoto, Japan), Dissolution test Apparatus (Lab India Pvt. Ltd, India) were used in this study.

Preparation of tablets

Eight formulations of Propanolol hydrochloride floating tablets were prepared by wet granulation technique. At first, all the excipients and Propanolol Hydrochloride(as shown in Table 1) were sieved through mesh size #80. After sieving, all the components were mixed geometrically and granulation was done using polyvinyl Pyrrolidine (PVP) K solution as a binder. The mixer was then dried in a hot air oven for 30 minutes or until the smell of Isopropyl alcohol (IPA) diffused off. Magnesium stearate and Talc were added to the mixture and passed through the sieve of mesh size #20. At the end, mixture was subjected to compression using a 12-station rotary tablet compression machine with a 10mm punch size each time with an average tablet weight of 300 milligrams

Table 1: Formulation matrix using different concentrations of excipients

Formulation Code / Ingredients	(F1)	(F2)	(F3)	(F4)	(F5)	(F6)
Propanolol HCl (mg)	40	40	40	40	40	40
HPMC K4M (mg)	40	80	120	-	-	-
HPMC K200M (mg)	-	-	-	40	80	120
Ethyl Cellulose (mg)	20	40	60	20	40	60
Sodium Bicarbonate(mg)	50	50	50	50	50	50
Citric Acid (mg)	-	-	-	-	-	-
Tartaric acid (mg)	-	-	-	-	-	-
Mg stearate (mg)	3	3	3	3	3	3
Talc (mg)	3	3	3	3	3	3
PVPK (mg)	8	8	8	8	8	8
Dicalcium Phosphate (mg)	136	76	16	136	76	16
Total (mg)	**300**	**300**	**300**	**300**	**300**	**300**

500 tablets per formulation were prepared and checked for all the pre and post-compression parameters if they met the criteria of pharmacopeia or not [11].

Pre-compression parameter evaluation

Various pre-compression parameters, including flow properties, Bulk density, tapped density, compressibility index, Hausner ratio, and angle of repose, were evaluated according to the Indian Pharmacopoeia 2007[11].

Post-compression parameter evaluation

Various post-compression parameters namely: weight variation, Hardness, Friability test, swelling studies, assay, floating time, In-vitro dissolution test, Thickness, Uniformity of content, and drug release mechanism were evaluated as per the Indian Pharmacopoeia 2007 [11].

Weight Variation

Individual weight of 20 tablets which were randomly selected was taken for the determination of weight variation and the mean was calculated. Weight variation specification as per Indian Pharmacopeia 2007(11).

Hardness

Five tablets were selected randomly and the hardness of each tablet was measured on a Monsanto hardness tester.

Friability test

6.5gm equivalent weight of tablets was weighed and kept in a rotating drum of the friability test machine. The initial weight of the tablets was labeled as X0. They were subjected to 100 falls of 6 inches' height and 25 rpm for 1 minute. After complete rotations, the tablets were de-dusted and the final weight (X) was taken. The percent loss in weight or friability was calculated by using the formula (12).

$$F=1-X/X0 \times 100$$

Swelling studies

The swelling ability of tablets was determined using an acidic medium (0.1 N Hydrochloride acid). The tablet was introduced in swelling media. The tablet was removed periodically from the medium. After draining the free water weight gain of the

tablet was measured. The swelling index was calculated by the given formula [12].

$$\%SI = (W0-Wi) / Wi \times 100$$

Where W0= weight of swollen tablet

Wi =weight of the initial tablet

Floating time

All the formulated tablets were subjected to floating studies and for each bacth 5 tablets were used. The tablet was placed in a 900ml beaker containing 0.1N HCl at 37±0.5°C. The time required for the tablet to rise to the surface and float was determined as floating lag time. The duration of the tablet constantly remaining on the surface of the medium is the total floating time(13).

In-vitro dissolution test

The release of active pharmaceutical ingredients (API) from the tablet was studied using the USP II paddle apparatus. For this 900 ml 0.1N HCl was taken and maintained at 37 ±0.5°C temperature. Dissolution was done at 100 rpm. 10 ml of samples were withdrawn at time intervals of 30 min, 2 hours, 4 hours, 6 hours, 8 hours, and 24 hours. The samples were replaced by the equivalent of media. The samples were filtered through Whatman filter paper and absorbance was measured at 290 nm using a UV spectrophotometer taking 0.1 N HCl as blank(13).

Thickness

The thickness of the compressed tablet was measured by using a Vernier caliper.

Drug release mechanism

The drug release mechanism was determined by fitting the dissolution data into different mathematical models like zero order, first order, Higuchi's, and Peppas' model(14–16).

Model	*Equation*
Zero-order	C= C0-K0 t
First-order	Log C= Log C0-Kt/2.303
Higuchi	C= [D (2qt-Cs) Cs.t] ½
Hixon-Crowell	Ct/C∞= ktn

C0= Initial amount of drug in solution, C = total amount of drug released per unit area of the matrix, D=diffusion coefficient for the drug in the matrix, qt =total amount of drug in a unit volume of the matrix, Cs=dimensional solubility of the drug in the polymer matrix. K0and Kt are release rate constants, n: the release exponent indicative of the mechanism of drug release.

Uniformity of content

20 tablets were taken in an individual 100ml volumetric flask and 5ml of 0.1N HCL was added.20mg of propranolol hydrochloride was taken in a volumetric flask with 20ml water. The solution was shaken for sometimes and 70ml of methanol was added and shaken. Then volume makeup was done with methanol. Then the solution was centrifuged and the supernatant layer was taken. 20 ppm solution was prepared from obtained supernatant and absorbance was measured using a UV/VIS spectrophotometer at 290nm as per Indian Pharmacopeia 2007 [11].

Result and Discussion

Pre-compression

The compressibility index of all formulations ranged from 13.63% to 18%, the Angle of repose ranged from 30.96 to 34.21, and Hausner's ratio ranged from 1.15 to 1.22 indicating that the powder has the required flow property for wet granulation and meets all the official requirement for the wet granulation which means the flow properties of the blends were good(11).The details of flow properties of all the formulations are shown in Table 1.

Table 2: Flow properties of lubricated granules

Formulation	Compressibility Index (%)	Angle of Repose (0)	Hausner Ratio
F 1	14.28	30.96	1.167
F 2	18	31.79	1.22
F 3	14.28	31.59	1.167
F 4	13.63	34.21	1.15
F 5	14.63	32	1.17
F 6	14.28	30.96	1.167

Post compression parameters

The detail evaluation results for the post-compression parameters are shown in Table 2. The thickness of all formulations ranged from 3mm to 4 mm and friability of all formulations was found to be less than 1%. The breaking force of all formulations was found to be 4.5± 0.2 kg/cm2. The weight variation for all the formulations was found to be less than 5 %. The uniformity of the content for all the foundations is more than 98% and less than 105%.

All the physical properties like weight variation, thickness, hardness, and friability of all formulations have complied with pharmacopeia (IP) 2007 limits(11)(standard uniformity range 85-115%).All the formulated tablets assay values were found to be within the range of 98.29 % to 101.25 % which meets the standard criteria for assay of Propanolol HCl tablets as per the Indian Pharmacopoeia 2007(11) which is between 92.5 % and 107.5 %.

Table 3: Propanolol HCl floating tablets post compression evaluation

Formulation Code	Weight a (mg)	Assay b (%)	Content Uniformity * (%)	Thickness* (mm)	Hardness* (kg/cm2)	Friability ** (%)
HPMC K4M and Ethy Cellulose (Ratio 2:1)						
F1	300 ± 0.82	98.29 ± 1.11	99.02-101.4	3-4	4.8-5	0.14
F2	300 ± 1.01	102.62 ± 0.77	101.1-104.5	3-4	4.8-5	0.07
F3	300 ± 0.94	100.85 ± 1.34	99.07-101.6	3-4	4.8-5	0.3
HPMC K200M and Ethy Cellulose (Ratio 2:1)						

F4	300 ± 1.12	99.77 ± 0.90	98.8-102.8	3-4	4.8-5	0.1
F5	300 ± 1.37	101.25 ± 0.95	100.3-102.5	3-4	4.8-5	0.45
F6	300 ± 1.41	98.98 ± 0.64	97.4-99.8	3-4	4.8-5	0.2

a: mean ± s.d (n=20); b: mean ± s.d (n=10); *n=5; **n=20; HPMC= Hydroxypropyl methylcellulose

In vitro buoyancy studies

The floating lag time of all formulations ranged from 4 seconds to 30 seconds which is less than 2 minutes. Propanolol Hydrochloride is absorbed in the stomach (upper GIT) and floating is required to increase its Gastro retention time and avoid its degradation by P-glycoprotein(17). So lag time should be fast enough to avoid the flush out of the drug from the stomach. Since the lag time of all formulations was less than 2 minutes and the floating time of all the formulations was up to 24 hours. The result complies with the study conducted by Gharti et al(17).

Table 4: Floating properties of propranolol HCl floating tablets

Formulation	Floating lag time(Seconds) n=5	Total Floating time(Hours) n=5
F 1	50-58	>24 hours
F 2	55-70	>24 hours
F 3	79-90	>24 hours
F 4	15-35	>24 hours
F 5	50-65	>24 hours
F 6	70-85	>24 hours

Swelling Index

The swelling Index of formulations are depicted in Figure1. It was observed that the matrices undergo swelling after placing them in dissolution media. In all the formulations, the swelling index has been increased gradually with time which is evident in the constant release of drugs from the matrices which is due to the retardation by the swelling hydrophilic polymers depending on its molecular weight. The gas generated from the sodium bicarbonates get entrapped within the polymers which provide the buoyancy to the tablet and this has also been supported by the study conducted by V.S Meka et al. The swelling of the polymer reached its saturation at around 8 hours based on the quantity of the polymer used for that particular formulation (18).

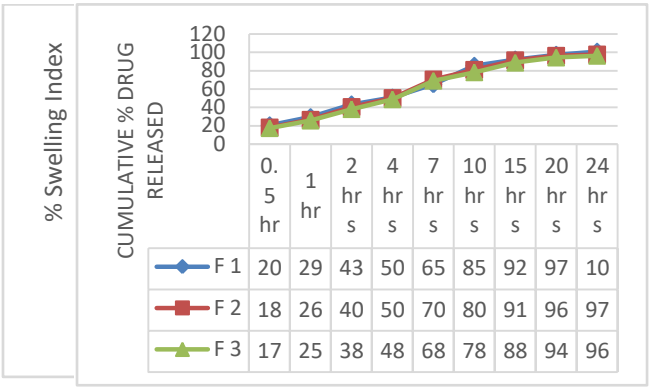

Figure 1: Swelling Index of Propanolol HCl, HPMC: Ethyl Cellulose

In vitro Dissolution studies

The results of the dissolution studies of formulation with HPMC K4M (F1-F3) and HPMC K200M (F4-F6) in the ratio of 2:1 are shown in Figures 2 and 3 respectively. HPMC K4M-based formulations (F1-F3) showed a higher amount of drug release as compared to the formulation (F4-F6) using HPMC K200M does not show any difference in the amount of drug release after 24 hours. From this result, it is concluded that changing the viscosity of the hydrophilic polymer does not change the amount of drug release with time and this resultis also supported by the study conducted by Gharti et al(17).

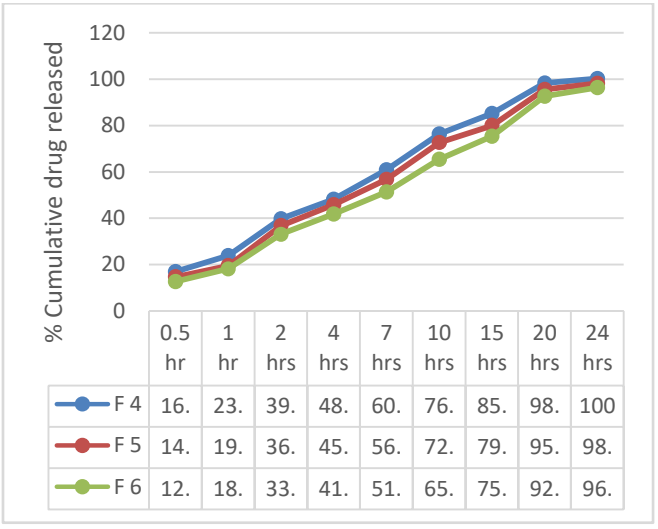

Figure 2: Dissolution profile of propanolol HCl floating tablet using HPMC K4M

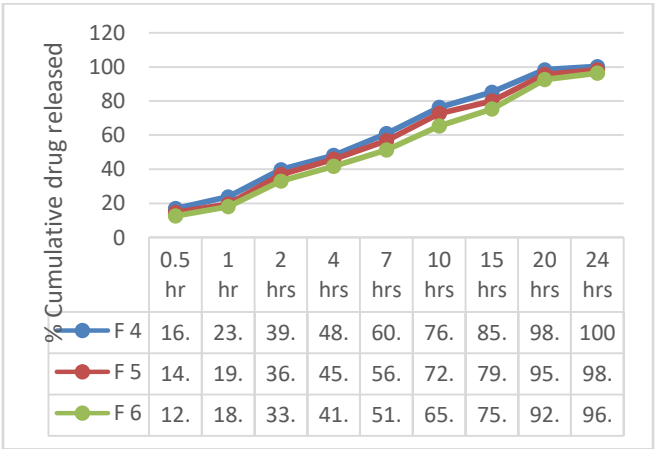

Figure 3: Dissolution profile of propanolol HCl floating tablet using HPMC K200M

Release kinetics

The dissolution data for all the formulations were fitted in different mathematical models like zero order, first order, Higuchi's, and Korsemeyer-Peppas were used. The dissolution data of up to 15 hours were used for calculating the release kinetics. Around 75-80 % of the drug will be released during this period and can be used to find out which kinetics of the drug release(19). Highuchi model was found to be a good fit for all the formulations as the regression coefficient R2 value was found to be within 0.99 to 1 (0.99 ≥ R2<1). Changing the viscosity did not show any difference in R2 values therefore it can be concluded that drug release was proportional to the square root of time. From the Korsemeyer-Peppas model, diffusion exponent "n" values were obtained in the range of 0.3652 to 0.4324. The results show that the drug release from the formulated tablet was Fickian diffusion(16,20–22) which is due to the use of using Fickian diffusion matrix while formulating the tablet.

Table 5: Comparison of R2 value

FORMULATIONS	Zero-order	First order	Higuchi s model	Korsemeyer-Peppas model	
	R2	R2	R2	R2	n
F1	0.9286	0.9864	0.996	0.9861	0.3799
F2	0.9467	0.9901	0.991	0.9731	0.3869
F3	0.9389	0.9784	0.9934	0.9918	0.3991
F4	0.9785	0.9726	0.99	0.9825	0.4324
F5	0.9697	0.9656	0.9911	0.9856	0.3694
F6	0.9817	0.979	0.99	0.9782	0.3652

Conclusion

The Gastro retentive Floating Tablet of Propranolol Hydrochloride were developed by using HPMC K4M, HPMC K200 M, and Ethyl cellulose employing wet granulation followed by direct compression of tablets. Sodium carbonate was used as gas generating effervescent agent. All the formulations showed floating lag time less 2 minutes and floating time of more than 24 hours. Though increasing the concentration of the polymer slightly delayed in the drug release but no effect on the release profile. Moreover, even after changing the viscosity of hydrophilic polymer (HPMC K4M and HPMC K200M) there was no difference on the drug release profile. Hence for the present study, it can be concluded that using appropriate concentration of hydrophilic polymers like HPMC effervescent floating drug tablets of propanolol HCl can be prepared. Such type of tables can remain buoyant for more than 24 hours decreasing the frequency of dosing.

Conflict of Interest

None

Acknowledgement

We would like to thank Deurali Janata Pharmaceutical Limited and CTL Pharmaceutical Ltd for providing us with the active pharmaceutical ingredients and excipients required. We also would like to thank everyone who has directly and indirectly involved completing this project.

Funding

Required active pharmaceutical ingredients and excipients were received from Deurali Janata Pharmaceutical Limited and CTL Pharmaceutical Ltd. No other funding was available.

References

1. Pant S, Badola A, Kothiyal P. A review on gastroretentive drug delivery system. Indian J Pharm Biol Res. 2016 Jun 30;4(2):01–10.
2. Khan MA, T Shafeeq. Role of Mathematical Modeling in Controlled Drug Delivery. J Sci Res. 2009 Aug 29;1(3):539–50.
3. RJPT - [Internet]. [cited 2024 Nov 11]. Available from: https://rjptonline.org/HTMLPaper.aspx?Journal=Research+Journal+of+Pharmacy+and+Technology%3bPID%3d2008-1-4-63
4. Dixit N. Floating drug delivery system. J Curr Pharm Res. 2011;7(1):6–20.
5. Chhetri HP, Thapa P. An Overview on Gastroretentive Drug Delivery System. Kathmandu Univ J Sci Eng Technol. 2014 Nov 30;10(1):90–103.
6. Kumar MR, Satyanarayana B, Paladugu ND, Muddasar S, Pasha SI, Vemireddy S, et al. A Comprehensive Review on Gastro Retentive Drug Delivery System, Acta Chimica & Pharmaceutica Indica: 3(2), 2013, 149-164
7. Chowdary KPR, Chaitanya KL. Recent research on floating drug delivery systems-a review. Journal of Global Trends in Pharmaceutical Sciences.Volume 5, Issue 1, pp -1361-1373, January-March 2014
8. Jagdale SC, Agavekar AJ, Pandya SV, Kuchekar BS, Chabukswar AR. Formulation and Evaluation of Gastroretentive Drug Delivery System of Propranolol Hydrochloride. AAPS PharmSciTech. 2009 Sep 1;10(3):1071–9.
9. Meka VS, Dharmanlingam SR, Kolapalli VRM. Formulation of gastroretentive floating drug delivery system using hydrophilic polymers and its in vitro characterization. Braz J Pharm Sci. 2014 Apr;50(2):431–9.
10. Tripathi K. Antihypertensive drugs, essentials of medical pharmacology. In: Essentials of Medical Phamacology. 5th ed. Newdelhi: Jaypee Brothers; 2003. p. 235–6.
11. Pharmacopoeialaboratory C, Nagar R. MINISTRY OF HEALTH & FAMILYWELFARE. 1–3.
12. Ray D, Prusty AK. DESIGNING AND IN-VITRO STUDIES OF GASTRIC FLOATING TABLETS OF TRAMADOL HYDROCHLORIDE. In 2010 [cited 2024 Nov 11]. Available from: https://www.semanticscholar.org/paper/DESIGNING-AND-IN%C2%ADVITRO-STUDIES-OF-GASTRIC-FLOATING-Ray-Prusty/209418bd15e7050d4f1492377bfd52f1e9099d2f

13. Meka V, Ram B, Songa S, Rao N, K R V. Gastroretentive drug delivery systems: Novel approaches and its evaluation-A review. Int J Pharm Sci Rev Res. 2011 Oct 5;10:203–16.
14. Lazarus J, Cooper J. Absorption, Testing, and Clinical Evaluation of Oral Prolonged-Action Drugs. J Pharm Sci. 1961 Sep 1;50(9):715–32.
15. Higuchi T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci. 1963 Dec 1;52(12):1145–9.
16. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. Int J Pharm. 1983 May;15(1):25–35.
17. Gharti KP, Budhathoki U, Thapa P, Bhargava A. Formulation in vitro evaluation of floating tablets of hydroxypropyl methylcellulose and polyethylene oxide using ranitidine hydrochloride as a model drug. J Young Pharm. 2012 Oct;4(4):201–8.
18. Stamm A, Tritsch JC. Some Considerations on the Liberation of Drugs from Inert Matrices. Drug Dev Ind Pharm. 1986 Jan;12(11–13):2337–53.
19. Lachman L, A. Lieberman H, L. Kanig J. The Theory and practice of industrial pharmacy. 3rd ed. Bombay: Varghese Pub. House; 1991. 317 p.
20. Alizadehgiashi M, Shaw JM. Fickian and Non-Fickian Diffusion in Heavy Oil + Light Hydrocarbon Mixtures. Energy Fuels. 2015 Apr 16;29(4):2177–89.
21. Pandey NK, Ghatuary SK, Dubey A, Jain PK. Formulation and In Vitro Evaluation of Sustained Release Floating Matrix Tablet of Levofloxacin by Direct Compression Method. J Drug Deliv Ther. 2019 Aug 15;9(4-s):398–403.

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