Advances in Bioresearch
Adv. Biores., Vol 17 (5) May 2026: 231-242
©2026 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.17.5.231242

Advances in Bioresearch

ORIGINAL ARTICLE

Development and Optimization of Extended-Release Tablet of Duloxetine Hydrochloride

Rani G. Neharkar, Nilesh S. Mhaske*
Department of Quality Assurance, Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy Vilad Ghat, Ahilyanagar, Maharashtra 414111, India
***Corresponding author email:** nilesh.2273@gmail.com

ABSTRACT
The present study aimed was to develop extended-release tablet of Duloxetine Hydrochloride to achieve controlled drug release over an extended period of time and improve patient compliance. Duloxetine Hydrochloride is a selective serotonin and norepinephrine reuptake inhibitor (SSNRI). It is widely used in management of major depression disorder (MDD), generalised anxiety disorder and diabetic neuropathic pain. Although drug possesses a biological half -life 12 hrs, repeated dosing may still be required to maintained consistent plasma concentration. Therefore, an extended- release formulation was designed to provide controlled drug release over a 24 hrs period and minimize fluctuation in plasma drug levels. The extended-release tablet was formulated by direct compression using HPMC K100m as rate-retarding polymer. Different formulation batches were prepared by varying polymer concentrations. Optimize formulation were carried out using Central Composite Design with Design Expert Software. FTIR studies confirmed the compatibility between drug and excipients. Pre-Compression parameters such as angle of repose, bulk density, Carr's index and Hausner's ratio indicate good flow properties of the powder blend. The prepared tablets were evaluated for post compression parameters including thickness, hardness, friability, weight variation, drug content, in-vitro dissolution study and cell cytotoxicity. The optimized batch (NF9) show satisfactory physiochemical characteristics with % drug release after 24 hrs was found to be 98.53 % and following zero-order Kinetics. The study concludes that the combination of HPMC K100m and Eudragit RS 100 successfully developed an effective extended-release tablet formulation of Duloxetine Hydrochloride with prolonged drug release.
KEYWORDS: *Extended-Release, Duloxetine Hydrochloride, HPMC K100M, Eudragit RS 100, Cell Cytotoxicity.*

Received 07.04.2026 Revised 01.05.2026 Accepted 26.05.2026

How to cite this article:
Rani G. N, Nilesh S. M. Development and Optimization of Extended-Release Tablet of Duloxetine Hydrochloride. Adv. Biores. Vol 17 [5] May 2026. 231-242

INTRODUCTION

Duloxetine hydrochloride is a selective serotonin and norepinephrine reuptake inhibitor (SSNRI) widely used in the management of major depressive disorder (MDD), generalized anxiety disorder (GAD), diabetic peripheral neuropathic pain, fibromyalgia, and chronic musculoskeletal pain [1,2]. The drug exerts its therapeutic action by inhibiting the reuptake of serotonin and norepinephrine at presynaptic nerve terminals, thereby increasing the concentration of these neurotransmitters in the central nervous system. Preclinical and clinical studies have demonstrated that duloxetine possesses a strong inhibitory effect on serotonin and norepinephrine transporters, while exhibiting comparatively weak activity toward dopamine reuptake, contributing to its favorable antidepressant and analgesic properties [3,4].

Despite its clinical effectiveness, conventional oral formulations of duloxetine hydrochloride often require frequent administration to maintain therapeutic plasma concentrations. Following oral administration, the drug undergoes extensive first-pass metabolism and exhibits an elimination half-life of approximately 12 hours, which may result in fluctuations in plasma drug levels and reduced therapeutic consistency. Such variations can increase the risk of adverse effects, compromise treatment outcomes, and negatively affect patient adherence, particularly in chronic conditions requiring long-term therapy [5,6]. Therefore, the development of modified or extended-release dosage forms has gained considerable attention as an effective strategy to overcome these limitations.

Extended-release drug delivery systems are designed to release the drug at a predetermined rate over an extended period, maintaining therapeutic drug concentrations while minimizing peak-to-trough fluctuations. These systems offer several advantages, including reduced dosing frequency, improved patient compliance, enhanced therapeutic efficacy, and decreased incidence of dose-related side effects [7–9]. Hydrophilic matrix systems are among the most widely employed approaches for extended drug release due to their simplicity, cost-effectiveness, and reproducibility [10,11]. Polymers such as hydroxypropyl methylcellulose (HPMC) and Eudragit derivatives are extensively utilized because of their excellent swelling, gel-forming, and release-retarding properties.

In the present study, extended-release matrix tablets of duloxetine hydrochloride were developed and optimized using HPMC K100M and Eudragit RS100 as release-controlling polymers. The combination of these polymers was expected to provide a robust matrix structure capable of sustaining drug release over an extended duration. The prepared formulations were evaluated for pre-compression parameters, post-compression characteristics, in vitro drug release behavior, cell cytotoxicity, and release kinetic modeling. The primary objective of this investigation was to develop a stable and effective extended-release formulation capable of delivering duloxetine hydrochloride in a controlled manner, thereby improving patient compliance, reducing dosing frequency, and enhancing overall therapeutic performance.

MATERIAL AND METHODS

Materials

Duloxetine Hydrochloride were obtained from Swapnroop Drugs and Pharmaceuticals. Other excipients were received from different manufacturer HPMC K100M and Eudragit RS100 purchased from Modern Industries Nashik, PVP K30 and microcrystalline cellulose from SD Fine -Chem Limited Mumbai, India and Talc and magnesium stearate from Loba Chemie, Palghar.

Drug-Excipients Interactions

FTIR spectroscopy was used to determine whether there were any chemical interactions between Duloxetine Hydrochloride and the various excipients in the mixture. Pure drugs and physical mixes were examined using an FTIR spectrometer (IRAffinity-1S, made by Shimadzu Japan)[12–14].

DSC Analysis

The DSC thermogram of pure Duloxetine HCL exhibited a sharp endothermic peak at 172.61°C corresponding to its melting point, indicating its crystalline nature. In the physical mixture of Duloxetine HCL with polymer, the characteristic peak was shifted to 171.78°C with reduced intensity. This significant shift in melting endotherm suggests possible interaction between drug and polymer and a reduction in the crystallinity of Duloxetine HCL. The decrease in peak temperature may be attributed to partial amorphization and molecular dispersion of the drug within the polymer matrix, which is desirable in Extended -release formulation to modulate the drug release profile [15–17].

Formulation of Extended-Release Tablet of Duloxetine Hydrochloride

The procedure follow was direct compression. The drug and excipients except magnesium stearate and talc were weighed. Approximately and were passed through sieve no #60 Magnesium stearate and talc passed through sieve no #80. All the ingredient were mixed thoroughly in a polythene bag and compressed into tablets utilizing a single-punch tablet compression machine (L ab Press,8-Station) with 6 mm flat faced punches**.**

Table 1: Composition of extended-release tablet of Duloxetine Hydrochloride

Ingredient	NF1	NF2	NF3	NF4	NF5	NF6	NF7	NF8	NF9
Duloxetine Hydrochloride	30	30	30	30	30	30	30	30	30
HPMC K100m	78.75	78.75	78.75	90	90	67.5	67.5	90	67.5
Eudragit RL	33.75	22.5	45	33.75	45	45	33.75	22.5	22.5
PVP K30	18	18	18	18	18	18	18	18	18
Microcrystalline Cellulose	276	287.25	264.75	264.75	253.5	276	287.25	276	298.5
Magnesium Stearate	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Talc	9	9	9	9	9	9	9	9	9

Pre-compression Parameters

Angle of Repose

The angle of repose is used to determine the flow properties of powders. It is the greatest angle created between the surface of a pile and a horizontal surface [18,19]. The angle is computed based on the pile's height and radius.

$\tan \theta = \frac{h}{r}$

$\theta = \tan^{-1}(h/r)$

Where, Θ=angle of repose
h=height of the heap
r=radius of the heap

Bulk Density

The bulk density of the powder mixture was estimated by pouring a known mass of powder in to a graduated measuring cylinder [20]. The volume was measured without tapping. It can be measured by using the formula:

Bulk Density: $\frac{\text{Mass}}{\text{Volume}}$

Tapped Density

The mass-to-volume ratio of a powder sample after it has been physically tapped (compacted) in a cylinder until there is no more volume change [21].

Tapped Density: $\frac{\text{Mass}}{\text{Tapped Volume}}$

Compressibility Index (Carr's Index)

The flowability of a powder can be assessed by comparing its bulk density (ρo) and tapped density(ρ_t), which indicate how easily the powder consolidates during tapping [22]. It was calculated as:

Compressibility Index (%): $\frac{\rho t - \rho o}{\rho t} \times 100$

Hausner's Ratio

It is used to evaluate the flow properties of powders. It is determined by comparing the tapped density with the bulk density of the powder.

Hausner Ratio: $\frac{\text{Tapped Density}(\rho t)}{\text{Bulk Density}(\rho o)}$

Post compression evaluation of extended-release tablet

The prepared tablet was evaluated for hardness, friability, weight variation, thickness and drug content.

Hardness

The Monsanto hardness tester was used to measure the hardness of 10 tablets of each formulation in kg/cm^2. The mean and standard deviation values were reported.

Friability

Roche Friabilator was used to determine the tablet's friability (%). Twenty tablets were initially weighed and kept in a friabilator. It runs at 25 rpm for 4 minutes. Following that, the tablets were removed, dedusted, and their final weight was recorded.

Friability (%) was determined using the following formula:

Friability (%): $\frac{Initial\ weight - Final\ weight}{Initial\ Weight} \times 100$

Weight Variation

20 tablets were chosen at random from each batch and weighed separately in order to conduct the weight variation test. 20 tablets average weight and standard deviation were computed. If there are no more than two of each tablet, the tablets pass the weight variation test. Allow weights to differ from the mean weight.

Thickness

Ten randomly chosen tablets were measured for thickness in millimetres using a vernier calliper, and the mean and standard deviation were noted.

Drug content

10 tablet was randomly selected from each batch and was crushed using mortar and pestle. Powder equivalent to 100mg was dissolved in 100ml phosphate buffer (6.8Ph) The solution was sonicated for 15 minutes, then filtered and diluted as needed. The absorbance was measured at 290 nm with a UV-Visible spectrophotometer (Jasco V-630).

Dissolution study

Dissolution testing was carried out using USP 2paddle apparatus (Electro lab) for 2hr in 0.1N HCL followed by 6.8 pH Phosphate buffer for 24 hr. A tablet was kept in apparatus containing 900ml of 0.1N HCL at $37^0C \pm 0.5^0C$ and was rotated at 50rpm. Sample of 5 ml was withdrawn and analysed at 290 nm for 1 and 2hr. Then tablet was taken out and kept in media of 900ml of 6.8 pH phosphate buffer. Sample of 5ml was withdraw for 4,6,8,10,12,16,20 and 24hr and analysed at 290 nm using UV-Visible Spectrophotometer against buffer as blank and % cumulative dug release was computed [23,24].

Optimization of extended-release tablet of Duloxetine Hydrochloride

A Central Composite Design (CCD) was utilized to optimize the formulation of Duloxetine hydrochloride extended-release tablets using Design-Expert® software (Version 13.0, Stat-Ease Inc., USA). The design included a total of 9 experimental runs incorporating factorial points and center points to ensure adequate estimation of experimental error and model predictability. Two independent formulation variables were selected: HPMC K100M (X_1), varied at 15% and 20% w/w, and Eudragit RS 100 (X_2), varied at 5% and 10% w/w.

The influence of these variables was studied on two critical dependent responses: tablet hardness (Y_1) and percentage drug release after 24 hr.

Table 2: Factor levels used in CCD design:

Factor	Name	-1	0	+1
A	HPMC K100M	15	17.5	20
B	Eudragit RS 100	5	7.5	10

Drug release kinetics study

Different type of kinetics model was used for in-vitro release study such as zero order, first order, Higuchi, Hixson kinetic and korsmeyer-peppas model. The interpretation was performed and reported which is based on the value of the regression co-efficient.

Biocompatibility study using MTT assay

The cell cytotoxicity of Duloxetine Hydrochloride formulation was evaluated on MCF-7 human breast cancer cells using the MTT assay. The cells were cultured in modified Eagle Medium (MEM) supplemented with NEAA and fetal calf serum and maintained at 37OC in a5% CO2 atmosphere. Approximately 1×105 cells/well were seeded in 96-well plates and incubated for 24hr.The cells were then treated with different concentrations of the test formulation and further incubated under controlled conditions. After incubation, Morphological observations under an inverted microscope revealed that there is no significant cellular damage MTT reagent was added to asses cell viability based on the formation of purple formazan crystals by metabolically active cells. Absorbance was measured at 570nm using a microplate and percentage cell survival was calculated [25,26].

The calculation of percent cell viability followed the below mathematical formula:

Percentage viability = $\frac{\text{Absorbance of test}}{\text{Absirbance of control}} \times 100$

RESULT AND DISCUSSION

Drug excipient compatibility study

The IR spectrum of Duloxetine Hydrochloride in Figure 1 is characterized by principal absorption peak at 2419.26cm^{-1}(-NH stretching), 2974.66-2765.67cm-1(C-H stretching) 1626.26cm-1(C=C stretching)1232.29-1101.15cm-1(C-O stretching)523.49cm-1(C-S stretching). The FTIR spectrum of drug and excipient showed in Figure 2. IR spectra did not show any significant difference from those obtained for their physical mixture. The obtained result clearly indicate that excipient can be used without any interaction for preparation of extended-release tablet of Duloxetine HCL.

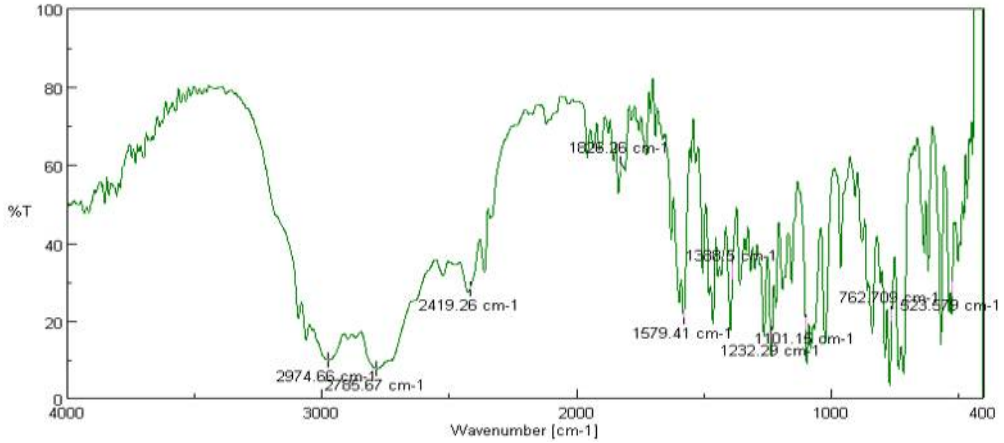


Figure 1: IR Spectrum of Pure Duloxetine HCL

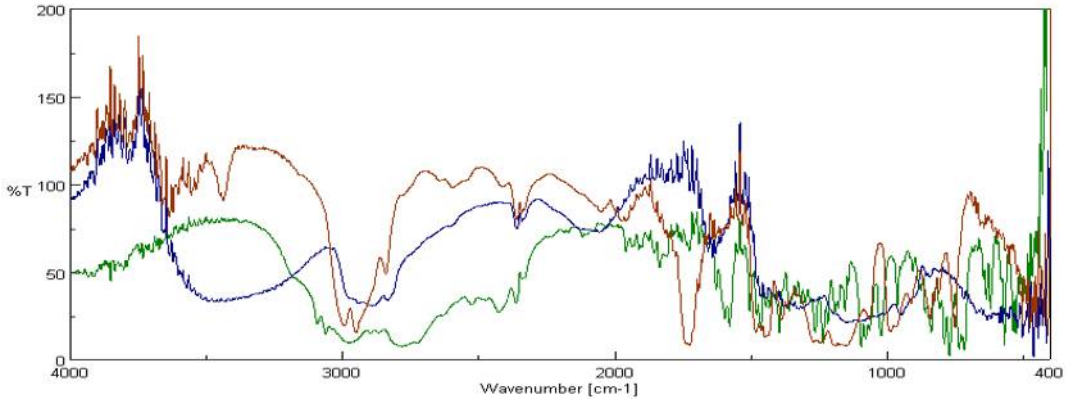


Figure 2: Duloxetine HCL with polymer overlay

Differential Scanning Calorimetry Analysis

The DSC thermogram of pure Duloxetine HCL exhibited a sharp endothermic peak at 172.61°C corresponding to its melting point, indicating its crystalline nature (Figure 3). In the physical mixture of Duloxetine HCL with polymer, the characteristic peak was shifted to 171.78°C with reduced intensity. This significant shift in melting endotherm suggests possible interaction between drug and polymer and a reduction in the crystallinity of Duloxetine HCL. The decrease in peak temperature may be attributed to partial amorphization and molecular dispersion of the drug within the polymer matrix, which is desirable in Extended -release formulation to modulate the drug release profile.

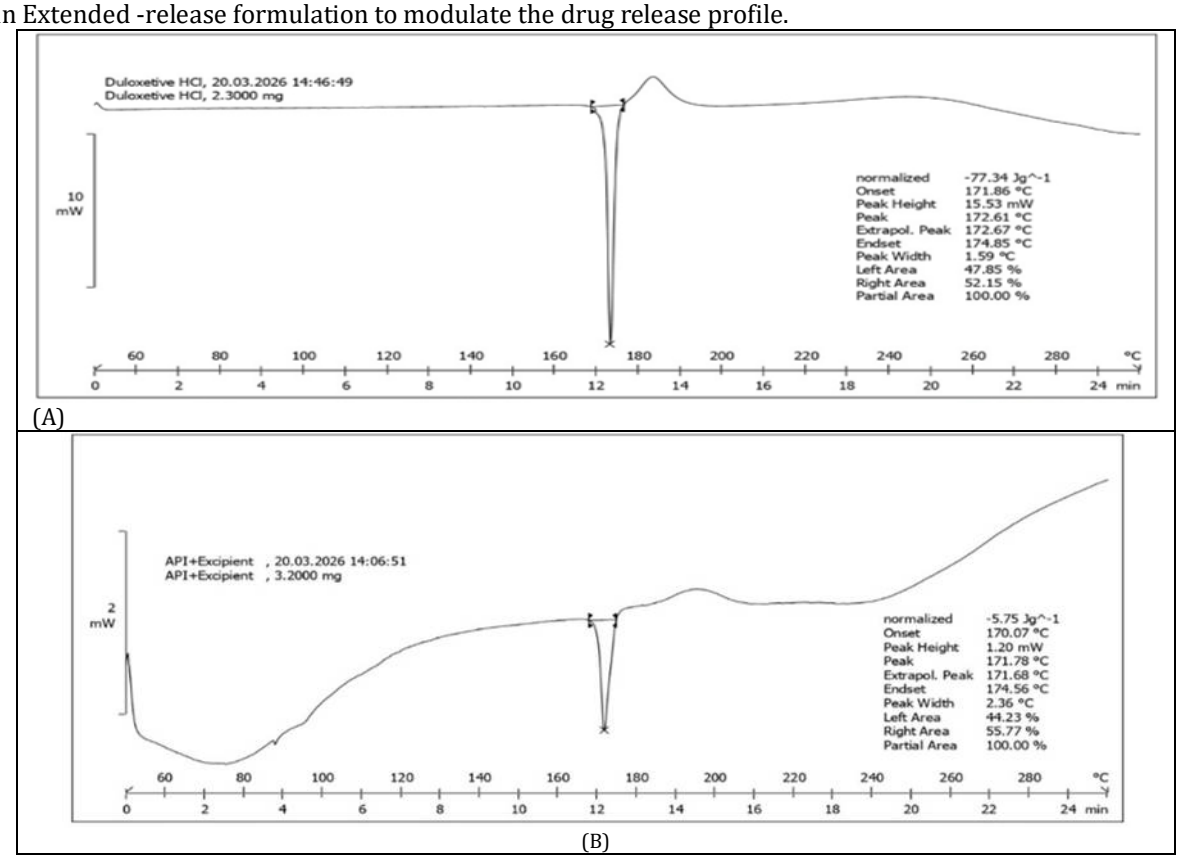


Figure 3: DSC Thermogram of (A) Pure Duloxetine Hydrochloride, (B) Drug + Excipient

Pre-compression study

All 9 batches were found to have good flow properties before compression. All results show acceptable compressibility and flow, ranging from 26.51^0 to 29.04^0 for angle of repose, 0.495 to 0.559 g/cm3 for bulk density and 7.03 to 16.8 % for Compressibility Index. The Hausner Ratio results verified the material filled the bottle easily and flow smoothly (Table 3).

Table 3: Pre-compression study of powder blend

Batch	Bulk Density gm/cm³	Tapped Density gm/cm³	Compressibility Index (%)	Hausner's Ratio	Angle of Repose (°)
NF1	0.559±0.004	0.647±0.005	13.2±0.08	1.15±0.008	26.51±0.06
NF2	0.555±0.004	0.581±0.004	13.2±0.04	1.03±0.008	28.26±0.02
NF3	0.555±0.005	0.652±0.006	14.8±0.05	1.16±0.008	28.57±0.06
NF4	0.495±0.003	0.595±0.004	16.8±0.05	1.18±0.008	28.41±0.05
NF5	0.555±0.004	0.629±0.004	11.6±0.08	1.13±0.005	27.88±0.08
NF6	0.533±0.006	0.607±0.005	12.15±0.02	1.12±0.005	28.25±0.05
NF7	0.542±0.008	0.583±0.006	7.03±0.01	1.07±0.005	28.62±0.02
NF8	0.518±0.003	0.659±0.006	11.8±0.04	1.27±0.008	28.94±0.07
NF9	0.538±0.005	0.588±0.004	9.8±0.04	1.08±0.005	29.04±0.05

Values are expressed as mean ±SD; n=3

Post compression study

All Duloxetine Hydrochloride Tablet from NF1 to NF9 met the required size and weight parameters. The tablets varied in thickness from 3.91± 0.03 mm to 4.08 ± 0.02 mm, but their diameter remained consistent at around 11.1 ± 0.02 mm. The average tablet weight was close to the aim (450 mg), with a slight deviation (±2.5 mg). The hardness ranged from 6.3 ± 0.3 kg/cm^2 to 7.8 ± 0.2 kg/cm^2, making them suitable for standard handling and packaging. The friability was found in range of 0.31±0.01% to 0.64±0.01%. The results demonstrated that uniformity between batches of the drugs was acceptable since the drug content ranged from 97.4± 0.77% to 99.2±0.49%. They prove that the process for making each composition is dependable and similar (Table 4).

Table 4: Post compression study of extended-release tablet

Batch	Thickness (mm)±SD	Average weight (mg)±SD	Hardness (kg/cm^2) ± SD	Friability (%) ± SD	Drug Content (%) ± SD
NF1	4.00±0.02	449.5±0.96	7.2±0.15	0.47±0.01	98±0.81
NF2	4.05±0.03	449.8±0.58	6.9±0.16	0.32±0.02	99±0.81
NF3	3.95±0.02	448.9±0.83	7.4±0.20	0.64±0.01	98.33±0.47
NF4	4.10±0.02	449.1±0.98	7.8±0.20	0.32±0.01	98.2±0.65
NF5	3.91±0.03	449.6±0.65	8.0±0.15	0.46±0.02	99±0.81
NF6	4.02±0.03	450±0.81	6.5±0.12	0.36±0.02	96.33±0.47
NF7	4.08±0.02	450.2±0.97	6.8±0.15	0.44±0.01	97.4±0.77
NF8	3.97±0.02	449.3±0.99	7.5±0.12	0.47±0.02	98.33±0.47
NF9	4.03±0.03	450.1±0.69	6.2±0.20	0.31±0.01	99.2±0.49

All values are expressed as mean ±SD (Where n=3)

In-vitro dissolution study of extended-release tablets of Duloxetine Hydrochloride

A study found that the Duloxetine Hydrochloride release slowly throughout the day. Each batch displayed controlled release, with the last total amount of drug released varying between80% to 98.53%. The highest release observed in Batch NF9 (98.53%) was very close to the study prediction (Figure 4).

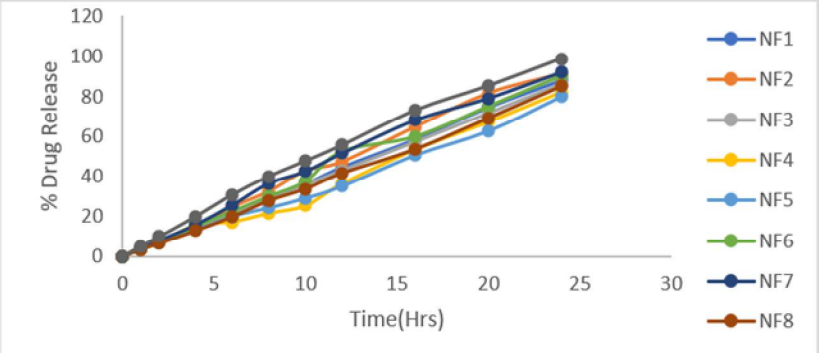


Figure 4: Cumulative % drug release profile of Duloxetine Hydrochloride extended-release formulation as per experimental design.

Optimization of formulation

Effect on Hardness(Y_1)

The linear model for hardness demonstrated statistical significance with a p-value of 0.0002 and showed good model fit, with Adjusted R^2 = 0.9278 and Predicted R^2 = 0.8669. The model was significant (F = 52.41), confirming that the selected variables contributed meaningfully to the response. The linear term for HPMC K100M (A) showed a highly significant effect (F = 93.83, p < 0.0001), whereas Eudragit RS 100

(B) also exhibited a significant effect (F = 10.98, p = 0.0161). Both factors significantly influenced hardness, with factor A showing a stronger impact compared to factor B. The final regression equation in terms of coded factors was:

Hardness (Y_1) = 7.14 + 0.6333A + 0.2167B

As observed from the model, increasing the concentration of HPMC K100M resulted in a pronounced increase in hardness, while Eudragit RS showed a moderate positive effect. The Predicted R^2 (0.8669) is in reasonable agreement with the Adjusted R^2 (0.9278), indicating good model reliability. Adequate Precision (18.386) indicates an adequate signal-to-noise ratio, confirming that the model is suitable for navigating the design space and optimizing tablet hardness.

Effect on % Frug Release after 24 hr (Y_2)

The linear model for % drug release after 24hr demonstrated high statistical significance with a p-value of < 0.0001 and showed excellent goodness of fit, with Adjusted R^2 = 0.9642 and Predicted R^2 = 0.9321. The model was significant (F = 108.69), confirming that the selected variables contributed meaningfully to the response. The linear term for HPMC K100M (A) showed a highly significant effect (F = 167.54, p < 0.0001), whereas Eudragit RS 100 (B) also exhibited a significant effect (F = 49.85, p = 0.0004). Both factors significantly influenced drug release. However, both A and B showed a negative effect, indicating that increasing their concentration decreases the drug release after 24 hours. Factor A showed a stronger impact compared to factor B. The final regression equation in terms of coded factors was:

% Drug Release (Y_2) = 88.00 − 5.50A − 3.00B

As observed from the model, increasing the concentration of HPMC K100M resulted in a pronounced decrease in drug release, while Eudragit RS also showed a moderate negative effect. The Predicted R^2 (0.9321) is in reasonable agreement with the Adjusted R^2 (0.9642), indicating good model reliability. Adequate Precision (28.2897) indicates an excellent signal-to-noise ratio, confirming that the model is reliable and suitable for navigating the design space and optimizing drug release.

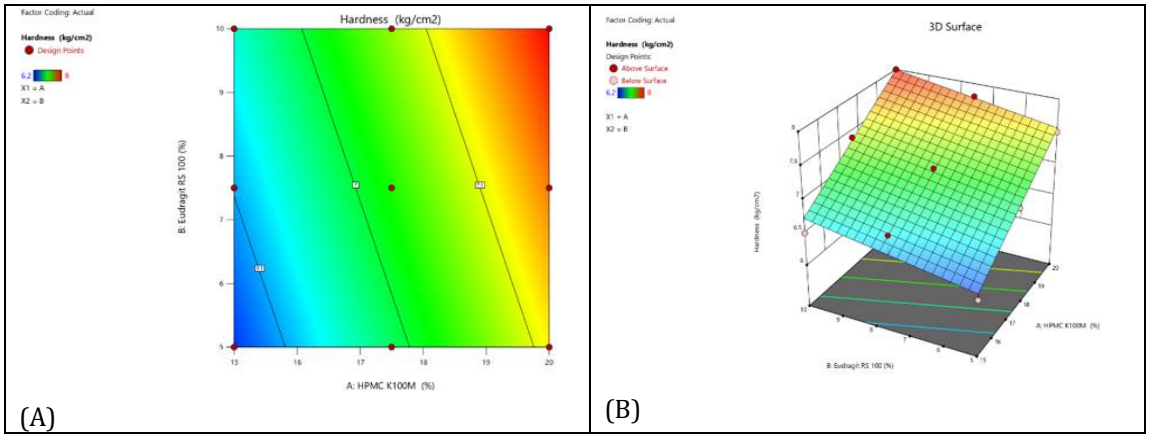
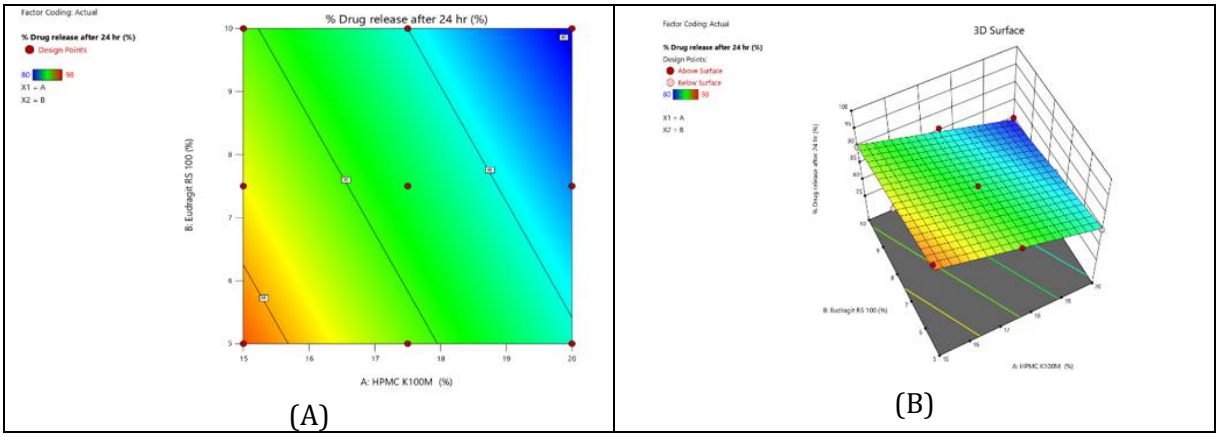


Figure 5: (A) Contour plot for hardness indicating that hardness increased progressively with increase in HPMC K100M and Eudragit RS100 concentration.The color transition from blue to red represents enhancement in tablet hardness from lower to higher polymer levels. (B) 3D surface plot showing a nearly linear upward trend in hardness with increasing concentrations of both polymers.The reponse surface confirms that both HPMC K100M and Eudragit RS 100 contributed positively toward improving tablet mechanical strength and compatibility.

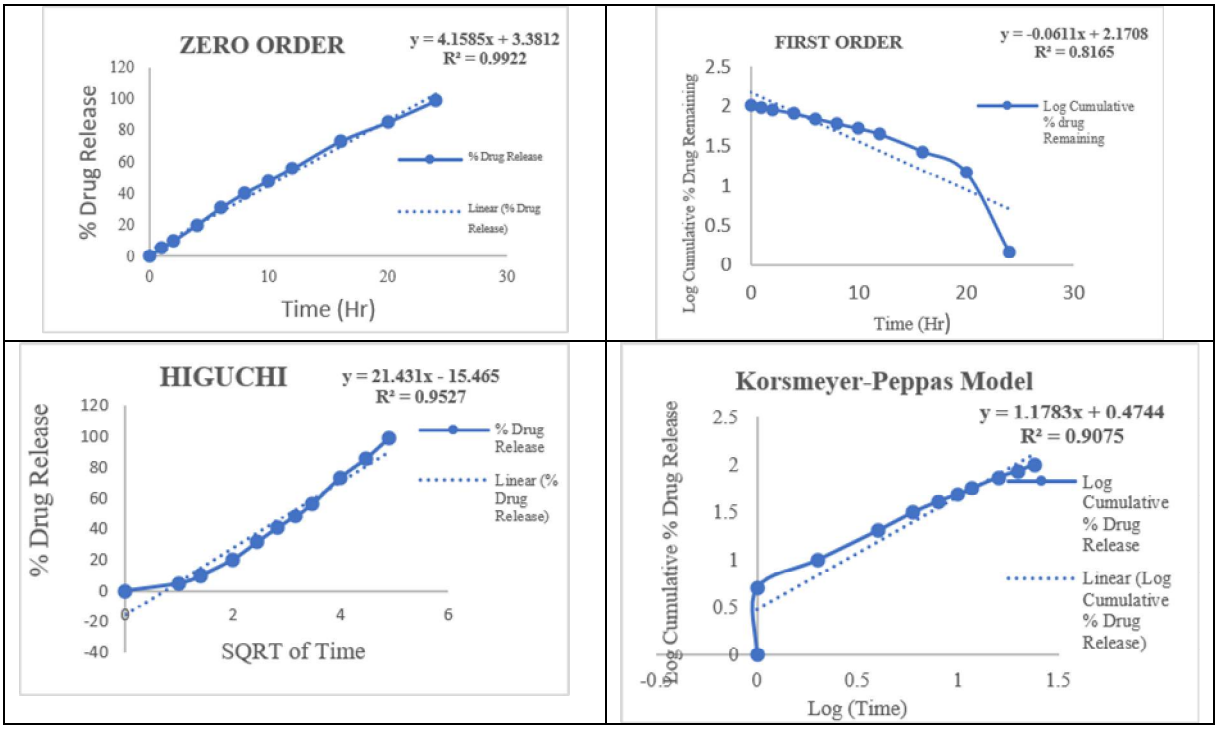


(A) (B)

Figure 6: (A)Contour plot and (B) 3D surface plot show the effect of HPMC K100M and Eudragit RS 100 on % drug release after 24 hr. Drug release decreased with increasing concentrations of both polymers. Higher drug release was observed at lower polymer levels, while higher polymer concentrations produced a sustained release pattern due to formation of a stronger matrix barrier. The 3D surface plot confirmed the negative effect of polymer concentration on drug release, indicating controlled and prolonged drug release behaviour.

Results of release kinetics

The optimized Duloxetine Hydrochloride Extended- release formulation drug release kinetic, that was analysed by using Zero order, First order, Higuchi and Korsmeyer-Peppas models, is given in Figure 7. Zero order model yielded the best fit with a correlation coefficient(R2=0.9922) meaning the drug was release at a constant rate for entire 24 hour.



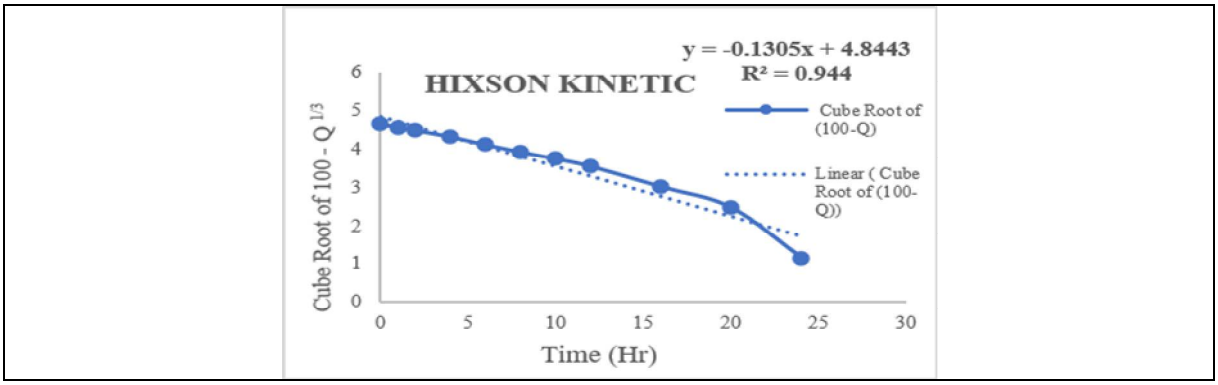


Figure 7: Kinetics modeling of drug release from optimized Duloxetine Hydrochloride Extended-Release Tablet

MTT assay results

The MTT assay revealed dose-dependent cytotoxic activity of Duloxetine Hydrochloride against MCF-7 cell lines following 24 hr. incubation. A gradual decline in cell viability was observed with increasing concentration, where percentage cell viability was decreased from 91.29% at 5µg/mL to 59.76% at 500 µg/mL. The formulation exhibited moderate cytotoxic potential toward MCF-7 cells while retaining considerable cell viability at lower concentrations, indicating acceptable biocompatibility within the tested concentration range.

Table 5: Effect of test sample on cell viability assessed by MTT assay at various concentration

Concentration (ug/mL)	Average % Cell Survival
CTRL	100.00
5	91.29
10	84.14
25	80.82
50	72.72
100	68.97
250	61.24
500	59.76

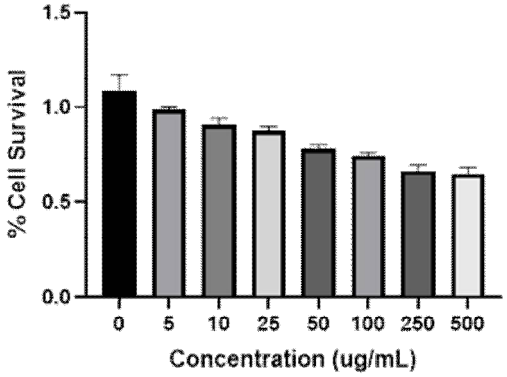
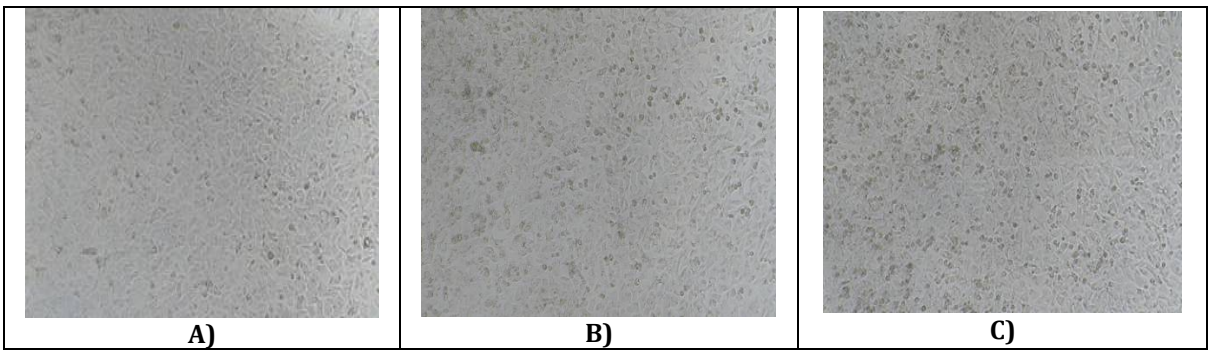


Figure 8: Effect of Duloxetine Hydrochloride on MCF-7 Cell Viability at varying conc. Assessed by MTT assay



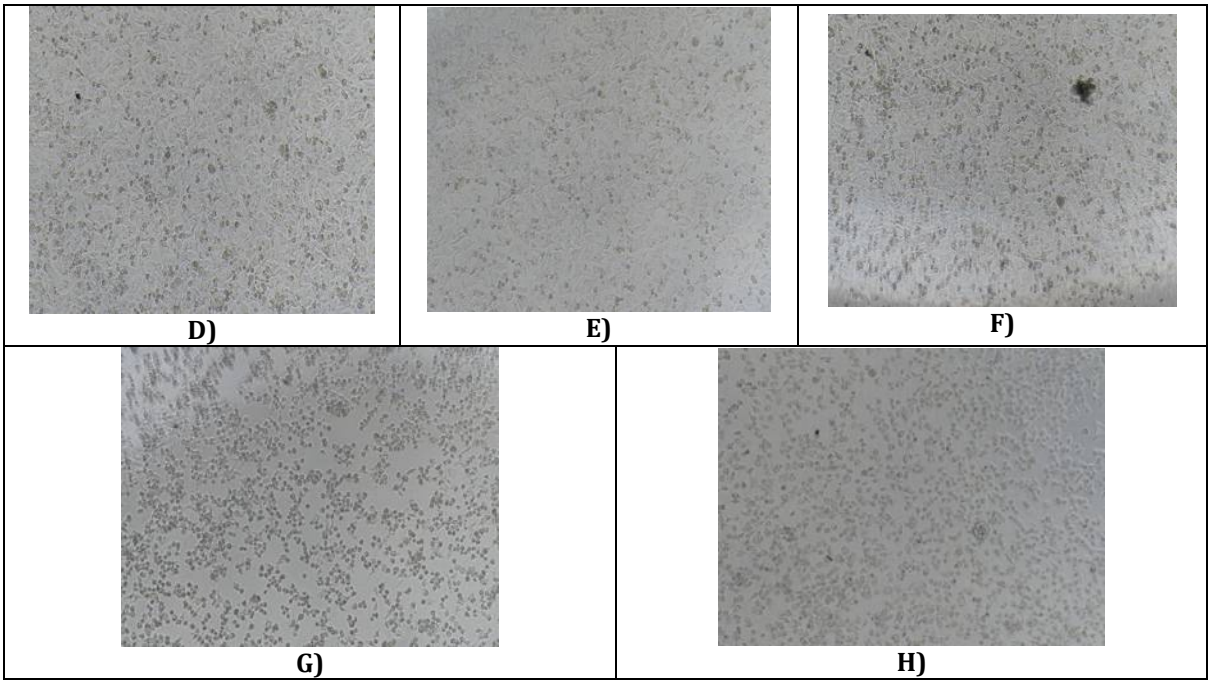


Figure 9: Microscopic images of MCF-7 Cells treated with Duloxetine Hydrochloride at various concentrations after 24 hours of incubation A) Control, B)5 µg/mL, C)10 µg/mL, D)25 µg/mL, E)50 µg/mL, F)100 µg/mL, G)250 µg/mL, H)500 µg/mL.

Accelerated Stability Study

The ICH recommended conditions (temperature 40±2°C and relative humidity 75± 5%) were used for three-month study of Batch NF9.Their appearance remained unchanged throughout the investigation. The tablets hardness dropped from 6.2 kg/cm² to 5.9kg/cm² after three months, but weight variation remained within the limit and only slightly declined from 450±0.69 mg to 449.2±0.78 mg. In-vitro testing of the drugs was slightly reduced from 98.53±0.50% to 98.41±0.38%. The results implied that optimized formula is stable under challenging.

Table 6: Accelerated Stability of optimized Batch NF9 (40±2°C/75±5%)

Study Duration	Appearance	Hardness (kg/cm2)	Weight Variation (mg)	In-Vitro Release after 24 hr(%)
Initial	White, Smooth Tablet	6.2±0.20	450.1±0.69	98.53±0.50
1 Month	No change	6.1±0.18	449.8±0.72	98.80±0.40
2 Month	No change	6.0±0.16	449.5±0.75	99.10±0.35
3 Month	No change	5.9±0.15	449.2±0.78	98.41±0.38

All values are expressed as mean ±SD (Where n=3)

DISCUSSION

The present study successfully developed an extended-release tablet of duloxetine hydrochloride to treat major depression disorder, generalized anxiety disorder, and diabetic peripheral neuropathy. Result of pre-compression parameter was satisfactory as angle of repose was in range of 26.51° to 29.04°, which indicate good flow properties of blended powder. The result was supported by Carr's index and Hausner's ratio. Carr's Index was ranging from 7.03 to 16.8 % and Hausner ratio ranging from (1.07 to1.18). HPMC K100M and Eudragit RS 100 polymers were evaluated for their ability to control drug release over 24 hours. DSC analysis revealed thermal behaviour with a distinctive peak at 172.61°C, indicating no chemical interactions between drug and excipients. All batches showed smooth, white. odorless tablets with consistent thickness and mechanical properties. The formulated dosage form fulfilled all the official specifications of tablet concerning hardness ranging from 6.3 ± 0.3 kg/cm² to 7.8 ± 0.2 kg/cm², Friability was found in range of 0.31±0.01% to 0.64±0.01%, weight variation from 448.9±0.83 to 450.2±0.97mg. The optimized formulation followed Zero-order kinetics(R2=0.9922) as the best fit model. The optimized NF9 batch show 98.53% drug release after 24 hours with acceptable biocompatibility in MCF-7 cytotoxicity assays. Accerated stability studies confirmed the formulation-maintained stability over three months, with no significant changes in hardness. Weight variation and % drug release.

CONCLUSION

The present research successfully designs and optimized an extended-release tablet formulation of Duloxetine Hydrochloride using HPMC K100m and Eudragit RS100 in a matrix system. The results from the optimized formulation (BATCH NF9) demonstrated superior strength, uniform drug distribution, and maintained sustained release kinetics over an extended period. No interaction between the drug and excipients were found during compatibility studies by FTIR and DSC. The developed Duloxetine Hydrochloride extended-release tablet exhibited excellent mechanical strength, released the active pharmaceutical ingredient in a controlled manner over 24 hrs. following zero-order kinetics, and remained stable when exposed to accelerated testing conditions. The formulation was also tested for compatibility and evaluated for safety and quality parameter. Duloxetine Hydrochloride showed concentration-dependent cytotoxicity with 59.76% cell viability at 500ug/ml, indicating moderate biocompatibility and safety. This approach improves patient management for MDD, Generalised Anxiety Disorder and Diabetic Peripheral Neuropathic pain. By reducing no. of dose, improve how patient will take their medicines and maintained plasma drug concentration. The successfully optimized Duloxetine Hydrochloride extended -release tablet formulation through design expert and batch NF9 Successfully represent a significant advancement in therapeutic drug delivery, offering improved bioavailability and enhanced patient compliance through reduced dosing frequency and consistent drug release profile.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

ACKNOWLEDGMENTS

I deeply expressed my sincere gratitude to Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy, Ahilyanagar for providing the essential resources and facilities that made these research possible. The members of the Department of Pharmaceutical Quality Assurance deserve special recognition for their unwavering support and valuable guidance that they provided consistently throughout every phase of my work.

REFERENCES

1. Maruoka J, Egami R, Akita Y, Kozuka K, Kakumoto Y, Kikuchi T, Kume K. (2026). Comparative sleep architecture profiles of antidepressants in mice: Pharmacological characterization of paroxetine, sertraline, duloxetine, mirtazapine and vortioxetine. Pharmacol Res Perspect. 14.e70246. doi: 10.1002/prp2.70246
2. Rajana N, Kulkarni GG. (2026). Simultaneous determination of duloxetine and N-nitroso-duloxetine in reactor cleaning solvent samples by LC-HRMS: Formation, quantitation, and green assessment. Chromatographia. https://doi.org/10.1007/s10337-026-04492-1
3. Yoosefian M, Bayramzadeh H, Abass KS, Mokhtari T. (2026). Potent LeuBAT inhibitors designed in silico as next-generation duloxetine analogs for enhanced major depressive disorder treatment. Sci Rep. 16.1 622 (2026). https://doi.org/10.1038/s41598-025-31085-z
4. Rath S. (2026). Advancing chronic low back pain management: Insights from amitriptyline and duloxetine comparison. World J Methodol. 16. 20;16(1):113191. doi: 10.5662/wjm.v16.i1.113191
5. Kong JS, Seo SW, Kim T, Moon HR, Yoo JW, Kim MS, Yun H, Hwang S, Hwang ET, Jung Y, Yoon IS. (2026). Physiologically based pharmacokinetic modeling for umbelliferone in rats and humans: Impact of extrahepatic phase II metabolism and hepatic/gut first-pass extraction on oral bioavailability and systemic disposition. J Pharm Investig. 56:185-202.
6. Liu LX, Wang F, Zhao ZC, Zhong ZH, Yang SM, Sun Y, Wang SF, Guo WL, Zhou YC. (2025). Pharmacokinetics of baicalin following single oral administration in tilapia (*Oreochromis niloticus*). J Fish Dis. DOI: 10.1111/jfd.70111
7. Kumar S, Kumar A, Gupta V, Malodia K, Rakha P. (2012). Oral extended-release drug delivery system: A promising approach. Asian J Pharma Tech. 2:38-43.
8. Mullaicharam AR. (2013). Novel approaches in vesicular drug delivery systems. Res J Pharm Biol Chem Sci. 4:211-217.
9. Wheless JW, Phelps SJ. (2018). A clinician's guide to oral extended-release drug delivery systems in epilepsy. J Pediatr Pharmacol Ther. 23:277-292.
10. Duong TT, Huynh DTM, Nguyen TUT, Tran Huynh QD, Thi Phan TT, Tran TT, Nguyen HV, Iskandar B, Nguyen DK. (2025). Formulation development of diclofenac sodium extended-release tablet using hydrophobic and hydrophilic matrix systems. J Appl Pharm Sci. https://dx.doi.org/10.7324/japs.2026.253028
11. Ghori MU, Conway BR. (2015). Hydrophilic matrices for oral control drug delivery. Am J Pharmacol Sci. 3:103-109.
12. Alhabardi SA, Almutairi JA, Al-Hamoud GA, Zakaraya ZZ, Hani U, Asiri ZAA, Al Freahat I, Alsafadi W, Dayyih WA, Khan SL, MBeghd ZA. (2025). Musa paradisiaca derived intrinsically heteroatom doped carbon dots as antioxidant and controlled drug release behavior. PLoS One. 1-19.

13. Jadhav PB, Jadhav SB, Zehravi M, Mubarak MS, Islam F, Jeandet P, Khan SL, Hossain N, Rashid S, Ming LC, Sarker MMR, Azlina MFN. (2023). Virtual screening, synthesis, and biological evaluation of some carbohydrazide derivatives as potential DPP-IV inhibitors. Molecules. 28.
14. Hani U, Mahammed N, Reshma T, Talath S, Wali AF, Aljasser A, Al Fatease A, Alamri AH, Khan S. (2025). Enhanced colon-targeted drug delivery through development of 5-fluorouracil-loaded cross-linked mastic gum nanoparticles. Sci Rep. 15:18355.
15. Rajurkar VG, Gite RD, Ghawate VB. (2015). Development of naproxen co-crystal formation: An efficient approach to enhance aqueous solubility. Anal Chem Lett. 5:229-238.
16. Pham DT, Nguyen DXT, Nguyen NY, Nguyen TTL, Nguyen TQC, Tu AVT, Nguyen NH, Thuy BTP. (2024). Development of pH-responsive Eudragit S100-functionalized silk fibroin nanoparticles as a prospective drug delivery system. PLoS One. 19.
17. Borah A, Sahu PP, Saikia HB, Haloi D. (2026). Polyvinyl alcohol based sensing materials: A comprehensive review. Colloid and Polymer Science 304(1):43-66. https://doi.org/10.1007/s00396-025-05519
18. Andrew E, Chidera A, Ekemezie O, Pauline O, Chinedu N, Godswill O. (2024). Preparation and evaluation of ranitidine hydrochloride floating microspheres. Am J Polym Sci Technol. 10:36-46.
19. Sidra Zaya, Jyoti Nayak, & Jai Narayan Mishra. (2023). Formulation And Evaluation Of Floating Tablet Of Atenolol for The Treatment of Hypertension. Journal of Population Therapeutics and Clinical Pharmacology, 30(4), 765-776. https://doi.org/10.53555/jptcp.v30i4.2848
20. Venkateswarlu K. (2012). Formulation and evaluation of sustained release glipizide matrix. IOSR J Pharm Biol Sci. 2:17-23.
21. Dwivedi C, Rao SP, Roy A, Saraf S, Kulsum U, Verma N, Pradhan DK. (2017). Formulation and characterization of metformin hydrochloride sustained release matrix tablet containing *Cassia tora* mucilage. J Drug Deliv Ther. 7.
22. Sarita S, PFIMAD. (2019). Formulation. World J Pharm Res. 2:1685-1703.
23. Chidi E, Ikenna NE, Zainab A, Francis JD. (2017). Development and evaluation of nanoemulsion formulations for improved oral delivery of carvedilol. Univers J Pharm Res. 2:5-11.
24. Baker MM, Hammad SF, Belal TS. (2019). Development and validation of a versatile HPLC-DAD method for simultaneous determination of the antiviral drugs daclatasvir, ledipasvir, sofosbuvir and ribavirin in presence of seven potential impurities. Application to assay of dosage forms and dissolution studies. Drug Dev Ind Pharm. 45:1111-1119.
25. Cieślik A, Raczkowska J. (2025). Biocompatibility of biomedical materials: Reliability of cell viability tests in the context of retinal prostheses. Appl Sci. 15. https://doi.org/10.3390/app151910684
26. Alshamrani A, Alhotan A, Kelly E, Ellakwa A. (2023). Mechanical and biocompatibility properties of 3D-printed dental resin reinforced with glass silica and zirconia nanoparticles: In vitro study. Polymers (Basel). 15. https://doi.org/10.3390/polym15112523