ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 19, Issue 2, 2026

Online - 2455-3891
Print - 0974-2441

Research Article

FORMULATION AND EVALUATION OF CONTROLLED RELEASE MATRIX TABLET OF KETOROLAC TROMETHAMINE PREPARED USING HPMC K100M AND XANTHAN GUM

RITESH R KARMARKAR[1]*, YASH S BACHHAV[1], POONAM J PATIL[2], RUTUJA S AHER[2], GOPAL V RATHI[2], NAKUL P KATHAR[3]

[1]Department of Pharmaceutics, Mahatma Gandhi Vidyamandir's Samajshri Prashantdada Hiray College of Pharmacy, Malegaon (Affiliated to Savitribai Phule Pune University), Pune, Maharashtra, India. [2]Department of Pharmaceutics, Mahatma Gandhi Vidyamandir's Pharmacy College (Affiliated to Savitribai Phule Pune University, Pune), Nashik, Maharashtra, India. [3]Department of Pharmaceutical Quality Assurance, R. C. Patel Institute of Pharmaceutical Education and Research (Affiliated to Kavayitri Bahinabai Chaudhari North Maharashtra University), Jalgaon, Maharashtra, India.
***Corresponding author: Ritesh R Karmarkar; Email: riteshkar@rediffmail.com**

Received: 11 July 2025, Revised and Accepted: 18 December 2025

ABSTRACT

Objective: The primary goal of this research was to create and assess the efficacy of ketorolac tromethamine (KT) controlled release matrix tablets formulated with Xanthan gum and polymers, hydroxypropylmethylcellulose (HPMC) K100M.

Methods: A 3×3 factorial design was employed, and the matrix tablets were tested. All of the manufactured tablets met the requirements for hardness, friability, weight fluctuation, medicine content, and thickness.

Results: The optimized formulation (F6, containing 36 mg HPMC K100M and 36 mg Xanthan Gum) showed 97.58% drug release over 24 h, fitting the Korsmeyer–Peppas model (R^2=0.9964) with non-Fickian diffusion (n=0.5922). The optimized formulation F6 remained stable under accelerated conditions for 3 months.

Conclusion: The study concluded that KT matrix tablets, particularly batch F6 with equal ratios of HPMC K100M and Xanthan gum, showed optimal drug release (94.52% in 24 h) and excellent stability.

Keywords: Ketorolac tromethamine, Hydroxypropylmethylcellulose K 100M, Xanthan gum, Matrix tablet, Release retardant.

 DOI: http://dx.doi.org/10.22159/ajpcr.2026v19i2.56018. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

For the temporary relief of moderate to severe acute pain that would otherwise necessitate the use of an opioid analgesic, ketorolac tromethamine (KT) is prescribed. One of the gastrointestinal adverse effects of KT, like other non-steroidal anti-inflammatory drugs, is a decrease in the synthesis of prostaglandins and thromboxanes from arachidonic acid. This is due to the fact that KT suppresses the activity of the enzyme cyclo-oxygenase. Only once the first parenteral administration is complete is oral KT indicated for further therapy. To keep its therapeutic benefits going, KT needs to be dosed often because of its short half-life (4–6 h) [1,2].

Following oral and intramuscular dosages, KT was efficiently absorbed (>87%) and absorbed quickly (Tmax <1.0 h). Ten to thirty milligrams was the recommended dosage, and its plasma half-life was 4–6 h [3]. When it came to systemic anti-inflammatory activity, when compared to phenylbutazone, indomethacin, and naproxen, it was 36 times stronger, almost twice as strong, and 3 times stronger, respectively [4,5]. Compared to aspirin, its analgesic effects were more potent. When it came to moderate to severe post-operative pain, KT outperformed morphine, pethidine, and pentazocine in clinical trials with a single dose. The drug's short plasma half-life and more water solubility make it an ideal candidate for an oral controlled release formulation.

An investigation into the development of a swellable-controlled release tablet containing ketorolac trometamine was documented. The tablet was formulated with hydrophilic polymers, hydroxypropylmethylcellulose (HPMC) and sodium carboxymethylcellulose, and the hydrophobic polymer ethylcellulose. Similarly, research on KT controlled release matrix tablets made using direct compression technique and various concentrations of cellulose derivatives (HPMC, hydroxyethyl cellulose, and carboxymethyl cellulose) demonstrated that drug release of KT is pretentious by type and concentration of polymer [2].

The bacterium *Xanthomonas campestris* produces the extracellular exopolysaccharide known as xanthan gum. Because of its rheological qualities, it finds extensive use in many different industries. The food, pharmaceutical, agricultural, textile, and other related industries all make use of this commercially significant polysaccharide. Because of its gelling properties and its propensity to entrap medication within the gel matrix, xanthan gum has the potential to impede drug release [6]. Aceclofenac [7], metronidazole [8], and furosemide are reportedly able to have their medication releases delayed by xanthan gum [9].

While HPMC is a standard matrix former, Xanthan Gum's high swelling capacity and gel strength may synergistically improve control, especially for a highly soluble drug like KT. This study investigates this combination to achieve a robust 24-h release profile.

MATERIALS AND METHODS

Materials

Sourced from FDC Ltd. (Waluj, Aurangabad), KT IP was used. A free sample of HPMC K100M was provided by Colorcon Asia Pacific Pvt. Ltd. of Mumbai. Kchabo Gums of Navi Mumbai provided the Xanthan Gum, and it was received as a complimentary sample.

Preformulation study of the drug

Organoleptic properties and description

The sample KT was studied for organoleptic.

Melting point

It was resolute by the capillary method.

Ultraviolet (UV) spectroscopy

In a 100 mL volumetric flask, dissolve precisely 20 mg of KT in a small amount of methanol, water, 0.1 N HCL, and pH 6.8 phosphate buffer solution to create a standard stock solution. Then, a stock solution of 200 µg/mL was obtained by bringing the volume up to 100 mL using methanol, water, 0.1 N HCL, and pH 6.8 phosphate buffer solutions consecutively. Appropriate dilutions of samples were prepared, and λ_{max} was determined. The results are shown in Table 1.

Calibration curve of KT in methanol

In a 100 mL volumetric flask, a precisely measured amount of 20 mg of KT was dissolved in a slight methanol solution until the volume reached 100 mL. To achieve drug concentrations ranging from 5 to 30 µg/mL, suitable portions were transferred to separate 10 mL volumetric flasks and then filled to a capacity of 10 mL using methanol solutions. Fig. 1 displays the outcomes.

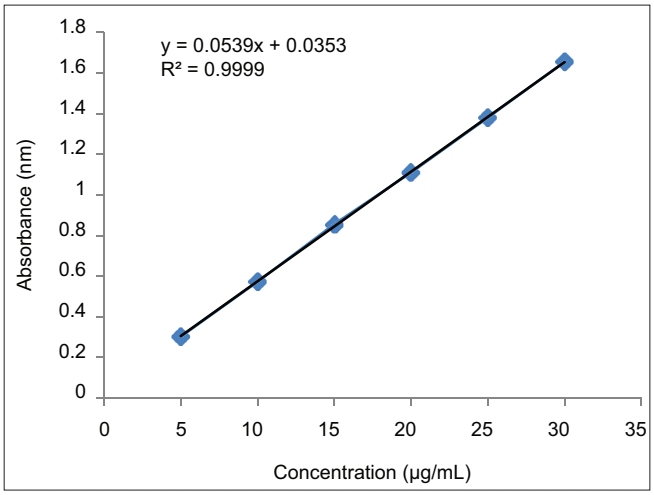

Fig. 1: Calibration curve of ketorolac tromethamine in methanol

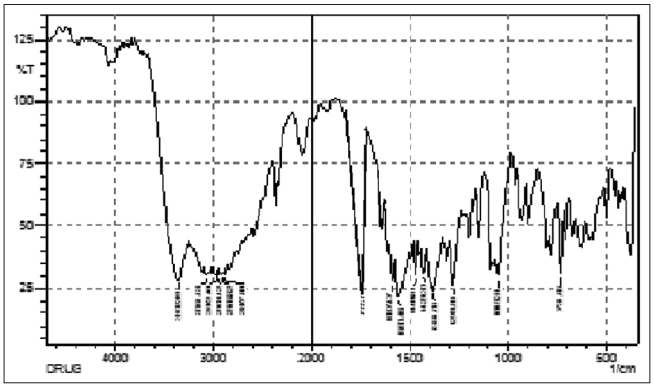

Fig. 2: Fourier transform infrared spectroscopy of ketorolac tromethamine

Table 1: Wavelength of maximum absorbance (λ_{max}) in different solvents

Solvent	λ_{max} (nm)
Water	322.2
0.1 N HCL	316.0
pH 6.8 phosphate buffer	322.1
Methanol	317.2

Fourier transform infrared spectroscopy (FTIR) spectroscopy

A FTIR spectrophotometer (Shimadzu 84005) was used to record the KBr pellet technique FT-IR spectra of KT. Fig. 2 displays the outcome.

Differential scanning calorimetry (DSC)

The sample was analyzed by a Shimadzu thermal analyzer DSC for KT. A sealed aluminum pan was used to heat 60.3 mg of the drug sample at a rate of 10°C/min. The heating process was carried out under a nitrogen flow of 2-bar pressure and at a temperature of 50–300°C. The outcome is shown in Fig. 3.

Formulation of KT matrix tablets

All nine batches of KT matrix tablets were prepared by the direct compression technique. The study uses 9 formulations (F1–F9) which implicitly form a 3×3 factorial design (3 levels of HPMC, 3 levels of Xanthan Gum). KT and all other excipients were passed separately through 40 mesh sieves before blending. The medication, with the exception of magnesium stearate, was measured out and mixed for 10 min in polythene bags. The mixture was lubricated for 5 min after adding the talc and magnesium stearate. The ready-made mixtures were pounded with 8 mm round punches on a 10-station rotary press. The formula for all nine batches is shown in Table 2 and Table 2a.

Pre-compression parameters

A pre-compression study was performed and tested for bulk and tapped density, Carr's index, and angle of repose. Outcomes of pre-compression parameters are shown in Table 3.

Evaluation of KT matrix tablets

Surface, dimensions, weight variation, hardness, medication content, friability, and *in vitro* dissolution profile were some of the quality control tests administered to the tablets both during production and afterward.

The finished tablets were examined visually for surface flaws such as cracks, depressions, pinholes, discoloration, and polish. Their thickness was measured with a Vernier calliper. The Monsanto hardness tester was used to measure their hardness. The mean hardness of all three measurements was calculated and reported.

Table 2: Formulation of ketorolac tromethamine matrix tablets

	Formulation code (Quantities in mg)								
Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Ketorolac tromethamine	30	30	30	30	30	30	30	30	30
HPMC K100M	18	27	36	18	27	36	18	27	36
Xantham gum	27	27	27	36	36	36	45	45	45
Dibasic calcium phosphate	95	86	77	86	77	68	77	68	59
Talc	5	5	5	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5	5	5	5
Total weight	180	180	180	180	180	180	180	180	180

Table 2a: Formulation of ketorolac tromethamine matrix tablets using 3×3 factorial design

Batch code	Xanthan gum	HPMCK100M
F1	−1	−1
F2	−1	0
F3	−1	1
F4	0	−1
F5	0	0
F6	0	1
F7	1	−1
F8	1	0
F9	1	1

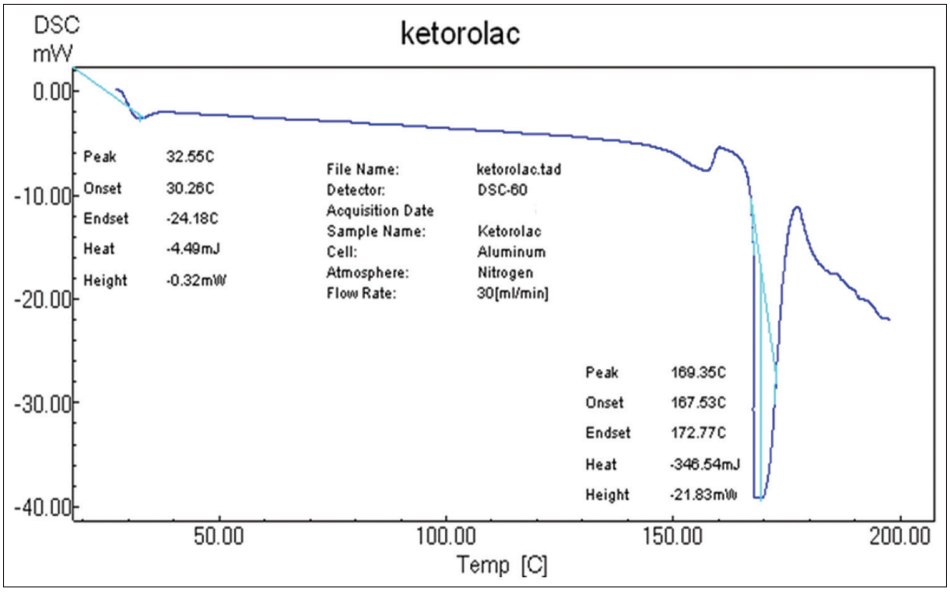

Fig. 3: Differential scanning calorimetry thermogram of ketorolac tromethamine

Table 3: Evaluation of powder blend for flow properties

Batch	Angle of repose (θ), Mean±SD n=3	Bulk density (g/mL), Mean±SD n=3	Tapped density (g/mL), Mean±SD n=3	Compressibility index (%), Mean±SD n=3	Hausner's ratio, Mean±SD n=3
F1	34.42±0.09	0.454±0.003	0.526±0.004	13.64±1.78	1.15
F2	35.20±0.07	0.434±0.003	0.508±0.002	14.57±1.84	1.17
F3	34.43±0.06	0.447±0.005	0.526±0.007	14.93±1.57	1.17
F4	34.59±0.05	0.425±0.036	0.508±0.002	16.30±1.34	1.19
F5	37.04±0.02	0.434±0.004	0.517±0.004	16.02±2.03	1.19
F6	38.34±0.03	0.441±0.003	0.526±0.003	16.18±2.38	1.19
F7	35.2±0.029	0.423±0.002	0.517±0.002	18.09±2.44	1.22
F8	35.98±0.095	0.434±0.002	0.526±0.005	17.40±1.36	1.21
F9	37.52±0.031	0.428±0.0063	0.524±0.002	18.21±1.84	1.22

Values represented as Mean±SD at n=3, Where n=Number of replicates. SD: Standard deviation

Uniformity of weight

Twenty tablets were measured out one by one. The total weight of all the tablets was used to determine their average weight. We compared the average weight to the individual weights. There should be no more than a 7.5% discrepancy in the weight variation as a percentage.

Friability

The tablets' friability was evaluated using the Roche Friabilator. The friabilator chamber was filled with 10 tablets that had been collectively weighed. For 4 min, it was spun at 25 revolutions per minute. The friabilator's chamber allowed the tablets to fall freely, exposing them to rolling forces. Once the friabilator had completed 100 spins, which took about 4 min, the tablets were removed and weighed again as a group. A friability limit of 1% is permissible. We used the following calculation to find the percentage of friability.

Drug content

The average weight was determined after randomly selecting 20 tablets. For analysis, a precisely averaged weight of tablet triturate was extracted after crushing the tablets in a mortar. We used methanol to dilute the samples until they reached the specified volume in many 100 mL volumetric flasks. After 30 min of shaking, the medication was fully dissolved. After the mixtures were filtered, the right concentrations were diluted. Each tablet's drug content was estimated using a blank as a reference at λ max 317 nm.

Table 4 shows the results for the organoleptic characteristics, dimensions, hardness, weight uniformity, friability, and concentration of the medication.

FTIR spectroscopy

Using the KBr pellet approach, an FTIR spectrophotometer (Shimadzu 84005) was used to record the FTIR spectra of the formulation mixture. Fig. 4 displays the peaks.

DSC

By Shimadzu-thermal analyzer DSC 60, 5 mg samples were subjected to DSC analysis to determine the formulation. The sample was subjected to a nitrogen flow at a pressure of 2 bar while being heated in an aluminum pan at a rate of 10°C/min. Temperature 50–300°C. See the results of the DSC investigation are shown in Fig. 5.

In vitro dissolution rate study

By USP – Type II dissolving device (Paddle type), we conducted *in vitro* medication dissolution rate investigations on the manufactured tablets. The experiments were conducted in a dissolution flask with 900 mL of phosphate buffer kept at 37±0.5°C and 100 rpm. The dissolving equipment had KT matrix tablets in each of its bowels. We let the machine run for a full day. Manual withdrawal of 5 mL samples was performed every 1 h for up to 24 h. Samples were passed over a 0.22 μ membrane filter while they were being sampled. Every time a sample was taken, a new dissolving medium was added to keep the sink condition constant. A pure phosphate buffer was used as a blank for the analysis of collected samples at 322 nm. Table 5 displays the results of the triplicate study that was conducted to determine the cumulative percent drug release versus time.

Table 4: Evaluation of tablet parameters

Formulation code	Thickness (mm) Mean±SD n=3	Hardness (Kg/cm²) Mean±SD n=3	Weight variation (mg) Mean±SD n=3	Friability (%) Mean±SD n=3	Drug content (%) Mean±SD n=3
F1	1.98±0.1	6.13±0.01	179.37±0.82	0.21±0.06	99.56±1.49
F2	1.99±0.2	6.40±0.01	179.69±1.25	0.43±0.09	98.68±0.77
F3	1.97±0.1	6.66±0.03	179.671.02	0.28±0.05	99.91±1.34
F4	2.01±0.4	7.13±0.01	179.46±0.90	0.30±0.07	98.93±0.47
F5	1.98±0.2	7.43±0.03	179.76±1.36	0.47±0.05	99.75±1.36
F6	2.01±0.1	7.86±0.03	179.361.16	0.49±0.02	99.86±0.93
F7	1.97±0.1	8.16±0.04	179.84±1.16	0.51±0.05	98.41±0.90
F8	2.02±0.3	8.50±0.01	179.261.59	0.16±0.09	100.30±1.18
F9	1.99±0.4	8.56±0.03	179.14±1.53	0.32±0.06	98.90±0.58

Values represented as Mean±SD at n=3, Where n=Number of replicates. SD: Standard deviation

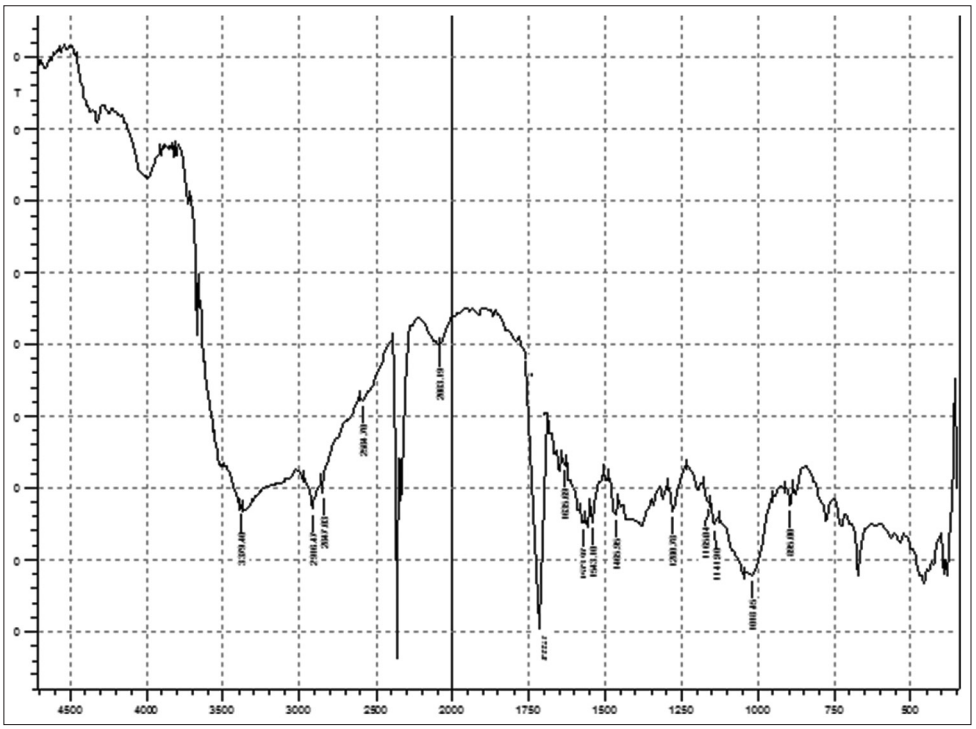

Fig. 4: Fourier transform infrared spectroscopy of the matrix tablet of ketorolac tromethamine

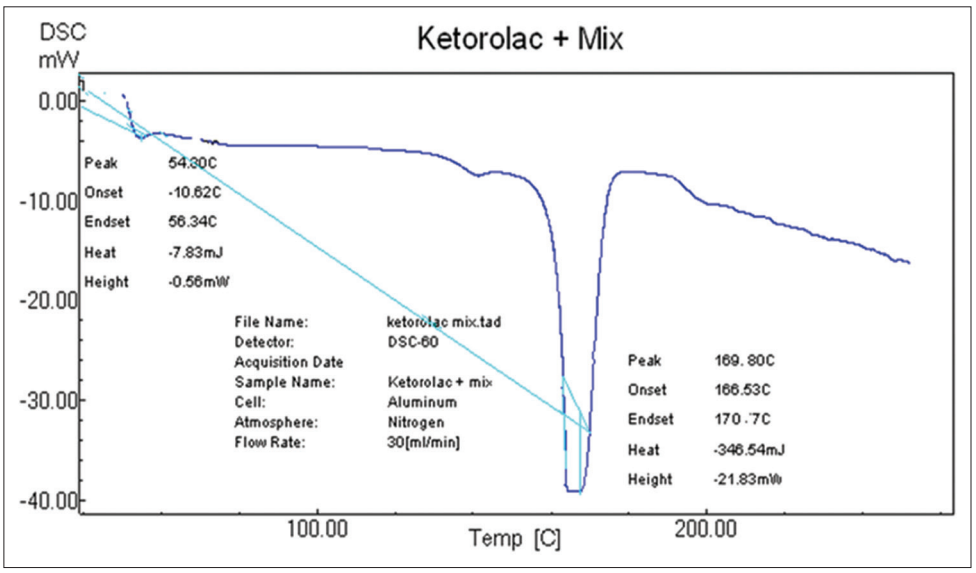

Fig. 5: Differential scanning calorimetry thermogram of the matrix tablet of ketorolac tromethamine

Table 5: Cumulative % drug released profile of ketorolac tromethamine matrix tablets

Time (h)	Cumulative % release (mean±SD), n=3 Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	25.75±0.79	23.96±0.77	23.27±0.41	20.17±0.68	18.65±0.26	15.13±0.41	16.55±0.33	12.2±0.71	11.02±0.87
2	31.41±0.42	27.48±0.84	28.1±0.86	25.82±0.64	22.96±0.31	21.1±0.72	23.48±0.69	19.72±0.55	16.94±0.25
3	36.87±0.63	36.63±0.13	33.83±1.37	32.38±0.41	29.02±0.57	26.68±0.43	28.98±0.77	26.63±0.75	20.99±1.15
4	43.14±0.43	41.76±0.78	37.14±0.41	36.21±0.59	33.83±0.63	31.26±0.57	35.72±0.43	30.84±0.83	26.18±0.63
5	48.21±0.37	48.1±0.36	42.93±0.26	42.97±0.35	38.81±0.26	35.59±0.63	37.92±1.19	35.91±0.92	29.52±0.85
6	54.3±0.38	52.4±0.64	51.14±0.33	46.65±1.25	42.99±0.71	40.83±0.35	41.06±0.72	39.4±0.71	35.74±0.28
7	58.7±0.52	55.41±0.46	56.92±0.26	51.8±0.43	48.06±0.53	44.48±0.51	43.04±0.91	41.64±0.42	39.67±0.73
8	64.9±0.72	58.97±0.36	60.06±0.42	54.28±0.67	52.53±0.28	48.36±0.39	45.81±0.99	43.9±0.59	42.73±0.58
9	68.33±0.53	61.5±0.47	64.78±0.42	57.88±0.64	55.45±0.26	50.05±0.86	47.35±0.29	48.99±0.63	47.93±0.58
10	74.6±0.63	63.05±0.86	67.03±0.36	63.38±0.53	58.19±0.27	54.52±0.35	50.06±0.52	52.13±0.32	51.32±0.83
11	78.19±0.82	65.71±0.43	69.26±0.66	68.28±0.62	61.07±0.73	56.42±0.52	53.47±0.81	54.18±0.81	54.47±0.59
12	82.8±0.94	68.98±0.58	71.27±0.63	71.38±0.37	65.08±0.32	60.6±0.64	58.47±0.84	57.67±0.46	57.79±0.26
13	85.9±1.25	72.72±0.27	73.88±0.38	75.1±0.42	69.01±0.63	64.7±0.35	62.79±0.93	61.42±0.29	63.04±0.67
14	90.22±0.93	76.47±0.65	76.6±0.53	80.18±0.73	73.52±0.37	67.58±0.74	67.75±0.74	64.74±0.83	66.12±0.56
15	91.78±0.56	80.05±0.42	79.67±0.48	84.16±0.26	76.37±0.63	70.07±0.83	71.79±0.90	68.38±0.58	69.81±0.41
16	95.46±0.91	84.15±0.47	82.73±0.31	86.31±0.53	80.17±0.85	72.51±0.65	74.94±0.22	71.86±0.81	74.22±0.54
17	96.42±0.63	88.09±0.37	85.08±0.74	89.07±0.27	84.85±0.77	74.90±0.47	78.96±0.30	73.09±0.37	74.33±0.63
18	98.21±0.72	90.7±0.47	87.15±0.52	92.21±0.73	87.43±0.83	77.61±0.83	83.48±0.54	77.98±0.86	76.31±0.38
19	98.18±0.47	93.74±0.53	90.02±0.73	94.44±0.75	89.68±0.88	80.98±0.66	86.76±0.39	81.86±0.78	79.43±0.72
20	98.17±0.62	95.29±0.52	93.8±0.76	96.83±0.26	92.56±0.27	84.31±0.46	90.66±1.04	83.68±0.50	82.93±0.62
21	98.17±0.72	96.19±0.62	95.69±0.37	97.62±0.43	94.43±0.76	87.29±0.56	93.48±0.34	86.08±0.86	84.34±0.38
22	98.14±0.27	95.32±0.37	96.38±0.52	97.54±0.26	96.25±0.54	91.85±0.78	96.82±0.88	89.59±0.90	87.00±0.73
23	98.10±0.52	95.73±0.63	96.18±0.85	97.42±0.77	97.43±0.55	95.59±0.76	97.5±0.69	91.89±0.84	88.34±0.63
24	98.07±0.62	95.28±0.53	95.14±0.54	97.31±0.67	97.12±0.62	97.58±0.62	97.29±0.46	93.55±0.66	90.13±1.27

Values represented as Mean±SD at n=3, Where n=Number of replicates

Kinetic assessment of *in vitro* release of drug from prepared matrix tablet To gain insight into the rate and mechanism of drug release, the collected dissolution release data were fitted to various equations, including zero order, first order, Higuchi, Hixson–Crowell, and Krosmeer–Peppasand Akaike information criterion (AIC).

Stability studies

Stability of the active ingredient is the primary criterion for accepting or rejecting any rationally designed and evaluated medicinal dosage form. In accordance with ICH Q1A standards, stability investigations were conducted. To conduct stability experiments, the product is left in circumstances of 40±2°C/75±5%RH for a duration of 3 months. Stability investigations were conducted in a photo stability cum humidity chamber (Thermolab, TH 200S, Mumbai) using aluminum foil to encase the optimized batch F6 tablets at time zero (T0) and after 3 months (T3). After 3 months, the samples were taken and tested for appearance, drug content, and *in vitro* dissolution rate studies.

RESULTS AND DISCUSSION

Preformulation studies

Organoleptic properties and description

Organoleptic testing revealed that the KT sample was an odorless, white crystalline powder.

Melting point

The melting point, as measured by the capillary method, was discovered to lie within the 165–169°C range.

UV spectroscopy

Table 1 displays the λmax values of KT in various mediums. The λmax values for KT in various solutions were determined to be 322 nm in water, 316 nm in 0.1 N HCl, 322 nm in phosphate buffer (pH=6.8), and 317 nm in methanol.

Calibration curve of KT in methanol

Methanol was used to conduct the calibration curve of the KT. In the concentration range of 5–30 µg/mL, the calibration curve was determined to be linear with a regression coefficient of 0.999, as follows: Law of Beers and Lambert. The results are shown in Fig. 1.

FTIR Spectrum of KT

The FTIR spectra of pure KT are shown in Fig. 2 and showed peaks at 1723.8 cm^{-1}, 3061 cm^{-1}, 3352 cm^{-1}, 1469.81 cm^{-1}, 1429.30 cm^{-1}, 1381.08 cm^{-1}, 1049.31 cm^{-1}, and 731.06 cm^{-1} that corresponds to C=O stretching, N-H and NH_2 stretching, C=C, aliphatic stretching, C-N vibrations, OH bending and C-H bending, respectively, which indicates functional groups existing in structure of drug.

DSC

The drug was thermally analyzed using DSC. At 169.35°C, which is its melting point and an indication of its purity, the DSC curve for KT displayed a pronounced endothermic peak. The DSC thermogram is shown in Fig. 3.

Evaluation of flow properties of powder blend

Several assessment criteria were applied to the developed mixture before compression. To test the powder mixture, we measured its bulk and tapped density, angle of repose, compressibility index, and Hausner's ratio. Table 3 displays outcomes for pre-compression parameters. The powder blend exhibited good flowing properties, as shown in the table of findings. A compressibility index of 11.92–14.83 and an angle of repose of 38.58–41.06 were the possible values. There was a wide range in bulk density (0.329–0.364) and tapped density (0.385–0.418) for the powder blend. Between 1.13 and 1.17 is the range of Hausner's ratio. Drug powder was found to be passable based on angle of repose values. Despite the poor flow properties, the blends were successfully compressed using the direct compression method, likely due to the use of glidants (Talc) and lubricants (Mg Stearate).

Evaluation of KT matrix tablets

Organoleptic properties

The finished matrix tablets were uniformly smooth and had a yellowish hue. Several tests were performed on the tablet formulations to assess their qualities. Table 4 displays the outcomes for each formulation.

Every formulation has a different thickness, ranging from 1.97 to 2.02 mm, which is determined by the drug: polymer ratio. The thickness of each formulation was consistent. The weight variation test was conducted according to the official technique, and results showed that all of the formulations had average % deviations that were within the allowed range (i.e., <5%, as per the pharmacopeial standard, for tablets with a weight of 180 mg).

Different batches demonstrate good content consistency, according to the results of the content uniformity test that was also conducted using the standard procedure. In addition, it was discovered that every batch had a drug content percentage higher than 95%. All of the formulations' tablet hardness values ranged from 6.0 to 8.5 kg/cm^2. Friability was another way to evaluate the hardness of tablets. In general, compressed pills with a weight loss of <1% are acceptable. The weight loss was <1% for all of the formulations tested here, which is well below the permitted range.

FT-IR of KT matrix tablet

Typical peaks were seen in FT-IR spectra of the KT matrix tablet, as illustrated in Fig. 4. FT-IR spectra of the matrix tablet displayed distinct peaks at 1723.8 cm^{-1}, 3061 cm^{-1}, 3352 cm^{-1}, 1469.81 cm^{-1}, 1429.30 cm^{-1}, 1381.08 cm^{-1}, 1049.31 cm^{-1}, and 731.06 cm^{-1}. These peaks correspond to C=O stretching, N-H and NH2 stretching, C=C, aliphatic stretching, C-N vibrations, OH bending, and C-H bending, respectively. Non-appearance of any well-defined, inexplicable peaks confirms the formulation's purity and indicates that the excipients have no interaction with the drug.

DSC of KT matrix tablet

The tablet was subjected to DSC thermal analysis. There is no evidence of drug-excipient interaction in the DSC thermogram of matrix tablets, which shows a sharp endothermic peak at 169.80°C, the tablet's melting point. The DSC of the matrix tablet is shown in Fig. 5.

***In vitro* dissolution rate study**

To find out whether the drug's release was sufficiently prolonged – that is, what proportion of polymer was sufficient to prolong the drug's release for at least 24 h – drug release tests were conducted. Formulation F6 demonstrates the highest drug retardation, with a drug release of 97.58% after 24 h, as shown by the dissolution curve. The time for 50% or 80% drug release (T50%, T80%) for all formulations were compared. 50% of drug release for formulation F1, F2, and F3 with HPMC: Xanthan Gum polymer ratio of 18:27, 27:27, and 36:27 showed 50% drug release at 6 h, whereas 80% drug release occurred at 12 h for F1 and 15 h for F2 and F3. 50% of drug release for formulation F4, F5, and F6 with HPMC: Xanthan gum polymer ratio 18:36, 27:36, and 36:36 indicates that 50% drug release for F4 batch occurs at 7 h, F5 batch occurs at 8 h, and F6 batch occurs at 9 h, whereas 80% drug release for F4 batch occurs at 14 h, F5 batch at 16 h, and F6 batch at 19 h. 50% of drug release for formulation F7, F8, and F9 with HPMC: Xanthan Gum polymer ratio of 18:45, 27:45, and 36:45 showed 50% drug release for F7, F8, and F9 occurs at 10 h, whereas 80% of drug release for F7 occurs at 18 h, for F8 at 19 h, and F9 at 20 h.

F6 (36:36) performed better than F4 (18:36) and F3 (36:27), suggesting an optimal ratio is needed, not just a high polymer load. Hence, the F6 batch was found to be the optimized batch and was used for further studies of stability. Outcomes of the *in vitro* dissolution rate study are shown in Table 5 and in Figs. 6-8.

Kinetic treatment of optimized KT matrix tablet

By comparing the *in vitro* release data with the zero, first-order, Hixson–Crowell, Higuchi, and Korsmeyer–Peppas models, we were able to determine which release model most accurately reflects the drug release pattern. A particular mechanism was chosen for release

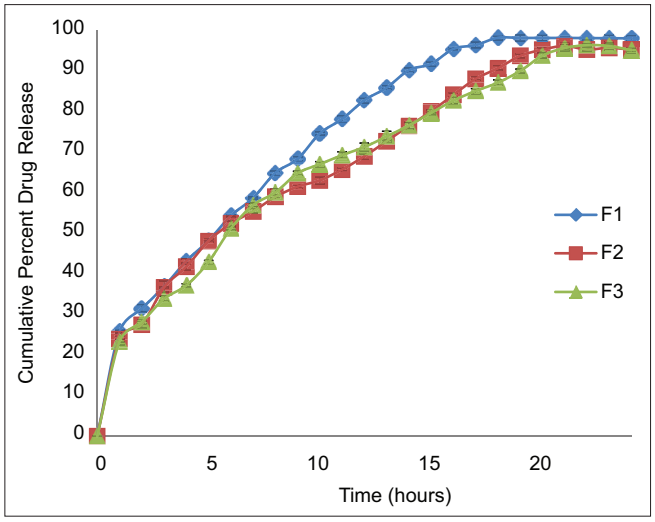

Fig. 6: Comparative dissolution profile of matrix tablets (F1-F3) of ketorolac tromethamine

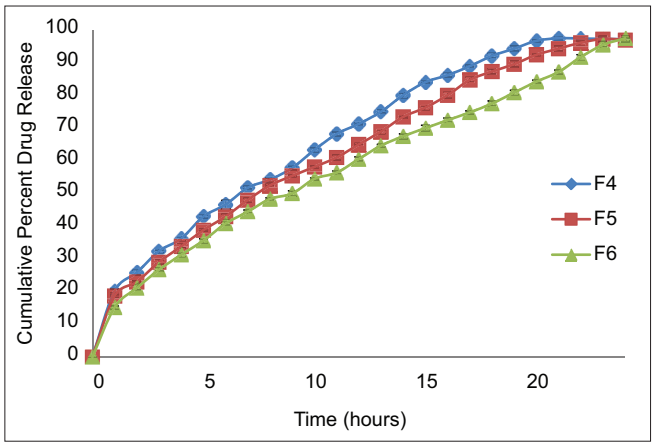

Fig. 7: Comparative dissolution profile of matrix tablets (F4-F6) of ketorolac tromethamine

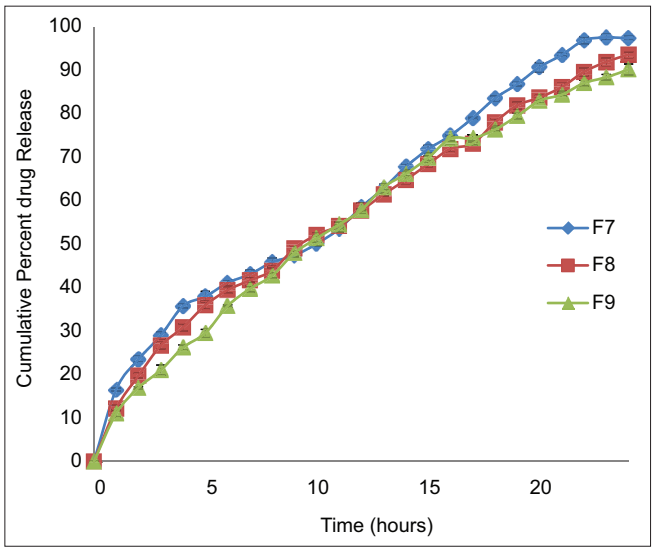

Fig. 8: Comparative dissolution profile of matrix tablets (F7-F9) of ketorolac tromethamine

Table 6: Kinetic treatment data of controlled release matrix tablet of ketorolac tromethamine

Formulation code	Coefficient of determination (R^2)					Krosmeyer Peppas plot n (Release exponent)
	Zero order R^2	First order R^2	Higuchi R^2	Hixson-crowell R^2	Krosmeyer-peppas R^2	
F1	0.8902	0.8001	0.9621	0.8312	0.9761	0.4810
F2	0.9597	0.9165	0.9881	0.9497	0.9924	0.4867
F3	0.9513	0.9012	0.9909	0.9570	0.9882	0.4946
F4	0.9609	0.9226	0.9871	0.9541	0.9890	0.5450
F5	0.9824	0.9605	0.9928	0.9903	0.9925	0.5797
F6	0.9912	0.9742	0.9905	0.9918	0.9964	0.5922
F7	0.9916	0.9843	0.9696	0.9802	0.9795	0.5788
F8	0.9899	0.9704	0.9912	0.9965	0.9961	0.6297
F9	0.9854	0.9530	0.9934	0.9899	0.9962	0.6938

Table 6a: AIC-Based model comparison table (optimized formulation F6) based on release data

Model	SSE	AIC
Zero order	121.02	42.83
First order	2827.48	118.46
Higuchi	118.46	42.32
Hixson–Crowell	448.17	74.25
Krosmeyer–Peppas	4.64	−35.43 (Lowest)

AIC: Akaike information criterion

Table 7: *In vitro* dissolution study of optimized batch after 3 months stability study

Time (h)	% Drug release (mean±S.D.), n=3
1	16.28±0.39
2	23.72±0.42
3	29.16±0.51
4	34.38±0.31
5	37.95±0.53
6	42.68±0.73
7	46.47±0.62
8	52.33±0.46
9	54.42±0.37.
10	58.33±0.47
11	60.30±0.71
12	63.42±0.38
13	67.64±0.58
14	70.54±0.63
15	73.02±0.74
16	74.69±0.59
17	76.91±0.69
18	80.01±0.81
19	82.94±0.48
20	88.94±0.53
21	91.82±0.62
22	94.71±0.83
23	96.50±0.64
24	97.86±0.55

Values represented as Mean±SD at n=3, Where n=Number of replicates.
SD: Standard deviation

based on the correlation coefficient "r" for the parameters that were evaluated; the highest correlation coefficient was chosen. For the optimized F6 formulation, the Korsmeyer–Peppas model yielded the highest "r" value. In the end, the drug was released through swelling or chain relaxation of polymers, diffusion, and erosion, as the value of release exponent "n" calculated from Krosmeyer–Pappas equation was more than 0.5, which indicates non-Fickian transport. The rate of drug release is independent of concentration in optimized formulation F6, which follows zero-order drug release. Tables 6 and 6a display the outcomes.

Krosmeyer–Peppas has the lowest AIC (−35.43) and hence the best fit model. Higuchi and zero order are moderate fits. First order fits worst, indicating the release is not concentration dependent. These strongly support the conclusion that optimized formulation F6 follows non-Fickian (anomalous) transport driven by polymer relaxation plus diffusion, with an overall zero-order release pattern.

Stability study

The optimized F6 matrix tablet formulation was subjected to stability experiments, which revealed that the tablets' color and odor remained unchanged and that drug content was determined to be 98.60±0.43%. The percentage of drug release after 24 h was determined to be 97.86±0.55 in in vitro dissolution research, and calculating the similarity factor (f2) between the initial and 3-month dissolution profiles did not alter significantly, as the calculated F2 factor value comes to 99.28, which is between 50 and 100, and hence the dissolution profiles are similar to each other. Hence, showed that after charging it for the stability investigation, it proves that the formula that was created remains unchanged and stable. Table 7 displays the outcomes.

CONCLUSIONS

Preformulation studies, namely, organoleptic properties, melting point, UV Spectroscopy, FTIR, and DSC studies were carried out on KT. The studies showed that the drug was pure in quality and complied with the standard. A total of nine batches were prepared for matrix tablet formulations. An evaluation of the resulting blends' flow characteristics was carried out using bulk, tapped density, Carr's Compressibility Index, Hausner's ratio, and angle of repose. Drug powder was found to be passable based on angle of repose values. Despite the poor flow properties, the blends were successfully compressed using the direct compression method, likely due to the use of glidants (Talc) and lubricants (Mg Stearate). All nine batches of KT matrix tablets were prepared using the direct compression technique. Round 8 mm punches were used to compress the produced mixes on a 10-station rotary press. The finished matrix tablets were uniformly smooth and had a yellowish hue. Tablet formulations were evaluated using a battery of additional criteria, including drug content, hardness, friability, uniformity of weight, and thickness. Every formulation has a different thickness, ranging from 1.97 to 2.02 mm, which is determined by the drug: polymer ratio. The thickness of each formulation was consistent. After conducting the weight variation test according to the official procedure, it was determined that all of the formulations had average percentage deviations that were within the allowed range (i.e., <5%, as per the pharmacopeial standard, for tablets with a weight of 180 mg). Different batches demonstrate good content consistency, according to the results of the content uniformity test that was also conducted using the standard procedure. In addition, it was discovered that every batch had a drug content percentage higher than 95%. All of the formulations' tablet hardness values ranged from 6.0 to 8.5 kg/cm^2. Friability was another way to evaluate the hardness of tablets. In general, compressed pills with a weight loss of <1% are acceptable. The weight loss seen in all of the formulations tested here was <1%, which is within the

permitted range. *In vitro* medication dissolving rate investigations were conducted on the manufactured tablets using a USP – Type II dissolution instrument (Paddle type). For 24 h, the dissolution flask was maintained at a temperature of 37±0.5°C and spun at 100 rpm. In the tests, 900 mL of phosphate buffer with a pH of 6.8 was utilized. Research concluded that the F6 batch was the most efficient. The highest drug release (94.52%) up to 24 h is achieved for the F6 batch when the proportions of HPMC K100M and Xanthan gum are equal. *In vitro* data on matrix tablet dissolution were subjected to the release kinetics analysis. If the optimized tablet's n value is more than 0.5, then the release mechanism is non-Fickian transport as a result of the polymers' swelling and chain relaxation, diffusion, and erosion. Krosmeyer–Peppas has the lowest AIC (−35.43) and hence the best fit model. Higuchi and zero order are moderate fits. First order fits worst, indicating the release is not concentration dependent. These strongly support the conclusion that optimized formulation F6 follows non-Fickian (anomalous) transport driven by polymer relaxation plus diffusion, with an overall zero-order release pattern. There were no changes observed in the color or smell of tablets, and drug content was determined to be 98.60±0.43%, according to stability experiments conducted on optimized F6 matrix tablet formulation. The percentage of drug release after 24 h was determined to be 97.86±0.55 *in vitro* dissolution research, and the dissolution profile of the matrix tablet did not alter significantly after charging it for the stability investigation. This proves that the formulation that was produced remains stable. Furthermore, the use of dibasic calcium phosphate (DCP) as a diluent is problematic. DCP is a soluble, non-swelling diluent. In a hydrophilic matrix, it can create channels for faster drug release, potentially confounding the results. An insoluble diluent, such as microcrystalline cellulose (MCC), is typically preferred to avoid this effect. The use of DCP can be replaced with MCC as a diluent for future work.

ACKNOWLEDGMENTS

The author is grateful to FDC Ltd. (Waluj, Aurangabad) for providing the gift sample of Ketorolac Tromethamine IP. Colorcon Asia Pacific Pvt. Ltd. of Mumbai and Kchabo Gums of Navi Mumbai both contributed to our gratitude by presenting us with free samples of HPMC K100M and Xanthan Gum, respectively.

AUTHORS CONTRIBUTIONS

All authors have contributed to the research.

CONFLICTS OF INTEREST

No conflict of interest.

FUNDING

Self-funded.

REFERENCES

1. Rajveer C, Rathinaraj BS, Fareedullah M, Bangale GS, Shinde GV. Design and evaluation of ketorolac tromethamine sustained release matrix tablets. Deccan. J Pharm Cosmetol. 2010;1(2):57-71.
2. Genç L, Jalvand E. Preparation and *in vitro* evaluation of controlled release hydrophilic matrix tablets of ketorolac tromethamine using factorial design. Drug Dev Ind Pharm. 2008;34(8):903-10. doi: 10.1080/03639040802266170, PMID 18686094
3. Brocks DR, Jamali F. Clinical pharmacokinetics of ketorolac tromethamine. Clin Pharmacokinet. 1992;23(6):415-27. doi: 10.2165/00003088-199223060-00003, PMID 1458761
4. Vatsaraj N, Zia H, Needham T. Formulation and optimization of a sustained-release tablet of ketorolac tromethamine. Drug Deliv. 2002;9(3):153-9. doi: 10.1080/10426500290095656, PMID 12396732
5. Rao MR, Ranpise AA, Thanki KC, Borate SG, Parikh GN. Effect of processing and sintering on controlled release wax matrix tablets of ketorolac tromethamine. Indian J Pharm Sci. 2009;71(5):538-44. doi: 10.4103/0250-474X.58188, PMID 20502573
6. Benny IS, Gunasekar V, Ponnusami V. Review on application of xanthan gum in drug delivery. Int J PharmTech Res. 2014;6(4):1322-6.
7. Ramasamy T, Kandhasami UD, Ruttala H, Shanmugam S. Formulation and evaluation of xanthan gum based aceclofenac tablets for colon targeted drug delivery. Braz J Pharm Sci. 2011;47(2):299-311. doi: 10.1590/s1984-82502011000200011
8. Jackson C, Ofoefule S. Use of xanthan gum and EthylCellulose in formulation of metronidazole for colon delivery. J Chem Pharm Res. 2011;3:11-20.
9. Jain S, Yadav SK, Patil UK. Preparation and evaluation of Sustained release matrix tablets of furosemide using natural polymers. Res J Pharm Technol. 2008;1:374-6.