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FORMULATION AND EVALUATION KETOROLAC LOADED HYDROGEL FOR INFLAMMATION

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ABSTRACT

This project is all about making and testing Ketorolac-loaded hydrogels for delivering drugs via the skin. We used a number of analytical methods, including as organoleptic evaluation, melting point analysis, solubility testing, UV-Visible spectrophotometry, and FTIR spectroscopy, to describe ketorolac, a strong non-steroidal anti-inflammatory medicine (NSAID). Carbopol-940 and guar gum were used as gelling agents to make eight distinct hydrogel formulations (F1–F8). We looked at these formulations' physical characteristics, pH, spreadability, extrudability, washability, viscosity, drug content, and drug release in vitro. Among all of them, formulation F4 had the best properties, with great homogeneity, spreadability, and drug release profile (98.74% at 30 minutes), which was very similar to the marketed formulation. Accelerated stability tests on F3 showed that it was physically and chemically stable for more than 90 days. The results imply that the manufactured Ketorolac-loaded hydrogels, especially F4, are a viable and reliable option for topical distribution with more therapeutic potential.

KEYWORDS: Ketorolac, hydrogel formulation, topical drug delivery, Carbopol-940, guar gum, physicochemical evaluation, in vitro drug release, FTIR spectroscopy, UV-visible spectrophotometry.

INTRODUCTION

Topical drug delivery systems have gotten a lot of interest because they can administer medications directly to the site of action, which lowers systemic adverse effects and makes patients more likely to follow their treatment plans. Hydrogels have become one of the best carriers since they are biocompatible, easy to use, and can hold a lot of water. Ketorolac tromethamine is a non-steroidal anti-inflammatory medication (NSAID) that is commonly used to treat pain and inflammation that is moderate to severe. However, taking it by mouth typically causes problems in the digestive system, which makes it hard to use for a long time.[1-2]

A hydrogel topical formulation is a safer and more targeted option that can help get around these problems. We made several hydrogel forms of Ketorolac in this work utilising Carbopol-940 and guar gum. We looked at the physicochemical features, drug release behaviour, and stability of several formulations to see whether they may make the medicine more effective and easier for patients to use. This work shows that hydrogel-based methods might be good candidates for delivering anti-inflammatory medications like Ketorolac directly to the skin.[3-5]

2. MATERIAL AND METHODS

2.1 Preformulation study

2.1.1 Characterization of Ketorolac

The physical properties of Ketorolac were assessed through organoleptic evaluation, including color, odor, and taste, to preliminarily verify its identity and quality.[6]

2.1.2 Melting Point Examination

The melting point of Ketorolac was determined using the capillary method and Thiele tube, providing a key indicator of its purity.[7]

2.1.3 Drug Solubility Examination

Solubility studies were conducted in various solvents (e.g., methanol, ethanol-water, phosphate buffer) under constant agitation to determine Ketorolac's equilibrium solubility.[8]

2.1.4 Determination of λmax

Ketorolac's maximum absorbance (λmax) was found to be at 260 nm using UV-Vis spectroscopy in pH 7.4 phosphate buffer, confirming its optical properties.[9]

2.1.5 Preparation of pH 7.4 Phosphate Buffer

The buffer was prepared by mixing potassium dihydrogen phosphate and disodium hydrogen phosphate solutions to obtain a final pH of 7.4.[10]

2.1.6 Standard Curve of Ketorolac

A standard calibration curve was created using UV-Vis spectrophotometry to determine the drug concentration based on absorbance at 260 nm.[11]

2.1.7 FTIR Spectroscopy

FTIR analysis identified functional groups in Ketorolac by recording its infrared spectrum, confirming its chemical structure.[12]

2.2 Preparation of Ketorolac-Loaded Hydrogel

Hydrogels were formulated using Carbopol-940, guar gum, and penetration enhancers. pH adjustment with NaOH enabled gel formation, resulting in a stable Ketorolac-loaded hydrogel.[13]

Table 1: Composition of Ketorolac-Loaded Hydrogel.

S. No.	Ingredients	Formulation code							
		F1	F2	F3	F4	F5	F6	F7	F8
1	Ketorolac (mg)	100	100	100	100	100	100	100	100
2	Carbapol- 940 (mg)	0.6	0.450	1.1	0.765	0.457	0.563	0.654	0.786
3	Guar gum (mg)	0.386	0.5	0.698	0.543	0.876	0.457	0.563	0.762
4	Isopropyl myristate (ml)	1.3	1.6	1.2	0.9	1.8	1.3	0.8	0.9
5	Isopropyl alcohol (ml)	0.22	0.30	0.18	0.34	0.16	0.18	0.35	0.17
6	Distilled water q.s	100	100	100	100	100	100	100	100

2.3 Assessment parameter of Ketorolac-Loaded Hydrogel

2.3.1 Physical Characterization of Hydrogel Formulations

Hydrogels were evaluated for pH, color, homogeneity, texture, consistency, grittiness, and phase separation to ensure uniformity, smoothness, and physical stability.[14]

2.3.2 pH Examination

The pH of each hydrogel was measured using a digital pH meter after dispersing 1 g of gel in 25 mL of distilled water. Triplicate measurements ensured accuracy and consistency.[15]

2.3.3 Washability Test

Hydrogels were applied to the skin and rinsed with plain water to assess ease of removal and residue. This tested post-application cleanliness and user-friendliness.[16]

2.3.4 Extrudability Study

Formulations were filled into collapsible tubes and manually pressed to evaluate how easily the gel was expelled, indicating suitability for packaging and patient use.[17]

2.3.5 Spreadability Test

Using two glass slides and a 20 g weight, the time taken for the gel to spread was recorded. Spreadability (S) was calculated using the formula.[18]

S = (m × l) / t, reflecting gel application ease.

2.3.6 Viscosity Measurement

A Brookfield viscometer measured the viscosity of hydrogels at room temperature. This assessed flow properties and formulation consistency.[19]

2.3.7 Drug Content Determination

Drug content was quantified by dissolving the gel in phosphate buffer (pH 7.4), filtering, diluting, and analyzing it at 260 nm using a UV spectrophotometer.[20]

2.3.8 In Vitro Drug Release Using Cellophane Membrane

A Franz diffusion cell setup was used to monitor drug release from hydrogels over 8 hours at 37°C. Samples were analyzed at 260 nm to determine release rate and profile.[21]

2.3.9 Stability Studies

Stability testing followed ICH guidelines under long-term and accelerated conditions. The selected formulation was monitored at 25°C/60% RH, 30°C/65% RH, and 40°C/75% RH for 3 months to assess physical and chemical stability.[22]

3. RESULT AND DISCUSSION

3.1 Results

3.1.1 Physical characteristic of Ketorolac

Table 2: Physical Characteristics of Ketorolac.

Parameter	Observation
Appearance	White to off-white crystalline powder
Odor	Odorless
Taste	Slightly bitter
Melting Point	96

Solubility	Slightly soluble in water, freely soluble in ethanol, methanol, and acetone
Molecular Weight	255.27 g/mol
Partition Coefficient (log P)	~3.1
UV Absorption (λmax)	4000–400 cm^{-1} nm in phosphate buffer (pH 7.4)

3.1.2 Standard calibration curve

Table 3: Observation Table Standard calibration curve.

S. No.	Concentration (µg/mL)	Absorbance at 322 nm
1	2	0.145
2	4	0.289
3	6	0.436
4	8	0.580
5	10	0.725
6	12	0.868

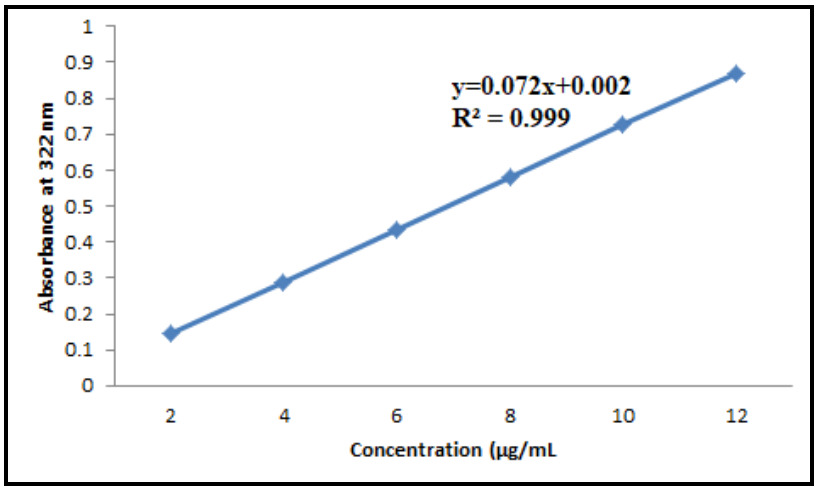

Figure 1: Calibration curve of Ketorolac at 332 nm.

3.1.3 FTIR Examination

Table 4: FTIR Interpretation Data for Ketorolac.

S. No.	Observed Peak (cm^{-1})	Functional Group	Vibrational Mode
1	~3312	O–H (from carboxylic acid)	Stretching
2	~1695	C=O (carboxylic acid)	Strong stretching
3	~1620	C=C (aromatic ring)	Stretching
4	~1570	N–H (amide or secondary amine)	Bending
5	~1470	C–H (aromatic)	Bending
6	~1320	C–N (secondary amine)	Stretching
7	~765–720	C–H (aromatic, out-of-plane)	Bending (monosubstituted benzene)

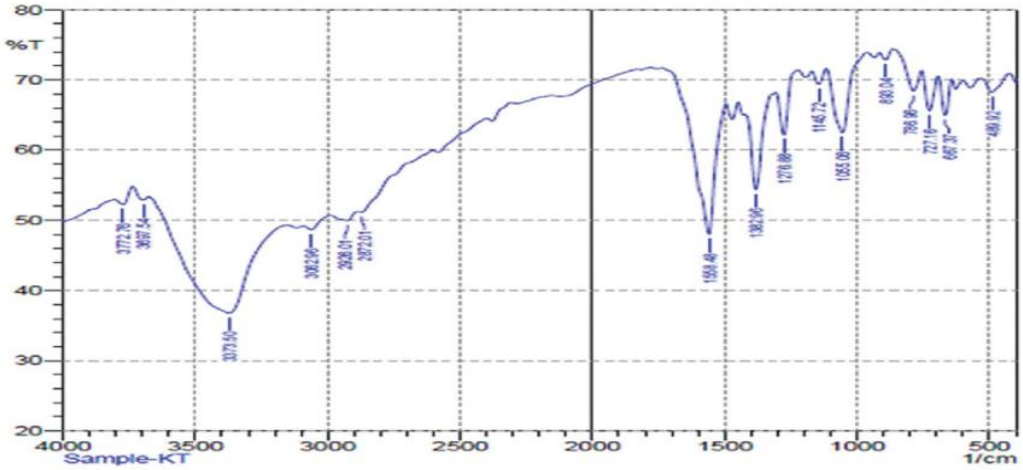

Figure 2: FTIR spectra of Ketorolac.

3.2 Evaluation parameters of Ketorolac loaded hydrogel.

3.2.1 Physical appearance of Ketorolac loaded hydrogel all formulations.

Table 5: Physical appearance of Ketorolac loaded hydrogel all formulations.

Formulation code	Colour	Homogeneity	Consistency	Phase separation
F1	White	Good	Average	None
F2	White	Average	Average	None
F3	White	Good	Good	None
F4	White	Excellent	Excellent	None
F5	White	Average	Good	None
F6	White	Good	Average	None
F7	White	Average	Good	None
F8	White	Average	good	None

3.2.2 pH Examination

Table 6: Results of pH of Ketorolac loaded hydrogel all formulations.

Formulation code	pH
F1	7.6±0.03
F2	7.5±0.02
F3	7.1±0.02
F4	7.4±0.08
F5	7.5±0.03
F6	7.2±0.01
F7	7.5±0.07
F8	7.4±0.06

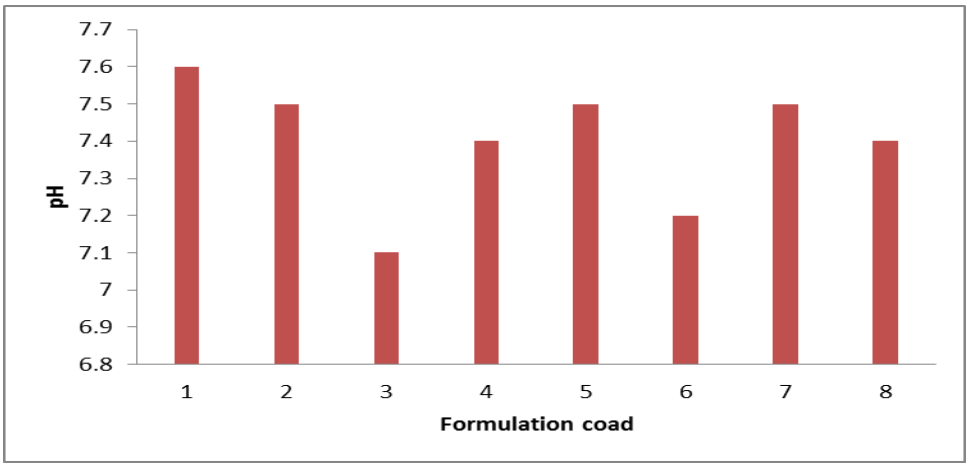

Figure 3: pH examination Ketorolac loaded hydrogel (F1-F8).

3.2.3 Outcomes of Washability and extrudability.

Table 7: Outcomes of Washability and extrudability.

Formulation code	Washability	Extrudability
F1	Excellent	Good
F2	Excellent	Excellent
F3	Excellent	Excellent
F4	Excellent	Good
F5	Excellent	Good
F6	Excellent	Good
F7	Excellent	Good
F8	Excellent	Good

3.4.4 Spreadability Examination of Ketorolac loaded hydrogel (F1-F8)

Table 8: Spreadability Examination of Ketorolac loaded hydrogel (F1-F8).

S. No.	Formulation code	Spreadability(gcm/sec)
1	F1	12.33±0.01
2	F2	13.47±0.02
3	F3	17.92±0.98
4	F4	15.28±0.98
5	F5	11.03±0.95
6	F6	15.81±0.81
7	F7	14.15±0.78
8	F8	13.47±0.72

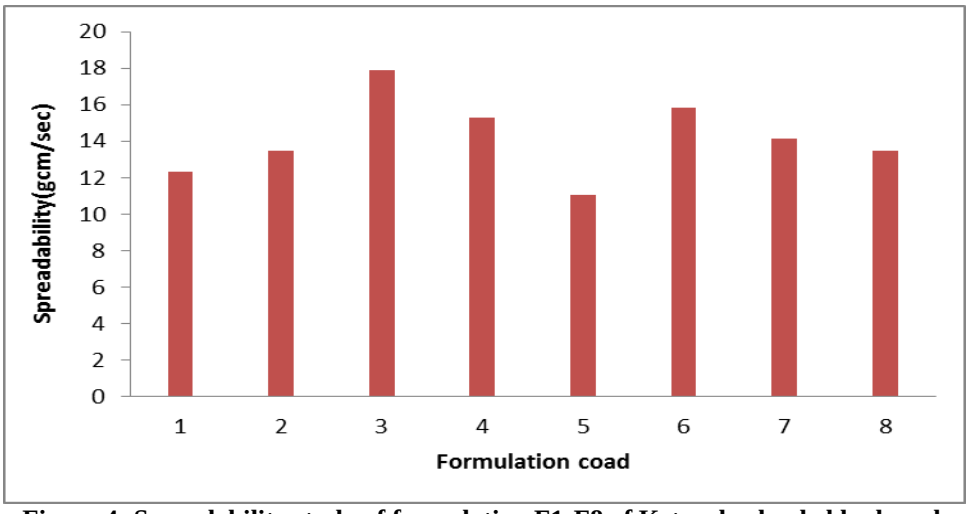

Figure 4: Spreadability study of formulation F1-F8 of Ketorolac loaded hydrogel.

3.2.5 Viscosity determination

Table 9: Results of viscosity of formulation F1-F8 of Ketorolac loaded hydrogel.

S. No.	Formulationcode	Viscosity(cps)
1	F1	934±2.6
2	F2	913±2.7
3	F3	946±1.4
4	F4	931±1.9
5	F5	919±2.7
6	F6	935±1.3
7	F7	936±2.3
8	F8	931±1.9

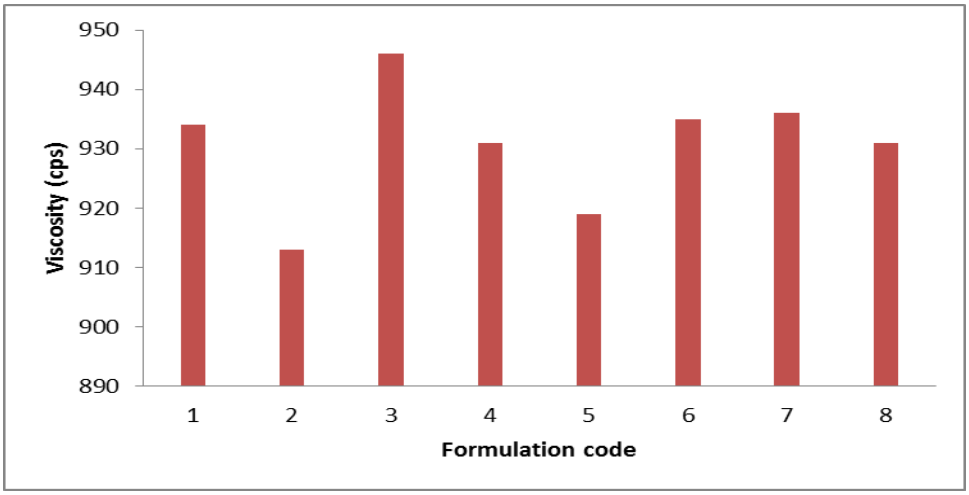

Figure 5: Results of viscosity of formulation F1-F8 of Ketorolac loaded hydrogel.

3.2.6 Drug contents

Table 10: Results of drug content of Ketorolac loaded hydrogel.

S. No.	Formulation code	Drug content
1	F1	94.03±0.4
2	F2	95.03±0.8
3	F3	98.74±0.4
4	F4	97.84±0.3
5	F5	94.98±0.7
6	F6	92.04±0.1
7	F7	92.24±0.2
8	F8	91.13±0.4

Table 11: Cumulative % drug release of best formulation F4 and Marketed formulation.

Time (min)	F3	Marketed formulation
0	0	0
5	45.01±0.2	42.01±0.5
10	65.81±0.9	64.67±0.1
15	80.90±0.6	79.90±0.7
20	91.56±0.2	88.09±0.8
30	98.74±0.2	97.03±0.3

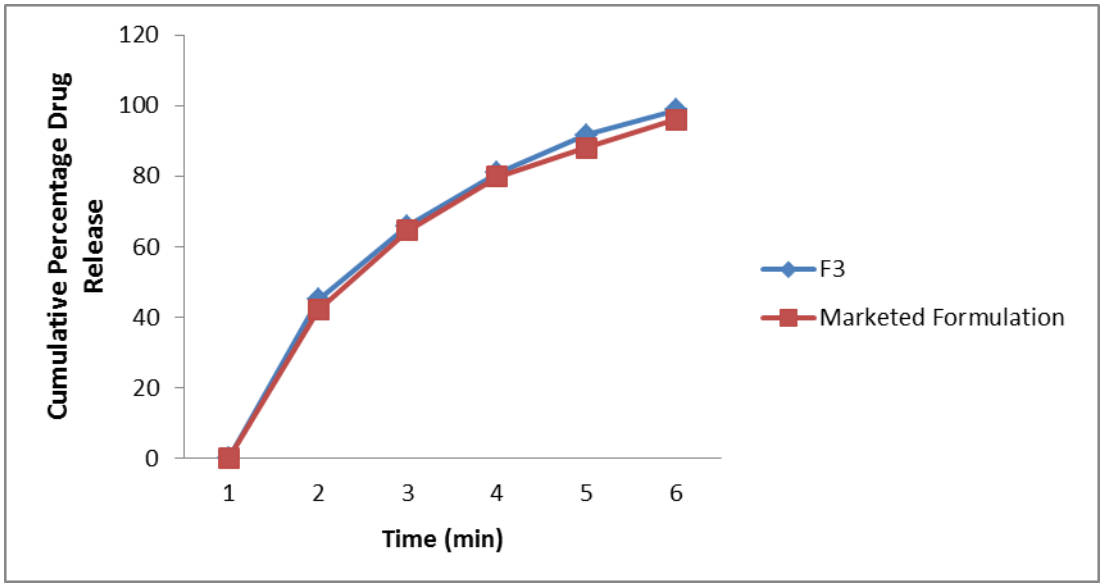

Figure: 6 Cumulative % drug release of best formulation F4 and Marketed formulation.

3.2.7 Accelerated Stability Studies

Table 12: Accelerated Stability Studies of best formulation F3.

S. No.	40 ±2^{0}C, 75 ±5% RH			
	O Days	30 Days	60 days	90 Days
pH	7.1±0.02	6.8±0.04	6.8±0.04	6.8±0.04
Viscosity	946±1.4	952±12.3	961±1.5	982±1.2
Cumulative % drug release	98.74±0.2	97.2±0.1	96.1±0.6	95.4±0.1

3.3 DISCUSSION

Ketorolac looked like a normal white to off-white crystalline powder that tasted a little bitter and had no smell. It melted at around 96°C, didn't dissolve well in water, but did dissolve well in ethanol, methanol, and acetone. This means it was moderately lipophilic, with a log P of about 3.1. The UV absorption peak at 332 nm in phosphate buffer proved that it was what it said it was.

The standard calibration curve for Ketorolac was quite straight and could be used for reliable quantitative analysis. FTIR spectrum analysis showed that Ketorolac had functional groups such O–H, C=O, C=C (aromatic), N–H, and C–N. This proved that the structure of Ketorolac was intact.

The physical tests on the hydrogel formulations (F1–F8) indicated that they were all white, even, and did not have any phase separation. F4 was the best since it was very consistent and uniform. The pH of all the formulations was between 7.1 and 7.6, which means they were safe to use on the skin. Tests for washability and extrudability showed that all of the formulations were easy to get rid of and came out of containers easily. Tests for spreadability showed that F4 had the best application properties. The viscosity readings, which varied from 913 to 946 cps, confirmed that the gel had the right consistency, with F3 having the maximum viscosity. Drug content analysis showed that the drug was evenly distributed in all formulations. F4 had the highest cumulative drug release (98.74%), which was very similar to the marketed formulation. Testing F3's stability over 90 days showed very small changes in pH, viscosity, and drug release, which confirmed that it is stable even when circumstances are sped up.

CONCLUSION

The current work was able to effectively show how to make and test hydrogel formulations with Ketorolac. Organoleptic study, melting point determination, solubility investigations, UV spectroscopy, and FTIR research all showed that ketorolac had the right physical and chemical properties. F4 had the best physical properties, the best pH, the best spreadability, the most constant viscosity, the most drug content, and the most cumulative drug release of all the formulations. It was similar to the marketed formulation. Stability experiments showed that formulation F3 was strong even when put under stress. Overall, the hydrogels that were made show promise as excellent topical drug delivery methods for Ketorolac since they are stable and work better as drugs.

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