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FORMULATION AND EVALUATION OF KETOROLAC TROMETHAMINE EMULGEL

Pharmaceutical Science

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ABSTRACT

Emulgel has emerged united of the foremost intriguing topical delivery techniques because of its twin unleash mechanism, that contains each gel and emulsion. Topical drug applications provide a variety of benefits, including the ability to transport medicine to the site of action and keep it there for a prolonged period of time. The primary purpose of this formulation is to enhance the topical dispersion of a hydrophobic drug (Ketorolac tromethamine). Carbopol 974P NF, eudragit S100 and Sodium CMC are a gelling agent used in a Ketorolac tromethamine emulgel. The emulgel was created with liquid paraffin because the oil, span 80 because the emulsifier agent. Physical look, pH, drug content, in-vitro diffusion investigations, and a skin irritation check were all performed on the ready emulgels. In-vitro diffusion studies disclosed that formulation EF6 discharged 97.89 % of the drug once 10 hours, with the results indicating that formulation EF6 discharged the drug loads of effectively than various formulations. In ex-vivo diffusion studies, EF6 discharged 97.92 % of the drug in 12 hours. Albino Wistar Rats were studied for their anti-inflammatory (carrageenan-induced paw edema) and analgesic (hot plate latency test) properties.

KEYWORDS

Emulgel, Carbopol 974P, Tween 80, Gelling agent, Ketorolac tromethamine, Emulsifying agent.

1. INTRODUCTION

Topical medication administration is the easiest and finest approach for controlled drug distribution throughout the body via ocular, rectal, and cutaneous routes. Topical medication distribution is defined as the localized administration of formulations throughout the body via ocular, rectal, nasal and cutaneous routes in order to maximize bioavailability and reduce side effects.[1] Emulgels function as a regulated medication delivery mechanism for substances that are administered topically. They have advantages over both gels and emulsions. They are either w/o or o/w emulsions that are gelled by combining with a gelling agent.[2] Emulgels are more stable than other topical treatments such as ointments, which can become rancid owing to the oil phase, creams, which can become phase inverted or broken, and powders, which can become hygroscopic.

Ketorolac tromethamine is a medication (NSAID). It is a racemic combination with analgesic action in the S-form. It has an impact because it inhibits both (COX-I and II).[3]

The goal of this study is to manufacture Ketorolac tromethamine as an emulgel in order to minimize the GIT side effect, to include this insoluble medication in a hydrophilic gel matrix and to improve the drug's percutaneous absorption and pharmacodynamics.

Anatomy of skin

Structure of the skin

The epidermis, which is the skin's topmost layer, is made up of stratified, keratinized squamous epithelium, and its thickness varies from area to area of the body. The soles of the feet and the palms of the hands have the thickest coatings. The deeper layers of the epidermis are bathed in interstitial fluid from the dermis, which provides oxygen and nutrients and is drained away as lymph. The epidermis does not contain blood vessels or nerve endings. From the deepest germinative layer to the surface stratum corneum, the epidermis is made up of numerous layers of cells, or strata (a thick horny layer). The cells on the surface are flat, thin, non-nucleated, dead cells, or squames, in which the fibrous protein keratin has taken the place of the cytoplasm in the cells. These cells are continually being rubbed off and replaced by cells that began in the germinative layer and underwent progressive alteration as they moved toward the surface. About 40 days are needed for the epidermis to completely regenerate.[4]

Dermis

The dermis is elastic and resilient. It is made of connective tissue, and the matrix is made up of elastic and collagen fibers. Stretch marks, also known as permanent striae, are a result of the skin's elastic fibers rupturing when it is overstretched during pregnancy and obesity. Water is held together by collagen fibers, which also give the skin its tensile strength. As collagen fibers age, wrinkles start to appear. The primary cells present in the dermis include fibroblasts, macrophages, and mast cells. Areolar tissue and various levels of adipose tissue are present underneath its lowest layer (fat).[4]

The structures in the dermis are:
blood vessels.
lymph vessels.
sensory (somatic) nerve endings.
sweat glands and their ducts.
hairs, arrector pili muscles and sebaceous glands.

2. MATERIALS AND METHODS

2.1. Materials

Ketorolac tromethamine from Dr. Reddy's laboratories Ltd, Hyderabad. Carbopol 974P from Lubrizol Advanced Materials, INC Cleveland. Tween 80 and span 80 from Finar limited, Ahmedabad. Propylene glycol and liquid paraffin from Research-lab Fine chem Industries Mumbai. Eudragit S100 from Evonik Industries Germany.Sodium CMC from Labogens fine chem industry, Punjab. Methyl paraben from Oxford laboratory Mumbai. Triethanolamine from SDFCL s d fne chem limited Mumbai.

2.2. Methods

2.2.1. Uv spectrum

Determination of absorption max (lambda max) of Ketorolac:

From the stock solution, a series of dilutions were made to produce concentrations of 0.1, 0.2, 0.3, 0.4, 0.5, and 1.0 ml using water to obtain 1, 2, 3, 4, 5, and 10 µg/ml of Ketorolac tromethamine solution.

The spectrum shows the maximum absorption at 323 nm. The max 323 nm wavelength was chosen and used for further investigation in the current study.[1]

Construction of Calibration curve

Preparation of standard stock solution of Ketorolac tromethamine in water:

100 mg of Ketorolac tromethamine was weighed and transferred to 100ml volumetric flask, dissolved in distilled water.

Preparation of working solution

1 ml of standard solution was taken and final volume was made upto 10 ml using distilled water.

From the working solution, series of concentration of 1, 2, 3, 4 and 5 µg/ml of Ketorolac tromethamine solution were prepared and the

absorbance was scanned between 200-700nm by using A Shimadzu 1700 UV Visible spectrophotometer.

Table-1: Linearity of Ketorolac tromethamine.

Sample ID	Type	Conc.	Wl235.0
0ppm	standard	0	0
1ppm	standard	1	0.078
2ppm	standard	2	0.121
3ppm	standard	3	0.194
4ppm	standard	4	0.254
5ppm	standard	5	0.334

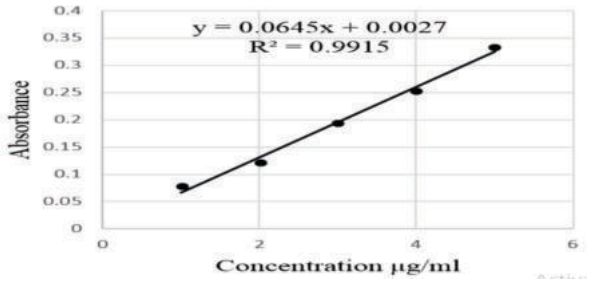


Fig-1: Linearity plot of Ketorolac tromethamine

2.2.2. FTIR analysis of drug and excipients

To make sure the excipient and medicine were compatible, this investigation was done. Ketorolac tromethamine's pure drug FTIR spectra were acquired, and liquid FT-IR investigations were done for the formulations that were ready with various excipients, and their compatibility was examined. The technique of potassium bromide discs was used to acquire the drug spectrum. By exerting 10 tons/inch2 of pressure for 10 minutes, the pellet was made with the dry samples. For liquid samples, the samples were collected and quantified in a liquid sample container.[5]

3. Preparation of Ketorolac Tromethamine Emulgel

3.1. Preparation of Gel

Carbopol 974P NF was dissolved in purified water and stirred continuously with a mechanical stirrer at a moderate speed to create the gel.[6]

3.2. Preparation of Emulsion

The oil phase was made by dissolving Span 80 in light liquid paraffin and heating it to a temperature between 70 and 80 °C. To produce the aqueous phase, Tween 80 was dissolved in clean water and heated to 70–80 °C. The drug was dissolved in water. Then propylene glycol and methyl paraben were combined, and then the aqueous phase and oil phase were progressively combined.[7]

3.3. Preparation of emulgel

To prepare emulgel, emulsion was continuously mixed with the gel basis in a 1:4 ratio using a mechanical stirrer.

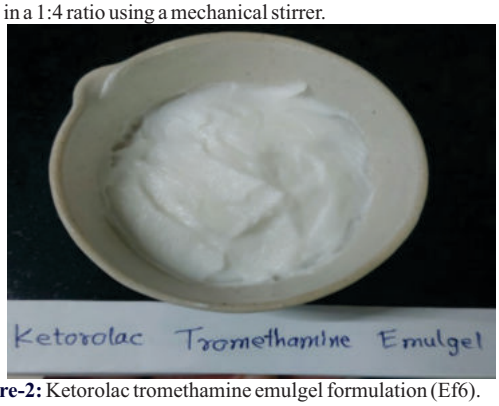


Figure-2: Ketorolac tromethamine emulgel formulation (Ef6).

Table-2: Formulation of Ketorolac tromethamine emulgels.

Ingredients (g)	EF1	Ef2	EF3	EF4	Ef5	EF6	EF7	EF8	EF9	EF10
Ketorolac tromethamine	1	1	1	1	1	1	1	1	1	1
Eudragit S100	0.1	0.2	0.3	_	_	_	_	_	_	_
Carbopol 974P NF	_	_	_	0.1	0.2	0.3	0.4	_	_	_
Sodium CMC	_	_	_	_	_	_	_	0.1	0.2	0.3
Tween 80	0.1	0.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Liquid paraffin	2	2	2	2	2	2	2	2	2	2
Span 80	0.1	0.2	0.3	0.4	0.5	0.5	0.5	0.5	0.5	0.5
Propylene glycol	2	2	2	2	2	2	2	2	2	2
Methyl paraben	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Triethanolamine	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

4. Evaluation Test

4.1. Physical appearance

The homogeneity, colour, consistency and phase separation of the prepared emulgel formulations were all visually assessed.[8]

4.2. Spreadability

Spreadability is assessed using the Mutimer et al. (1956) proposed equipment, which is appropriately adjusted in the lab and employed for the investigation. It is made up of a wooden block that has a pulley at one end. This approach bases the measurement of spreadability on the emulgels' "Slip" and "Drag" properties. A ground glass slide is fixed to this block. On this ground slide, more emulgel (approximately 2 gm) is being studied. The emulgel is then placed in a sandwich between this glass slide and another glass slide with a hook and a set ground slide dimension[9]. To remove air and create a consistent emulgel coating between the slides, a 500 g weight is put on top of the two slides for five minutes. The weight was measured out and put into the pan that had a hook attached to a pulley. It was observed how long, in seconds, it took for the top slide to disengage from the bottom slide. A shorter gap indicates a better spread coefficient.[10]

Spreadability (S) was calculated as follow:
S=M.L/T
Where,
S = Spreadability.
M = Weight tied to upper slide.
L = Length of glass slides.
T = Time required to totally separate the slides from one another.

4.3. Extrudability

The method accustomed measure emulgel formulations for extrudability during this study is predicated on the proportion of emulgel and emulgel extruded from a lacquered metallic element folded tube. Using the load in grams, needed to make a minimum of a 0.5 cm ribbon of emulgel in 10 seconds. Extrudability improves because the amount extruded will increase.[11]

4.4. Determination of pH

A pH meter was used to determine the pH levels of the emulgels' 1% percent aqueous solutions.[12]

4.5. Drug Content Determination

1 g of emulgel that had been precisely measured was added to a 100 ml volumetric flask, and the capacity was then filled with phosphate buffer (pH 7.4). Next, pipette 1 ml and dilute it up to 10 ml. A Shimadzu 1700 UV Visible spectrophotometer was used to detect the absorbance at 323 nm following the appropriate dilution.[2]

4.6. In Vitro Drug Release study

1gm of emulgel containing 2% Ketorolac tromethamine was kept over a cellophane membrane and then placed in a Franz diffusion cell phosphate buffer (pH 7.4). The test was carried out at 37°± 0.5° and at a rotation speed of 50rpm. Aliquots of 1ml were withdrawn from the medium at 0.25, 0.5, 0.75, 1, 2, 3, 4, 6, 8, 10 hours' time intervals, replaced at each time with 1ml of buffer to maintain a constant volume. The sample was diluted with 9 ml of distilled water and the concentration was determined using a UV Spectrophotometer.[13]

4.6.1. Drug Release Kinetics

The data were subjected to kinetic analysis in order to identify the release model, which is described as follows: zero order (cumulative% drug release vs. time), first order (log cumulative% drug retention vs. time), and Higuchi model (cumulative% drug retained vs. SQRT).[14]

4.7. Ex-vivo Permeation

A modified Franz diffusion cell was used for this experiment. Goat skin was used in the investigation into skin permeability. A known amount

of a 1 gm gel containing 20 mg of medication was evenly distributed across the donor side of the skin, which was placed in a modified Franz diffusion cell.

The acceptor media was phosphate buffer, pH 6.8, from which samples were obtained continuously for 12 hours in order to maintain the receptor phase volume at 25 ml. The concentration was calculated using the equation of the calibration curve and detected using a UV-Spectrophotometer at 323 nm.[11]

4.8. Analgesic Activities

The hot plate technique was used to perform the analgesic activity. The latency period for the Albino Wistar rat's weighing 180-200 g response to the hot plate was calculated for the groups that were created.[15] The number of rats used in this experiment 9. These were divided into three groups having 3 rats in each group.

Control Group (Group 1):

No topical treatment was given and the latency period was calculated (blank emulgel).

Standard Group (Group 2):

The rats were treated with Ketorolac tromethamine gel 2% (Dr. Reddy's laboratories Ltd) and its latency period was calculated.

Test Group (Group 3):

The test formulation Ketorolac tromethamine (EF6) was administered to the rats, and the latency period was determined.

4.9. Anti-inflammatory Activity

The number of Albino Wistar rats (female) weighing 180-200 g were used in this experiment 9. These were divided into three groups having 3 rats in each group. To do this, 0.1 ml of 1% w/v carrageenan was injected in the sub-plantar area of the left hind paw of rats. Rats' left hind paws were topically treated with Ketorolac tromethamine emulgel and the commercially available Ketorolac tromethamine gel 2% (Dr. Reddy's laboratories Ltd). Following carrageenan injection, the paw edema volume was measured with a plethysmometer immediately (Zero time), and then at 30 min, 60 min, 2 hours, 3 hours, 4 hours, 6 hours and 8 hours' intervals.[16]

Control group (Group 1):

Carrageenan (1%) was administered in the plantar surface of rat + blank emulgel.

Standard group: (Group 2):

Marketed Ketorolac tromethamine gel (2%) + Carrageenan.

Test Group (Group 3):

Formulation Ketorolac tromethamine emulgel EF6 + Carrageenan.

4.10. Skin Irritation test

Skin irritation test was performed onto shaved skin of Albion Wistar rats back side. Control, standard and test formulation (EF6) were observed for 72 hours after application.[17]

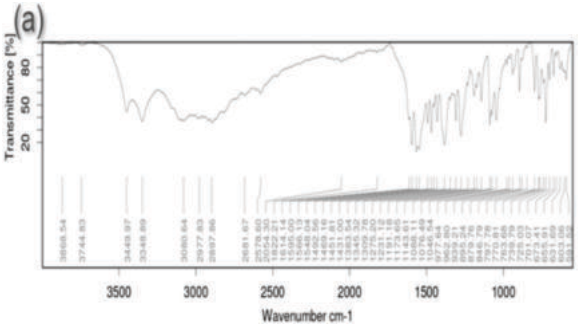
4.11. Stability Studies

The prepared emulgels were packed in aluminum collapsible tubes and stored for a period of one month [14].[16]

5. RESULT AND DISCUSSION

5.1. FTIR-Drug-Excipient compatibility studies.

The formulation's FTIR spectra reveals notable peaks of Ketorolac tromethamine showing no interactions between Ketorolac tromethamine and excipients.



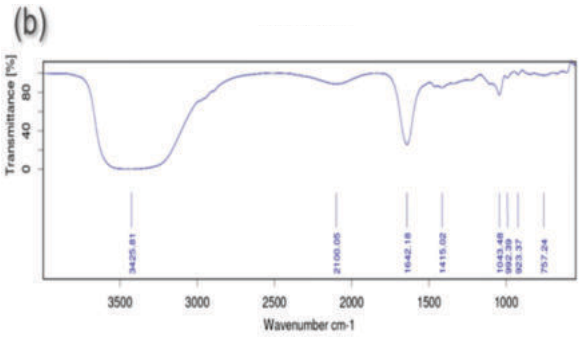


Figure-3: (a) FTIR Spectra of Ketorolac tromethamine pure drug. **(b)** FTIR Spectra of Ketorolac tromethamine emulgel formulation Ef6.

5.2. Physical appearance

Table-3: Physical appearance of Ketorolac tromethamine emulgel formulations.

Formulation	Colour	Consistency	Homogeneity	Phase separation
EF1	White	Good	Good	None
EF2	White	Good	Excellent	None
EF3	White	Excellent	Excellent	None
EF4	White	Good	Good	None
EF5	White	Excellent	Excellent	None
EF6	White	Excellent	Excellent	None
EF7	White	Excellent	Excellent	None
EF8	White	Good	Good	None
EF9	White	good	Excellent	None
EF10	White	Excellent	Excellent	None

5.3. Spreadability, Extrudability

The best formulation EF6 showing excellent extrudability, spreadability 25±0.7 g.cm/sec and pH 6.6±0.2.

Table-4: Spreadability and extrudability value.

Formulation	Spreadability (g.cm/sec)	Extrudability g/cm2
EF1	20±0.2	Good
EF2	22±0.5	Excellent
EF3	23±0.3	Good
EF4	20±0.6	Good
EF5	24±0.5	Good
EF6	25±0.7	Excellent
EF7	23±0.4	Good
EF8	21±0.2	Excellent
EF9	21±0.1	Good
EF10	23±0.4	Excellent

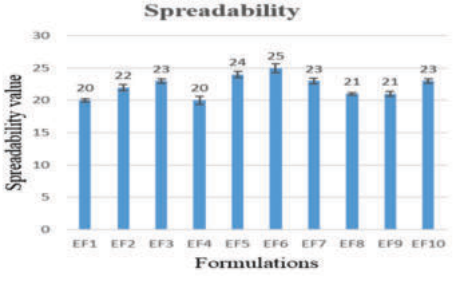


Figure-4: Spreadability value.

5.4. Determination of pH

pH of prepared emulgel was found to be 6.0±0.1 to 6.6±0.2 which compliance with skin pH range.

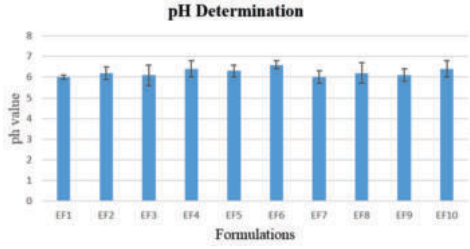


Figure-5: pH value of diferent emulgel formulations.

5.5. Drug Content Determination

Formulation EF8 indicated more drug content of 96.50 %. The formulation EF6 showed drug content of 90%.

Table-5: Drug content of Ketorolac tromethamine emulgel formulations.

Formulation	Sample Volume (ml)	Dilution Factor	Amount Present (mg)	% drug contents
EF1	10	100	18.2	91.00
EF2	10	100	17.5	87.50
EF3	10	100	17.3	86.50
EF4	10	100	18.9	94.50
EF5	10	100	18.4	92.00
Ef6	10	100	18	90.00
EF7	10	100	17.4	87.00
EF8	10	100	19.3	96.50
EF9	10	100	18.4	92.00
EF10	10	100	18	90.00

5.6. In Vitro Drug Release Study

All emulgel formulations exhibit better drug release, which can be classified in the following descending order: EF4 >EF1 > EF8 >EF6>EF5>EF3>EF9>EF10>EF2>EF7.

Table-6: In Vitro diffusion data of Ketorolac tromethamine emulgel formulations.

Time	% CDR									
(hrs)	EF1	EF2	EF3	EF4	EF5	EF6	EF7	EF8	EF9	EF10
0	0	0	0	0	0	0	0	0	0	0
0.25	28.21 ±1.3	26.25 ±2.2	20.12 ±2.1	27.56 ±1.6	22.25±2.3	11.42 ±1.5	9.23 ±1.2	29.56 ±1.4	25.23±1.2	11.23±2.2
0.50	52.23 ±4.5	46.54 ±3.4	30.45 ±1.2	46.23 ±2.6	36.45±3.1	18.15 ±1.2	16.23±1.4	56.23 ±2.3	45.56±3.1	15.23±1.4
0.75	74.24 ±3.3	55.36 ±4.6	42.12 ±1.5	55.23 ±4.3	42.56±4.2	19.52 ±2.3	18.54±3.2	78.56 ±2.1	56.12±2.4	25.56±3.4
1	86.56 ±4.2	75.25 ±4.2	50.58 ±3.2	68.12 ±3.2	54.12±1.3	24.61 ±4.2	20.45±2.1	86.56 ±1.3	65.23±4.1	36.12±4.2
2	98.64 ±3.1	85.78 ±2.1	70.12 ±4.3	75.46 ±1.5	64.45±5.2	33.62 ±3.5	24.65±4.2	98.45 ±2.3	76.45±2.3	45.12±2.1
3	_	94.45 ±4.1	86.21 ±2.1	84.23 ±5.2	74.56±2.2	46.45 ±2.1	33.56±3.2	_	84.56±3.2	64.21±1..5
4	_	_	97.45 ±2.4	90.79 ±2.3	83.45±3.1	52.21 ±3.2	46.45±2.5	_	96.15±4.1	86.12±3.2
6	_	_	_	98.87 ±2.1	90.23±2.5	64.58 ±2.4	52.12±3.6	_	_	95.46±2.4
8	_	_	_	_	97.89±3.2	82.45 ±3.1	79.56±3.1	_	_	_
10	_	_	_	_	—	97.89 ±3.4	94.23±2.4	_	_	_

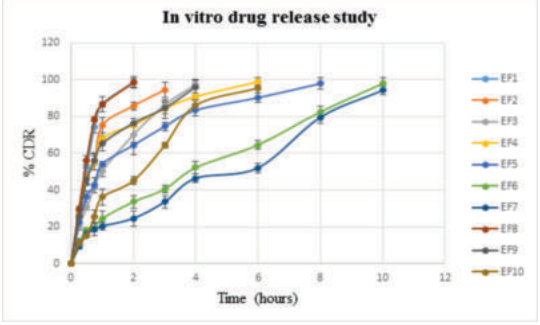


Figure-6: Comparative Drug Release Profile of Ketorolac tromethamine emulgel Formulations.

5.6.1. Drug Release Kinetics

A variety of mathematical models were tried to suit the outcomes of the improved batch's in vitro release trials. The regression coefficient (r^2) values for zero order, first order, Higuchi matrices, and Peppas for formulation (Ef6). When the regression coefficient 'r^2' values of the optimized formulation's zero order and first order plots were compared, it was discovered that the zero order plot's 'r^2' value was 0.977 while the first order plot's 'r^2' value was 0.878, indicating that the drug release from the optimized formulation (EF6) was found to follow zero order release kinetics with non-fickian diffusion.

5.7. Ex-vivo Drug Release Study

All emulgel formulations exhibit better drug release, which can be classified in the following descending order: EF1 >EF8 > EF4>EF6>EF3>EF5>EF9>EF10>EF2>EF7.

Table-7: Ex-vivo diffusion data of Ketorolac tromethamine emulgel formulations.

	% CDR									
Time (hrs)	Ef1	EF2	EF3	EF4	EF5	EF6	EF7	EF8	EF9	EF10
0	0	0	0	0	0	0	0	0	0	0
0.25	26.21 ±1.2	25.78 ±2.1	19.89 ±1.5	16.45 ±2.1	5.64±3.1	0.75 ±1.3	0.5±2.1	29.56 ±2.3	15.46 ±2.5	9.8±3.2
0.5	48.15 ±3.1	40.15 ±4.2	28.15 ±3.2	32.48 ±1.4	10.21 ±1.6	0.93 ±3.5	0.84 ±4.3	48.13 ±3.4	26.13 ±1.4	14.21±2.4
0.75	62.45 ±2.2	53.78 ±3.2	41.87 ±2.2	49.89 ±4.2	20.65 ±2.2	3.12 ±4.2	2.8±1.5	68.15 ±4.6	34.76 ±3.2	23.43±1.2
1	76.12 ±4.3	60.78 ±4.5	51.46 ±4.5	59.87 ±3.1	28.45 ±3.2	8.32 ±2.3	8.12 ±3.2	75.46 ±3.2	46.78 ±4.5	31.48±3.1
2	85.42 ±2.2	71.43 ±1.3	68.45 ±4.3	67.46 ±2.4	39.78 ±4.4	16.4 ±1.2	15.13±4.2	84.45 ±2.4	57.13 ±4.2	45.18±4.2
3	98.78 ±3.4	80.15 ±2.2	77.46 ±2.3	76.45 ±4.3	52.47 ±4.5	23.5 ±3.4	20.13±2.3	98.23 ±4.5	65.45 ±2.3	62.45±2.3
4		93.47 ±3.4	86.46 ±3.1	87.46 ±4.5	63.43 ±3.2	32.25±2.3	31.78±1.4		79.49 ±4.1	74.28±3.4
6			97.18 ±4.3	97.99 ±3.2	74.96 ±1.4	47.36±4.2	44.65±3.2		95.78 ±3.2	86.45±4.2
8					85.46 ±2.4	65.76±4.5	60.78±2.2			94.56±2.5
10					96.38 ±3.2	82.95±2.1	78.89±4.3			
12						97.92±4.3	91.98±3.4			

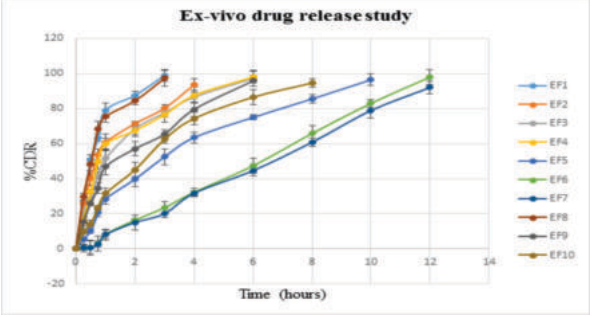


Figure-7: Comparative Drug Release Profile in ex-vivo of Ketorolac tromethamine emulgel Formulations.

5.8. Analgesic Activities

The analgesic effect of the Ketorolac tromethamine emulgel (EF6) was studied by hot plate method and compared with both the control group and the standard group (Ketorolac tromethamine gel 2%). The formulation (EF6) showed hike in lapse time.

Table-8: Analgesic values.0

Groups	Time							
	0 Mins	30 Mins	60 Mins	2 hours	3 hours	4 hours	6 hours	8 hours
Normal	2.54±0.3	2.47±0.3	2.67±0.3	2.78±0 3	2.81±0.3	2.84±0.3	2.88±0.3	2.91±0.3
standard	2.58±0.3	3.12#±0.4	3.78#±0.4	4.47#±0.5	4.94##±0.5	5.42##±0.5	5.53##±0.5	3.41#±0.4
Test formulation	2.58±0.3	3.34*±0.4	3.48*±0.4	4.87*±0.5	4.99**±0.5	5.47**±0.5	5.24**±0.5	3.84*±0.4

#: Significant. *: Significant.
##: Highly significant. **: Highly significant.
###: Relatively high significant. ***: Relatively high significant.

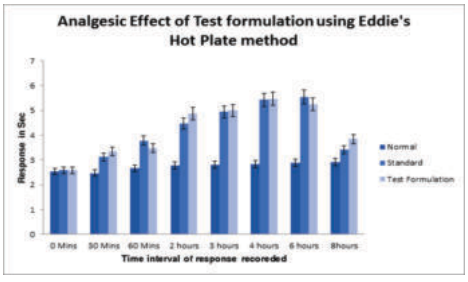


Figure-8:
The Test response was compared with the standard Ketorolac gel from 0 min to 8 Hours using ANOVA, Dunnetts test. It was found P<0.05, shows that the prepared formulation to be effective in showing analgesic effect. Single significant 0.05, high 0.01, highly 0.001.

5.9. Anti-inflammatory Activity

Edema size induced by the carrageenan injection was significantly inhibited by treatment with Ketorolac tromethamine emulgel (EF6). Moreover, it was found from statistical analysis using Student's t-test and one-way analysis of variance (ANOVA) following the Dunnetts tests that Ketorolac tromethamine emulgel (EF6) significantly inhibited and reduced the edema size. The p-value < 0.05 was considered significant.

Table-9: Anti-inflammatory values.

Groups	Time							
	0 Mins	30 Mins	60 Mins	2 hours	3 hours	4 hours	6 hours	8 hours
Normal	2.54±0.1	2.47±0.1	2.67±0.1	2.78±0.1	2.81±0.1	2.84±0.1	2.88±0.1	2.91±0.1
Toxic control	7.42±0.5	7.54±0.4	7.57±0.3	7.94±0.3	7.87±0.4	7.41±0.4	6.47±0.3	6.21±0.3
Standard	7.87±0.5	7.04±0.4	6.78±0.3	6.47±0.3	4.94±0.2	3.42±0.2	3.33±0.2	3.31±0.2
Test Formulation	7.58±0.5	7.34±0.4	6.48±0.3	6.01±0.3	4.39±0.2	3.57±0.2	3.23±0.2	3.24±0.2

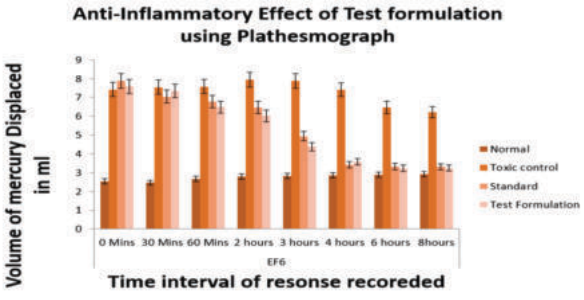


Figure-9: The Test response was compared with the standard Ketorolac gel from 0 min to 8 Hours using ANOVA, Dunnetts test. It was found P<0.05, shows that the prepared formulation (EF6) to be effective in showing Anti-inflammatory effects.

5.10. Skin irritation

No allergic symptoms like redness, inflammation or irritation appeared on rats up to 72 hours.

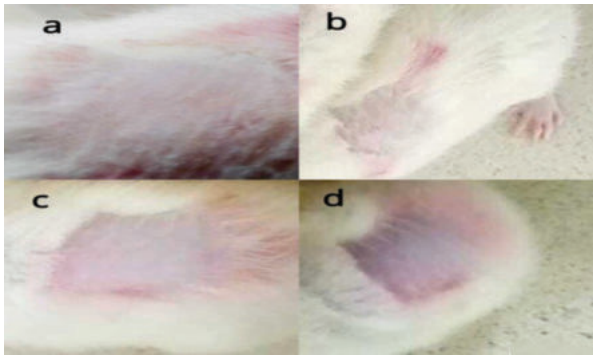


Figure-10: (a) Skin irritation study on rats before application of the formulations. (b) Skin irritation study on rats after application of standard (Ketorolac tromethamine gel 2%). (c) Skin irritation study on rats after application of control (blank emulgel) upto 72 hours. (d) Skin irritation study on rats after application of test Ketorolac tromethamine emulgel (EF6) upto 72 hours.

5.11. Stability Studies

The stability of this improved formulation was determined by conducting stability testing at room temperature for one month.

After being stored for a month, all of the synthesized emulgel formulations were discovered to be stable; there had been no changes in their physical characteristics, pH, or drug content.

CONCLUSION

Emulgels are comparatively more recent and superior topical medication delivery technologies because they combine the benefits of emulsion and gels. Additionally, they will serve as a means of long-term medication stability by loading hydrophobic substances into water-soluble gel bases. Similar to other formulations in the research, the topical emulgel of Ketorolac tromethamine was tested for appearance, spreadability, and in vitro drug release.

To ascertain the drug release from emulgel, in vitro testing of the test formulations was conducted. In vitro tests on formulation EF6 revealed a maximum release of 97.89% in 10 hours and in ex-vivo EF6 revealed a maximum release of 97.92% in 12 hours. Hot plate tests and carrageenan-induced paw edema demonstrated better analgesic and anti-inflammatory properties of the test formulation.

Conflict of Interest Statement

The authors declare no conflicts of interest in this work.

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Human and Animal Rights

No human volunteers were used in this study, although in vivo studies were conducted in animals that were approved by the Institutional Animal Ethics Committee (IAEC) India under reference no. (02/IAEC/VIPER/M.Pharm/2022-2023/I).

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