World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Formulation and evaluation of a novel controlled release mefenamic acid pluronic lecithin organogel

Madhuri Reddy Muppa [1,*], Annabathula meghana [2], Gandamala Chetan [2], Eluduti himabindu [2], Chakali Sai kiran [2] and Gonugoppula Rakesh [2]

[1] *Department of Pharmaceutics, St. Mary's Group of Institution, Deshmukhi (Village), Pochampally (Mandal), Yadadri Bhuvanagiri (Dist), Telangana-508 284, India.*
[2] *St. Mary's Group of Institution, Deshmukhi (Village), Pochampally (Mandal), Yadadri Bhuvanagiri (Dist), Telangana-508 284, India.*

World Journal of Advanced Research and Reviews, 2023, 19(02), 1226–1238

Publication history: Received on 11 July 2023; revised on 22 August 2023; accepted on 25 August 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.19.2.1678

Abstract

Based on pluronic lecithin, PLO gels were established in the present research as a topical carrier for the regulated delivery of mefenamic acid. To explore various factors utilizing *In vitro* diffusion experiments and in vivo study, ten organized formulations have been created using such methods that used lecithin as a lipophilic phase as well as pluronic F-127 as a hydrophilic phase in variable proportions. The pH values of all formulations were found to be between 5.60 and 5.75, which is nonirritating, and to be off-white, homogeneous, and unwilling to wash off easily. In formulations F1 to F5 (lecithin) but also F6 to F10 (pluronic), an increase in polymer concentration led to a drop in gelation temperature, an increase in viscosity, as well as a reduction within the spreadability of gels with a tendency for polymers to form rigid 3D networks. Higher viscosity organogels have been proven to be more stable and delay drug release from the gel. The formulations of F2 and F3 have been chosen for kinetic tests and stability studies because they had the most significant percentage of drug content and the highest drug release during eight hours, and all physical parameters were found to be within acceptable limits. It was discovered that the order of drug release through different formulations was F1to F10. A drug is removed from the improved formulation F2 in a regulated manner according to zero-order rate kinetics. The optimized mefenamic acid organogel (F2) in vivo anti-inflammatory effectiveness against a commonly used commercial product (Volini gel) was determined to be satisfactory but also significant.

Keywords: *In vitro*; Anti-inflammatory; Mefenamic acid; Pluronic; Lecithin; Organogels

1. Introduction

Mefenamic acid is an NSAID medication with anti-inflammatory and analgesic properties. By blocking the formation of prostaglandins, it is used to treat pain, inflammation, edema, and uterine contractions. Mefenamic acid's conventional oral dose form is in the form of capsules. Still, like other NSAIDs, mefenamic acid was also susceptible to causing intestinal bleeding, gastrointestinal ulcers, and skin rashes when taken orally [1].

Mefenamic acid has a very low solubility in water (20 mg/l), and because most of its metabolism and excretion takes place in the kidney and liver, its oral bioavailability is further diminished. Mefenamic acid is administered topically to improve absorption, promote local activity, and prevent adverse effects on the stomach. It has an apparent volume of distribution of 1.06 l/kg, is 90% protein bound, and has a half-life of two hours. Mefenamic acid has a log p value of 4.1 and a molecular weight of 241.285 g/mol, making it a good choice for transdermal delivery.

*Corresponding author: Madhuri Reddy Muppa

Because Mefenamic acid transdermal delivery has various benefits over other forms of traditional oral routes, including avoiding Transdermal administration of mefenamic acid would be promising due to its easy usage, controlled rate of drug release, constant drug blood level, lowered adverse effects to minimal disruption, but also drug degradation in the stomach as a result of internal body variations as well as several metabolizing enzymes, first-pass consequence, irritation of GI mucosa, but also simplicity of applications [2].

However, specific skin barriers, such as the stratum corneum, the skin's most complex and outermost layer, and corneocytes that contain dead keratin, make it challenging to distribute drugs through the skin.

Several methods have been used to improve drug permeation. Use of penetration enhancers. New drug deliverable systems such as vesicular systems, nanoparticles, microspheres, and polymeric lipids gels are techniques used to boost medication bioavailability via the epidermis.

Organogels made of pluronic lecithin (PLO gels) have the ability to penetrate the skin but also deliver enough medication for both local and systemic action. As a result, we selected PLO gels for the topical distribution of mefenamic acid, wherein the result should be improved outcomes because the medicine will be delivered over the skin. Phospholipid (lecithin) is the surfactant in PLO gels, which also contain an aqueous polar phase, and the external continuous phase is such an organic solution [3].

Each gelator molecule self-association causes the entangled microspheres to form a 3D network that traps an outer continual nonpolar phase and immobilizes it, converting it into a viscous gel. PLO gels have successfully integrated a variety of pharmacological classes, including NSAIDS, hormones, opiates, topical anesthetics, and anti-emetic medications. Drugs with molecular weights under 400 Da, including hydrophilic and lipophilic varieties, are easily absorbed into the composition of PLO gel. Phospholipid lecithin, an emollient for skin with a reasonable spreading rate, isopropyl myristate (IPM)/palmitate, an oil phase solvent for the lecithin, were sorbic acid serve as preservatives that make up the composition of PLO gel [4].

The aqueous phase contains pluronic F-127 as a surfactant, purified water as a solvent, and potassium sorbate as a preservative. Studies have shown that PLO gel formulations were significantly more effective at treating inflammation than oral pills. Therefore, the current work aimed to create a PLO gel formulation of mefenamic acid with anti-inflammatory effects utilizing an in vivo rat model [5].

2. Material and methods

2.1. Materials

Mefenamic acid has been received from K Pharma as a free sample. IPM, sorbic acid, potassium sorbate, potassium dihydrogen orthophosphate, sodium chloride, and sodium hydroxide have been obtained through Qualikems Fine Chem. Pvt. Ltd., soy lecithin, and disodium hydrogen phosphate were obtained through Himedia Labs Pvt. Ltd., and Pluronic F-127 was purchased from Sigma Aldrich. We bought menthol from Avon Flavors. All additional compounds have been of the analytical variety.

2.2. Methods

An organized PLO gel combines the aqueous and oil phases at a high shear rate. Ten PLO gel formulations (Table 1), each with a different amount of lecithin and pluronic F-127, have been made using a procedure involving an oil phase and an aqueous phase. Lecithin and sorbic acid are combined precisely with IPM as a solvent to create the oil phase. To guarantee that the lecithin and sorbic acid in the combination completely dissolved in IPM, it was left at room temperature for 12 hours [6].

2.3. Aqueous phase

Aqueous phases were created by weighing out pluronic F-127, potassium sorbate, and menthol and combining them with cold water. The liquid was refrigerated at or below 4^{o}C for 12 hours, allowing pluronic F-127 to dissolve [7] completely.

The following day, the gel was made by progressively combining the oil and water phases, using a mechanical stirrer to create an evenly distributed microemulsion. Producing a paste using polyethylene glycol 400 and combining it with the pluronic degree allowed the drug to be integrated into the oil phase. As a calming ingredient and penetration enhancer, menthol was used.

Characteristics in a visually organized system Light and scanning electron microscopes were used to study molecular packing, the creation of cross-linking ties inside the network of organogel, and trapping the aqueous phase in the lipid polymer phase [8].

2.4. Organoleptic characteristics [9-12]

Each formulation underwent testing for various organoleptic qualities, including flavour, texture, colour, phase separation, and greasiness.

2.4.1. Homogeneity test

To assess the gel's consistency and whether any coarse particles were stuck to or removed from the finger, 100 mg of gel was pushed among the thumb and index finger.

2.4.2. Wash ability

PLO gel (100 mg) has been applied to the hand's backside skin. Upon drying, each layer was rinsed with tap water to see if it could be cleaned.

2.4.3. pH determination

Using a digital pH meter calibrated before measurements with pH seven and pH four standard buffer solutions, the gel compositions' pH was ascertained. The electrode was calibrated and then submerged in an aqueous gel solution (1 g in 20 ml water) at 25 C, providing the gel formulation's pH.

Table 1 Formulation of PLO gels from F1 to F10

Types of Phase	**Ingredients (% W/W)**	**Formulations**									
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
Oil Phase	Mefenamic acid	1	1	1	1	1	1	1	1	1	1
	Lecithin	2	4	6	8	10	4	4	4	4	4
	Sorbic acid	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
	Distilled Water (up to)	100	100	100	100	100	100	100	100	100	100
Aqueous Phase	Pluronic F 127	20	20	20	20	20	5	10	15	25	30
	Potassium Sorbate	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
	Menthol	3	3	3	3	3	3	3	3	3	3
	Distilled Water	100	100	100	100	100	100	100	100	100	100

2.4.4. Viscosity (rheological characters)

Using a Brookfield digital viscometer, the viscosity of each formulation was calculated (in centipoises: cps). Tests were conducted at 25 C, with a water bath used to regulate the temperature. Viscosity was assessed using the spindle (LV 61) revolving at 10 rpm.

2.4.5. Spreadability

The degree of each formulation was assessed using a device with two glass slides developed by Mutimer et al. (1956). Gel (1 g) was inserted among such slides, and the upper decline was weighted with 1000 g to help the gel spread evenly. To determine the spreadability of various gels, weights were now placed at a time, a weight pan taken through the sliding mechanism to traverse a specific distance was observed, and the spreadability was computed using the following formula:

$$S = M \times L/T$$

Where;
L is the distance traveled by the movable slide in cm,

T is the entire amount of time required for the slide to travel the length of L and
S is a spreadability of gel in g cm/s.

2.4.6. Gel transition temperature

This gel transition temperature was measured in a 20 ml magnetic bead-equipped transparent vial. Every formulation (10 g) was put into a water bath that was kept at 4 C and gradually warmed by 1 C/min while the magnetic bead was stirred at 60 rpm. The gelation temperature of gels was determined to be the degree of heat at which the magnetic bead ceased to move.

Utilizing a UV spectrophotometer, the drug content of several formulations has been calculated. 100 cc of buffer was used to dissolve 100 mg of gel, then filtered using a 0.45 mm syringe filter. After filtering, the drug content was determined by measuring the absorbance at lmax 285 nm.

2.5. *In vitro* diffusion study [13]

To assess the percentage of total medication release combined over time, an *In vitro* diffusion study was conducted. A Franz diffusion cell was employed, which featured two storage areas: an upper A semi-permeable celluloid membrane separates the upper donor compartment from the bottom receiving compartment. P H 7.4 phosphate buffer was put in the receiver compartment, and PLO gel (1 g) was placed in the donor compartment. The group's size was maintained at 37 C while being constantly stirred. Samples were collected at intervals of 0, 1, 2, 3, 4, 5, 6, 7 and 8 hours. After each sampling, one milliliter of the sample was removed and replaced with an equal amount of phosphate buffer pH 7.4. After performing the necessary dilutions, models were analyzed using a UV spectrophotometer at max 285 nm to calculate the percentage of cumulative drug release.

2.6. Stability study [14]

According to ICH recommendations, The PLO gel formulations' stability testing has been done in a humidity chamber (I-Therm Inc.). For three months, the room has been run at 4 C, 25 C with 65% relative humidity, and 60 C with 75% relative humidity. Its physical stability, pH, and drug concentration were assessed to determine whether phase separation had occurred.

2.7. Animals

Following approval from the Institute Animal Ethics Committee (MMCP/IAEC/12/25), albino rats (Wistar strain), either male or female, weighing approximately 200–250 g, have been used. The animals were kept in standard housing with a 12:12 light-dark cycle and temperatures between 24 and 28 C and 60 and 70% relative humidity. The animals were given a regular pellet meal and unlimited water [15].

2.8. Skin irritation study

Each set of six rats underwent a study on skin irritancy. A hair-removing cream removed the hairs from the rat's back. On either side, a 4 cm2 space was marked. The compositions were deployed (100 mg/rat) once daily for seven days following 24-hour depilation, and the eyes were bandaged with cotton bandages. The reaction in the rat was graded as follows: 0 No response 0.5 Mild, scattered erythema, 1 Moderate yet patchy erythema or light but confluent erythema 2 Moderate Erythema with 3 Extreme erythema either with or without edema [16].

2.9. Designing experiments for in vivo research (analgesic and inflammation activity)

Three groups of six rats each were created, each receiving the following care. Group 1: Untreated control group; Group 2: Untreated positive control group; Group 3: Untreated standard-marketed formulation (Volini gel; 100 mg); Group 4: Untreated test formulation (PLO gel; 100 mg) [17].

2.10. Eddy's hot plate method

To test the analgesic activity of the medicine, heat has been utilized as a source of pain in this procedure. Each animal was placed individually on Eddy's hot plate (Techno Instrument India) at a constant temperature of 55 1 C. Whichever animal's reaction time—licking its paws, jumping, or elevating its limbs—is noticed first will be considered the endpoint. Reaction time was measured before and 30 minutes after the drug's administration [18].

2.11. Carrageenan-induced rat paw edema model

The medication was administered 30 minutes before carrageenan was given. After 30 minutes of medication delivery, all groups except the standard control group received an injection of 0.1 ml of 1% w/v carrageenan into the rat paw. After a gap of 0 h, 1 hour, two h, three h, as well as four h, the paw edema volume has been measured using a digital plethysmometer (Model 7140, UGO Basile) (Figure 1) [19].

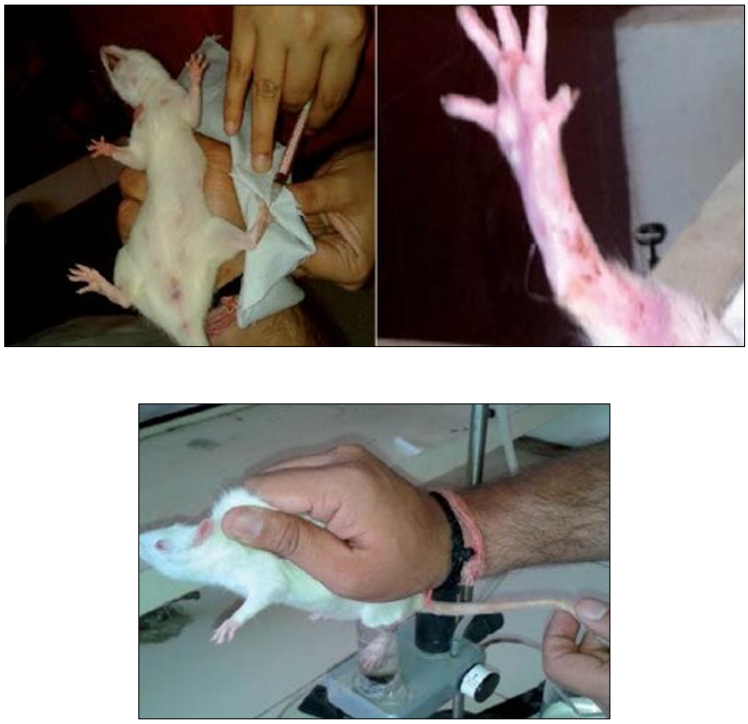

Figure 1 Carrageenan-induced paw edema test

The proportion of edema inhibition compared to the control was regarded as an indicator of anti-inflammatory effectiveness. The formula used to determine the percentage inhibition of edema is as follows: Percentage inhibition of edema 14 (AB)/A 100, where A is the paw volume of a group, and B is the group's paw volume that received the test drug [20].

2.12. Statistical analysis [21]

The information was presented as a standard deviation of the mean as a mean (SEM). Analysis of variance in one direction (ANOVA) has been used to examine the statistical significance between the standards, and Tukey's multiple comparison test was used after that. Statistical significance has been determined by such a p-value of 50.05.

3. Results

Ten formulations with different lecithin (F1-F5) or pluronic F 127 (F6-F10) concentrations have been created, as well as their various formulation properties were assessed.

3.1. Organoleptic characteristics

We examined the gel compositions' physical features and other organoleptic traits. All formulations were discovered to be stable, greasy, odorless, off-white in color, and without any indication of phase separation.

3.2. Surface morphology of organized

Organogel (F2) was examined under a light microscope at a resolution of 10–40 and revealed to be a bi-continuous system with water molecules trapped inside the gelator's self-constructed three-dimensional network (Figure 2).

The gel (F2) was visible in SEM images of the gel at 10 1000 resolutions, forming the three-dimensional network structure, which is quite dense. The resulting three-dimensional networked system stops the external apolar phase from flowing (Figure 2)

3.3. pH

Every PLO gel composition was discovered to have pH values between 5.60 and 5.75, which falls within the pH range that skin often has. The result is that none of the PLO gel formulations cause skin irritation (Table 2).

Spreadability The spreadability figures show that the gel may be spread with ease with little shear; however, the percentage of spreadability.

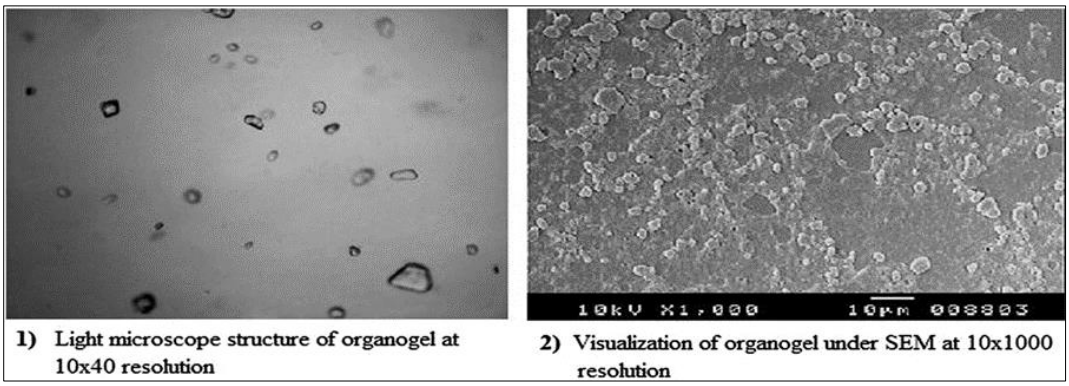

Figure 2 Light microscope structure at 10 40 resolution (1) and SEM image at 10 1000 resolution of organogel formulation (F2)

Table 2 Evaluation parameters of organogel formulations (F1–F10)

S.no.	Formulation	pH	Spreadability(g.cm/s)	Viscosity(incps)	Skinirritationstudy	Geltransitiontemperature
1.	F1	5.60±0.67	30.17±2.78	2738±4.78	Noirritation	35.5 ° C ±0.88
2.	F2	5.58±0.27	21.93 ±1.41	2931±8.41	Noirritation	33.3 ° C ±1.03
3.	F3	5.61±0.59	17.93±0.734	2935±10.94	Noirritation	32.7 ° C ±0.77
4.	F4	5.59±1.81	13.51±0.222	2988±1.92	Noirritation	30.2 ° C ±1.02
5.	F5	5.58±0.93	10.38±0.286	3048±27.85	Noirritation	29.2 ° C ±0.74
6.	F6	5.56±0.62	40.52±2.822	2621±15.86	Noirritation	33.8 ° C ±1.22
7.	F7	5.61±0.46	27.03±2.078	2668±11.31	Noirritation	32.2 ° C ±0.93
8.	F8	5.57±0.23	21.58±0.571	2771±9.41	Noirritation	31.6 ° C ±0.62
9.	F9	5.80±0.19	14.25±0.228	2988±24.16	Noirritation	31.1 ° C ±0.60
10.	F10	5.75±0.14	8.25±0.351	3158±11.97	Noirritation	29.9 ° C ±1.08

The spreadability of organogels from F1 to F5 (30.17-10.38 g.cm/s) decreased due to lecithin. The F6 through F10 saw an increase in the percentage of pluronic (40.52-8.25 g.cm/s), and a similar pattern was seen (Table 2). Due to increased cross-linking between polymers, which prevents gels from spreading freely, spreadability decreases as polymer concentration rises.

3.4. Viscosity

The range of the viscosity of gel formulations was determined to be between 2738 and 3048 cps (F1-F5), 2621 and 3158 cps (F6–F10). According to the viscosity curve shown in Figure 3, The incidence of increased cross-linking in polymers with the rise in polymer concentration could cause a corresponding greater viscosity. PLO gels exhibit pseudoplastic flow, shear thinning, and non-Newtonian behavior (Table 2).

3.5. Skin irritation study

It is allowed if the gel formulation doesn't irritate the skin. Erythema, edema, or skin reddening weren't present. All gel compositions discovered lacked any irritating symptoms (Table 2).

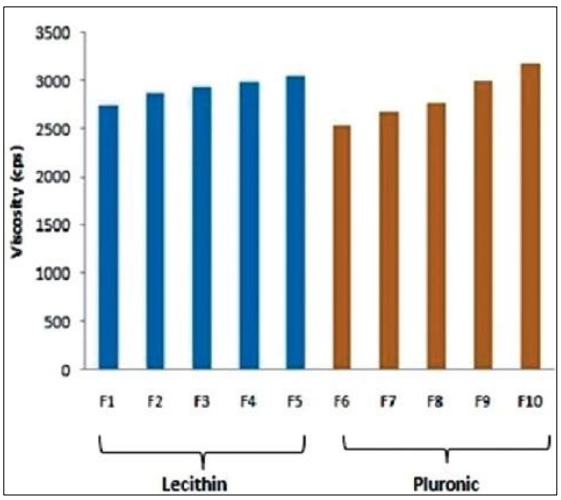

Figure 3 Viscosity values of formulations from F1 to F10

3.6. Gel transition temperature

Ten different organogel formulations' gel transition temperatures were measured among such ranges of 35.5 C and 29.2 C (F1-F5) as well as 33.8 -29.9^{0}C (F6–F10). The gel strength rises with increasing polymer content, and gelation occurs at lower temperatures (Table 2).

Drug content as a percentage Organogels' percentage drug content was discovered to be between 96.25% and 98.36%. It was determined using the MA standard curve in PBS 7.4 (Table 3).

3.7. Percent cumulative drug release

Table 3 Organogels' percentage drug content

S.no.	Formulations	Percentage drug content
1.	F1	97.18±0.314
2.	F2	96.25±0.310
3.	F3	98.29±1.440
4.	F4	97.16±0.236
5.	F5	96.73±0.205
6.	F6	95.92±0.201
7.	F7	97.21±0.310
8.	F8	96.79±0.115
9.	F9	98.36±0.115
10.	F10	98.09±0.831

Lecithin-rich formulations have a higher viscosity and slow down the release of the medication. The order in which the drug's cumulative percent release over eight hours was discovered was F1F2F3F4F5F6F7F8F9F10 (Table 4). It should be noted that an increase in lecithin concentration resulted in a delay in the release of MA in formulations F1 through F5. However, an increase in pluronic was seen in formulations F6 through F10.

Table 4 Cumulative medication release percentage over 8 hours

S.No	Formulation	Percent Cumulative Drug Release
1.	F1	74.8
2.	F2	88.4
3.	F3	85.7
4.	F4	78.2
5.	F5	67.4
6.	F6	58.6
7.	F7	63.8
8.	F8	67.6
9.	F9	72.7
10.	F10	78.8

Bold values indicated the top two formulations for additional research.

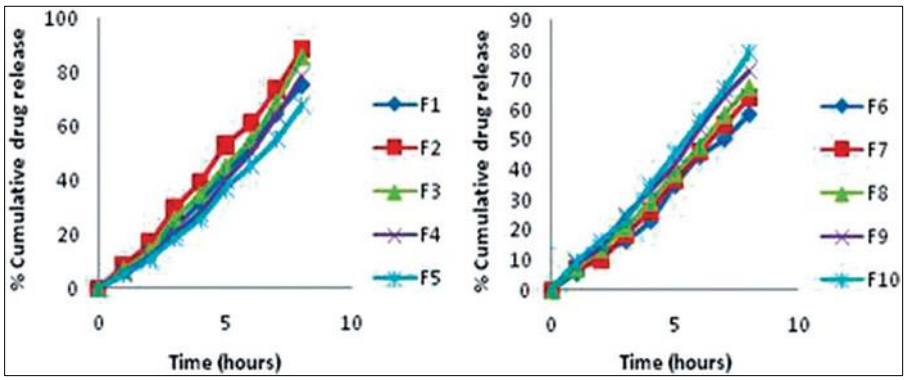

Figure 4 Percentage cumulative drug release profile of F1–F5 and F6–F10 formulations

The medication release profile showed less change under concentration, given that the likely rise within microviscosity in such a gel's three-dimensional structure reduces the number and size of aqueous regions available for drug diffusion. Figure 4 displays the cumulative % medication release profile for F1 to F5 and F6 to F10. The studies above concluded that formulations F2 and F3 have been appropriate for additional kinetic data fitting stability studies because they possess the greatest overall drug release percentage over eight hours and have all physical parameters within acceptable ranges.

As a result, F2 and F3 formulations were examined further for various rate equations. Compared to F3, the F2 formulation has been found to follow zero order rate kinetics with r 2 values of 0.996, indicating that it is a controlled drug release composition.

3.8. Stability study

At all temperature ranges during the study period, it was determined that Formulations F2 and F3 were suitably stable. Depending on the polymer concentration, Around 60 C, pluronic gels transitioned from semisolid to liquid, but no phase separation occurred for 60 days in the F2 formulation and 30 days in the F3 formulation. Nevertheless, after a lengthy

examination at 60 C, PLO gels exhibited phase separation (Table 6). Thus, F2 formulation were ultimately chosen for its in vivo anti-inflammatory effects.

3.9. *In vivo* study

3.9.1. Hot plate method

Mefenamic acid PLO gel's analgesic impact was evaluated in comparison to that of the control and standard groups (Volini gel). Animals in the control group typically took 4 to 8 seconds to react. Animals in the test group had considerably longer reaction times, although these times were still within the standard group's 10–13 s range. Additionally, the statistical study revealed no.

Table 5 Kinetic data of release studies for F2 and F3 formulations

Formulation	Zero Order		First Order		Higuchi		Hixson Crowell	
	R^2	K_0	R^2	K_1	R^2	K_H	R^2	K_{HC}
F2	0.996	11.32	0.887	0.114	0.968	43.49	0.920	-0.276
F3	0.987	10.98	0.863	0.887	0.946	41.91	0.944	-0.299

Table 6 Stability study data of F2 and F3 formulations

Time(days)	Temp(°C)	F2	F3	F2	F3	F2	F3
0	4	95.98±0.24	98.29±0.02	5.58±0.32	5.61±0.34	No separation	No separation
15	4	95.69±0.49	98.01±0.22	5.53±0.33	5.59±0.32	No separation	No separation
30	4	95.48±0.13	97.74±0.31	5.61±0.24	5.42±0.21	No separation	No separation
60	4	95.22±1.21	97.41±0.28	5.54±0.41	5.53±0.33	No separation	No separation
90	4	94.67±0.42	97.11±0.35	5.49±0.37	5.49±0.15	No separation	No separation
15	25	95.51±0.32	97.87±0.32	5.51±0.24	5.58±0.33	No separation	No separation
30	25	95.19±0.43	97.32±1.23	5.43±0.15	5.93±.37	No separation	No separation
60	25	94.47±0.62	96.63±0.95	6.23±0.33	6.21±0.34	No separation	No separation
90	25	93.98±0.15	96.19±0.54	5.69±0.37	6.10±0.41	No separation	No separation
15	60	95.13±0.32	97.45±0.65	5.83±0.54	5.79±0.23	No separation	No separation
30	60	94.52±1.51	96.82±1.75	6.11±0.41	6.27±0.46	No separation	No separation
60	60	93.29±0.96	96.12±1.42	5.97±0.57	6.13±0.58	No separation	Slight separation
90	60	92.65±1.63	95.54±1.76	5.71±0.59	5.91±0.61	Slight separation	Slight separation

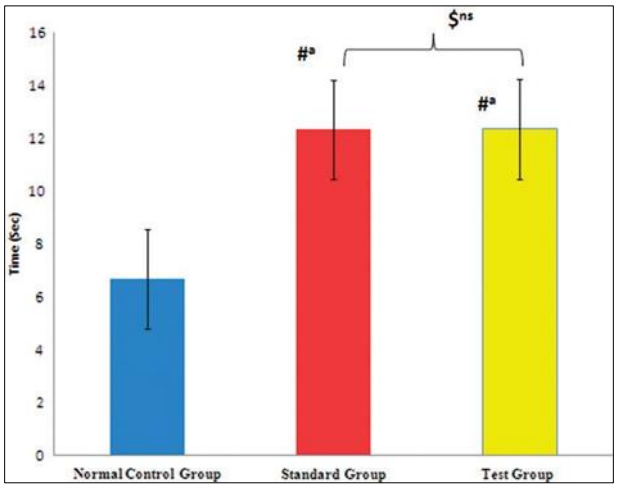

Figure 5 Using Eddy's hot plate, the mefenamic acid organogel formulation demonstrated analgesic efficacy significant difference between the standard and test formulations (F2), confirming that both formulations exhibited the same kind of effect (Figure 5)

3.9.2. Carrageenan-induced paw edema

The results (Figure 6) revealed that from the second hour on, both F2 and commercial formulations generated statistically significant inhibitions (p50.0001) of edema compared with the positive control group. However, at the third and fourth hours, our F2 formulation showed non-significant effects when compared with the marketed formulation, indicating similar types of inhibitory activity. In the third and fourth hours, the test formulation generated 28.55% and 33%; the marketed formulation produced 30.16% and 35.52%. (Table 7).

4. Discussion

These days, finding new medication molecules and creating pharmaceutical products in the lab is laborious. However, marketed products are well known for their medicinal activity as well as for having substantial adverse effects. For the drug to accomplish its purpose without having any adverse side effects, the best drug delivery mechanism is our focus.

The current study aimed to create and assess various tropical organogel mefenamic acid formulations with varied amounts of pluronic and lecithin. Our analysis discovered that all gel formulations had all physical criteria within acceptable ranges, including homogeneity, off-white hue, odorlessness, greasy consistency, and stability devoid of any evidence of phase separation. There was some resistance to washing with the organogel formulations. Our organogel compositions' pH has been discovered to be close to the pH range of skin and demonstrated strong skin compatibility.

One of the parameters used to determine the viscosity, spreadability, and percentage of cumulative drug release is polymer concentration. Our research demonstrated a direct relationship between viscosity and polymer concentration, with viscosity rising as polymer concentration did. The consistency of gel formulations increases due to an increase in pluronic or lecithin (F1-F5) concentration (F6-F10) and decreases spreadability due to an increase in layer resistance. As a result, as the formulations' viscosity grew, the percentage of total medication release over time decreased, and these findings were consistent with those of past studies (Pandey et al., 2010). Because our formulation exists in a gel state and Ba et al. also found comparable results, the gelation temperature range of our formulations is lower than the typical body temperature (2016).

Additionally, rats were used in the skin irritation research, and none of the formulations displayed any signs of skin irritation, demonstrating excellent skin compatibility. The optimized formulations F2 and F3 were chosen for further rate kinetics and stability research based on several assessment criteria (Table 2). According to the ICH recommendations and the stability research, the data of the Formulations F2 and F3 for three months are acceptable.

The physical characteristics, percentage drug content, and pH of our F2 and F3 formulations did not significantly change after storage or exhibit any evidence of phase separation. Given the rate kinetic data, formulation F2 was chosen for its in vivo analgesic and anti-inflammatory effectiveness since it exhibits zero-order release kinetics as opposed to F3, which will administer the drug at a controlled pace. Animal tests on in vivo analgesic efficacy (Figures 5 and 6 and Table 7) showed that our F2 and commercial diclofenac (Volini gel) formulation both demonstrated similar activity.

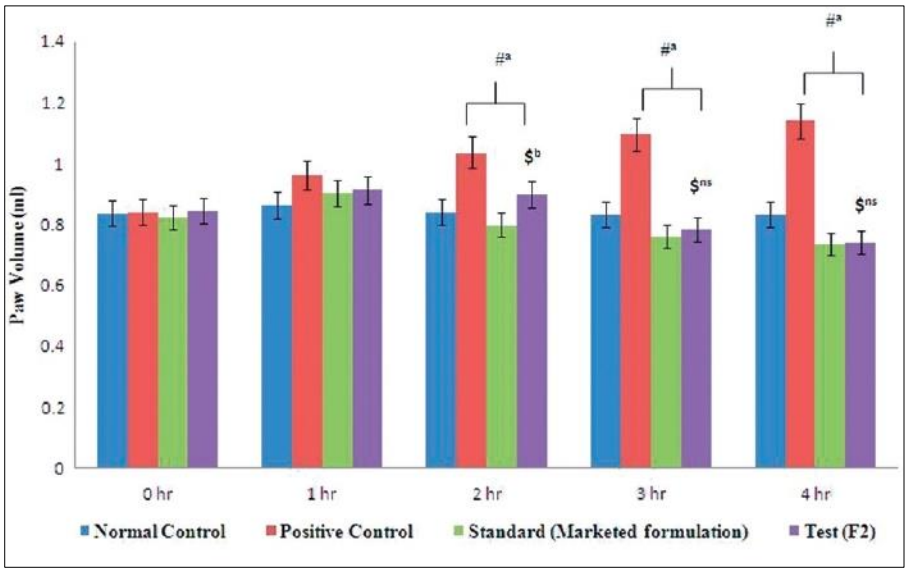

Figure 6 Mefenamic acid organogel with anti-inflammatory properties utilizing digitized plethysmograph

Table 7 Paw volume averages at various periods

Time(h)	Normal control	Positive control	Standard (marketed formulation)	Test(F2)	Overall value	Value
0	0.828±0.018	0.862±0.234	0.823±0.015	0.843±0.021	0.292	1.348
1	0.856±0.022	0.972±0.071	0.859±0.059^{ns}(6.13%)	0.913±0.062^{ns}(4.9%)	0.0412	3.333
2	0.851±0.020	1.041±0.065	0.797±0.015^{d,a}(23%)	0.899±0.035^{d,a,e,b}(13.22%)	50.0001	34.26
3	0.877±0.015	1.089±0.068	0.760±0.017^{d,a}(30.16%)	0.783 ±0.013^{d,a,e,ns}(28.55%)	50.0001	90.58
4	0.843±0.012	1.15±0.081	0.735±0.018^{d,a}(35.52%)	0.741±0.014^{d,a,e,ns}(33%)	50.0001	138.13

The data were statistically analyzed using one-way ANOVA, and Tukey's Multiple Range Test was used afterward. The trials were carried out extensively, and the values are Mean SD for each group (n 14 6). Positive control versus formulation, p50.0001, p50.01, p50.05. e Compare the formulation group to the control group. Nonsignificant, or ns.

In contrast, in the inflammation-induced rat model, the test formulation at 2 hours showed a marginally significant effect (p50.01) compared to the marketed formulation. Still, the F2 formulation at 3 hours and 4 hours showed no significant impact compared to the marketed formulation, indicating that our F2 formulation has the same therapeutic activity as the marketed formulations (Volini gel). Although the analgesic and anti-inflammatory effects of the F2 and commercial gel formulation were nearly identical, our formulation (Topical organogel) may be a more effective substitute for the marketed gel diclofenac due to its brief and low-intensity activity. These can quickly deliver the medicine across the skin due to their organic nature and the presence of lecithin, which has a very high capacity to penetrate the drug through the skin. Therefore, more research is required to improve organogel formulations and receive better outcomes.

5. Conclusion

As a result of the investigation described above, we conclude that organogels provide a novel base for medications administered topically and may provide an alternative to commercially available diclofenac gel formulations. After passing through several stages of clinical studies and adhering to ethical standards, our F2 formulation may be released as a novel medication on the market for anti-inflammatory drugs.

Compliance with ethical standards

Acknowledgments

The management provided technical assistance for the authors to complete this work, which they appreciate.

Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Statement of ethical approval

All animal experiments were carried out after approval of the protocol by the institutional animal ethical care committee (IAEC), Sanzyme Bio Labs Pvt Ltd, Hyderabad, Central Animal House registration No: 1688/PO/E/2022.CPCSEA was conducted according to the Indian National Sciences Academy guidelines for using and caring for experimental animals.

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