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Formulation, Development and Evaluation of Novel Topical Emulgel Based On Mefenamic Acid

Satyendra Mishra*[a], Vinay Kumar*[a] , Dr. Jai Narayan Mishra*[a],
Kailash Institute of Pharmacy & Management, GIDA Gorakhpur, Pin-273209, Uttar Pradesh,
Kailash Institute of Pharmacy & Management, GIDA Gorakhpur, Pin-273209, Uttar Pradesh, India
Kailash Institute of Pharmacy & Management, GIDAGorakhpur, Pin-273209, Uttar Pradesh, India

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ABSTRACT
Emulgels have become a potentially effective method of delivering hydrophobic medications. The study's goal was to create an NSAID called Mefenamic Acid Emulgel using Carbapol 940 as a gelling agent. Clove oil and Mentha oil were used to increase penetration. After being prepared, the emulsion was added to the gel base. Rheological tests, spreading coefficient studies, bioadhesion strength, skin irritation studies, in vitro release studies, ex vivo release studies, anti-inflammatory effectiveness, and analgesic activity were all tested for the formulations. In comparison to commercially available Diclofenac Sodium Gel, formulations F2 and F4 demonstrated comparable analgesic and anti-inflammatory effects. Therefore, it can be said that Mefenamic Acid topical Emulgel has potent analgesic and anti-inflammatory properties.

Keywords: Emulgels, Bioadhesion, Mefenamic Acid, Rheological Tests, Anti-Inflammatory.

I. INTRODUCTION

The market offers a variety of topical formulations for analgesic medications. Effective NSAID Mefenamic acid has long been used as an analgesic and anti-inflammatory medication. Traditionally, it has been sold as pills and suspensions. Mefenamic Acid has not yet been marketed as a topical formulation. Due to medication penetration into the deeper layers of skin or mucous membranes, the majority of topical treatments are utilised for localised effects at the application site [1].

Even though some inadvertent drug absorption may happen, it usually only involves small amounts and poses little threat. Large amounts of aqueous or hydroalcoholic liquid are trapped in a network of colloidal solid particles to form gels, a more recent type of dosage forms. These particles may be inorganic, like aluminium salts, or organic polymers with natural or synthetic origins [2-4].

Compared to the ointment or cream basis, they feature a larger aqueous component that allows for increased drug solubility and facile migration of the drug through a vehicle that is virtually a liquid. These offer greater usability and patient acceptance. Despite the fact that gels have many benefits, hydrophobic medication delivery is a significant drawback. Emulgels are created and used to get over this restriction so that even a hydrophobic medicinal moiety can benefit from the special qualities of gels. The dosage forms are referred to as Emulgels when gel and emulsions are used in combination [5].

The ability of novel polymers to gel allows for the formulation of stable emulsions and creams by reducing surface and interfacial tension while simultaneously increasing the viscosity of the aqueous phase, which has sparked a lot of interest in their use as emulsifiers and thickeners in recent years [6-9].

Emulsion gels are a class of soft solid-like materials. These composite materials are structurally either a polymeric gel matrix into which emulsion droplets are incorporated (emulsion-filled gels), or a network of aggregated emulsion droplets (emulsion particulate gels). [20]

Emulgels for dermatological usage are thixotropic, greaseless, readily spreadable, easily removed, emollient, nonstaining, long shelf life, bio-friendly, transparent, and have a beautiful look [10].

The purpose of this research was to create an Emulgel formulation of the hydrophobic medication Mefenamic acid using two different types of penetration enhancers, namely clove oil and Mentha oil, together with the gelling agent Carbopol 940. Investigated was the impact of penetration enhancers and gelling agents. The prepared Emulgels were further tested for rheological properties, spreading coefficient,

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bioadhesion strength, skin irritancy, in vitro release, ex vivo release, anti-inflammatory activity, and analgesic properties [11-14].

II. MATERIALS

Lexicon Biotech Pvt. Ltd. provided a free sample of Mefenamic acid. Carbopol 940 was acquired from Loba chemicals in Mumbai for Baddi (Himachal Pradesh). Dialysis supplies were purchased from Hi Media in Mumbai. The use of any additional chemicals was not necessary because all other chemicals were of analytical quality.

2.1. Emulgel preparation and formulations

Different formulas were created utilising varying amounts of penetration enhancers and gelling agents. The main difference in the procedure was the process for creating gels with various formulations. In all formulations, the emulsion was made in the same way. Carbopol is an acrylic polymer. Carbopol is non-toxic and non-irritating so that it is suitable for gel preparations.[21]Carbopol 940 was dissolved in purified water and mixed steadily at a reasonable speed using a motorized shaker to create the gel phase for the compositions. Triethanolamine was then used to bring the pH to 6-6.5. (TEA). Tween 20 was dissolved in pure water to create the aqueous portion of the emulsion, and span 20 in light liquid paraffin to create the oil phase. While methyl and propyl parabens were combined with propylene glycol, Mefenamic acid was dissolved in ethanol [15].

Table 1 Composition of different formulation batches (%w/w)

Ingredient	F1	F2	F3	F4
Mefenamic Acid	1	1	1	1
Carbapol 940	1	1	1	1
Liquid Paraffin	7.5	7.5	7.5	7.5
Tween 20	0.5	0.5	0.5	0.5
Span 20	1	1	1	1
Propylene glycol	5	5	5	5
Ethanol	2.5	2.5	2.5	2.5
Methyl parabene	0.03	0.03	0.03	0.03
Ethyl parabene	0.01	0.01	0.01	0.01
Clove oil	--	--	8	10
Mentha oil	4	6	--	--
Water	q.s.	q.s.	q.s	q.s.

Table 1: Ingrediant use in formulation of Emulgel with its composition various formulations' compositions in detail.

2.2. Emulgel Evaluation

2.2.1. Physical examination

The prepared Emulgel compositions were visually examined for colour, consistency, and appearance [16].

2.2.2. Study of Rheology

Using a cone and plate viscometer with a spindle, the viscosity of the batches that were created was measured (Brookfield Engineering Laboratories) [22]. The component was linked to a bath of circulating water that was thermostatically controlled and kept at a temperature of 25 °C. A beaker with a thermostatic jacket on it received the formula whose stiffness was to be measured. The reading was recorded as the spindle was free to move into the Emulgel [17].

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2.2.3. Coefficient of Spreading

The spreading coefficient was calculated using Mutimer's recommended apparatus. It is made up of a wooden block with a pulley attached to one end. The "Slip" and "Drag" properties of Emulgels were used as the foundation for measuring the spreading coefficient. On the wooden block was fixed a ground glass slide. On this ground slide, extra Emulgel (approximately 2 g) from the study was applied.

Then, a second glass slide with the same dimensions as the fixed ground slide was positioned between this slide and the Emulgel mixture. The hook is provided with the second glass slide. For five minutes, a load of 500 mg was placed on top of the two slides to remove air and create a consistent Emulgel film between them. A precise amount of weight was added to the pan before it was hooked to the pulley. The top slide's time (in s) needed to cover a distance of 5 cm was recorded. Greater spreading coefficient is indicated by a shorter interval [18].

2.2.4. Irritation test for skin (patch test)

Patch tests are tools used in the identification of the etiologic agent (s) of allergic contact dermatitis [22].For the investigation, a group of 8 rats was employed. On the appropriately shaved skin of the rat, the Emulgel was applied. For a period of 24 hours, undesirable skin alterations, such as colour and morphological changes, were seen [19].

2.2.5. Strength measurement of Bioadhesive

The bioadhesive strength was measured using the modified approach. Two arm balances make up the equipment. Strings are used to secure both ends to glass plates. There are two glass plates on one side. The opposite side has a single glass plate [5].A modified balance method also used for determining the ex vivo mucoadhesive strength [23].

2.3. Mefenamic acid Emulgel preparation and assessment

By placing more weight on the left hand pan, the right and left pans were brought into equilibrium. For five minutes, the balance was held in this position. A precisely weighed 1 g of Emulgel was sandwiched between these two slides, each of which included a piece of fresh, hairless rat skin. Additional weight from the left pan was then removed in order to create the sandwich, and pressure was then applied to remove any air pockets. For five minutes, the balance was held in this position. The left hand pan was steadily weighed down at a rate of 200 mg/min until the 2 glass slides separated from one another. The amount of weight (in grams) needed to separate the Emulgel from the glass plate served as a gauge for the bioadhesive strength [12]. The bioadhesive strength is calculated by using following:

Biodhesive strength ¼ Weight required ðin gÞ=Area ðcm2Þ:

2.4. Studies on in vitro release

A modified Franz diffusion (FD) cell was used for the in vitro drug release tests. On the dialysis membrane of the FD cell, which was situated between the donor and receptor compartments, the formulation was applied. As a dissolving medium, phosphate buffer with a pH of 7.4 was employed. The water jacket circulated to keep the cell's temperature at 37 °C. The solution was continuously stirred using a magnetic bead while the entire assembly was kept on a magnetic stirrer. As a control, a comparable blank set was run concurrently. At appropriate times, the sample (5 ml) was removed and equal parts of new dissolving medium were substituted.Samples were analyzed spectrophotometrically at 285 nm and the cumulative% drug release was calculated. In each instance, the real reading was the differential between the drug release and control readings [13]

2.5. A study of drug release EX vivo

Franz diffusion were utilized to investigate the topical permeation of the emulgel formulations [25]. Selected formulation (F2 and F4) were the subject of an ex vivo drug release research in a customized Franz diffusion cell utilising wistar male rat skin. With the dorsal side facing upward, a piece of skin was cut and inserted between both the donor and receptors compartments of the FD cell. As a dissolving medium, a phosphate buffer pH 7.4 was employed. By circulating water jacket, the temperatures of the cell was kept constant at 32 °C. The solution was continuously stirred using a magnet bead while the entire assembly was kept on a magnetic stirrer. The same blank collection was run concurrently. At appropriate intervals, the samples were removed, and equivalent quantities of new dissolving media were substituted [18].

2.6. Stability studies

The emulgel were packed in aluminum collapsible tubes, stored in extreme conditions, and the stability is checked [24].The manufactured Emulgels were placed in aluminium collapsible tubes (5 g), and stability tests were conducted on

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them for three months at 5 °C, 25 °C/60 RH, 30 °C/65 RH, and 40 °C/75% RH. At intervals of 15 days, samples were taken out and examined for physical characteristics, pH, rheological properties, and drug concentration [19].

III. RESULTS & DISCUSSIONS:

3.1. Phenotypic appearance

Emulgel compositions were creamy, thick, and yellowish-white in colour, with a uniformly smooth texture and glossy appearance. Table 2 provides a discussion of the findings.

Formulations	Consistency	Color	Phase separation	Homogeneity
F1	Excellent	White	None	Excellent
F2	Excellent	White	None	Excellent
F3	Excellent	Pale Yellow	None	
F4	Excellent	Yellow	None	Excellent

Table 2: Phenotypic appearance of the formulations

3.2. Spreading coefficient

Spreading coefficient of different formulation of Emulgel are provide below in figure 1.

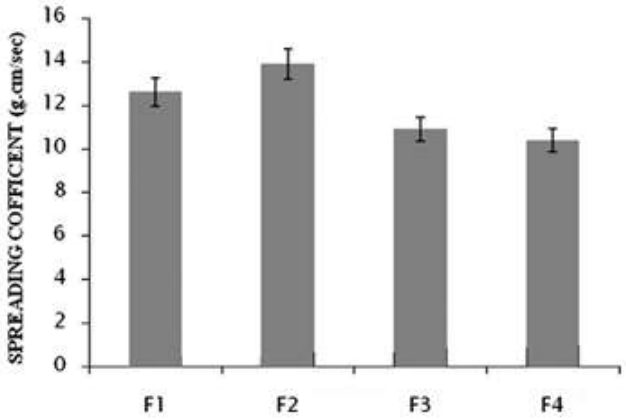

Figure 1: Spreading coefficient of the formulation F1–F4 (mean ± SD).

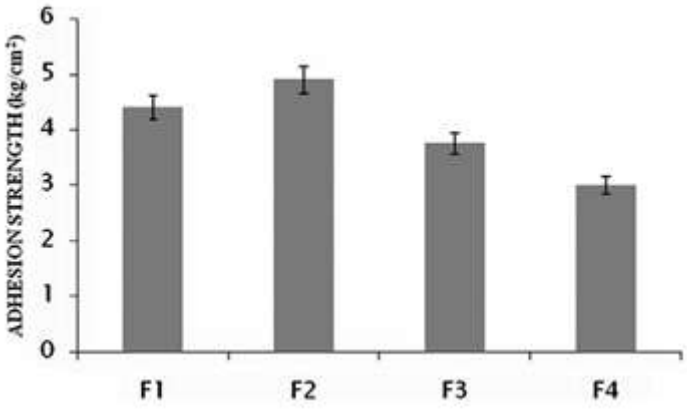

Figure 2: Bioadhesive strength of formulations F1–F4 (mean ± SD).

The bioadhesive strength of various Emulgel formulations have been shown above in Figure 2.

3.3. Rheological studies

Viscosity of different formulation of Emulgel are provide below in figure 3.

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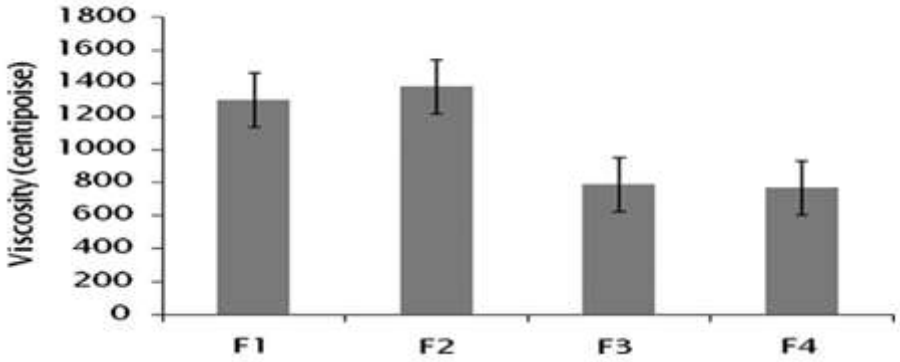

Figure 3: Viscosity of the formulations F1–F4 (mean ± SD).

3.4. Skin Irritation test

Up to 24 hours, rats did not exhibit any allergy signs including inflammation, redness, or irritation.

3.5. In vitro release study

According to the study, the sequence in which pharmaceuticals release from their emulsified gel formulations is F4 <F3 < F2 <F1, with the leve ls of the drugs released after 240 minutes being 56.01%, 53.48%, 52.23%, and 51.21%, respectively (Fig. 4).

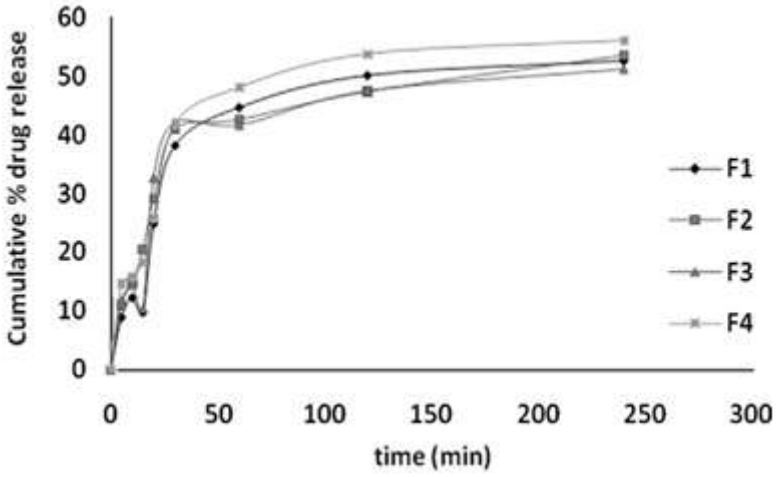

Figure 4: In vitro cumulative % drug release of formulation F1– F4.

3.6. Anti-inflammatory activity:

Calculating the formulations F2 and F4's anti-inflammatory activity and comparing it to Diclofenac Sodium (marketed preparation). Diclofenac Sodium was shown to block F2, F4, and F2 by 65.71%, 54.28%, and 55.72%, respectively. This demonstrated that the formulations were equally as potent as commercial ones.

3.7. Analgesic activity:

The formulas demonstrated an increase in lapse time. They were put up against gel Diclofenac Sodium (Marketed Preparation).

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3.8. Formulation and evaluation of Mefenamic Acid Emulgel

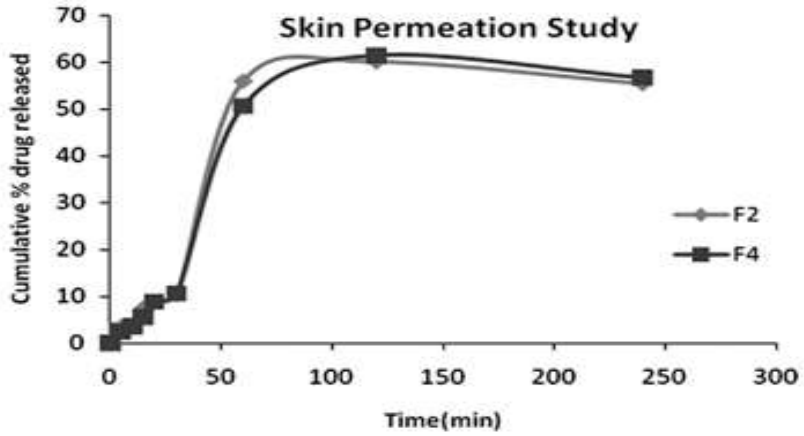

Figure 5: Ex vivo cumulative% release of formulations F2 and F4

Ex vivo cumulative% release of formulations F2 and F4 is shown in Figure 5. Diclofenac Sodium Gel, F2 and F4 were found to have lapse periods of 6.8 s, 5 s, and 5.1 s, respectively.

3.9. Stability study

All of the developed Emulgel formulations were shown to be stable after three months of storage; there had been no changes in their pharmacologic makeup, pH, rheological properties, or external appearance.

IV. CONCLUSION

Topical medicine delivery will be widely employed in the upcoming years to improve patient compliance. The spread ability, adhesion, viscosity, and extrusion of this innovative drug delivery method are improved by the use of Emulgel. Additionally, they will serve as a method for adding hydrophobic pharmaceuticals to gel bases that are water soluble for long-term stability. In a manner similar to this, Mefenamic acid topical Emulgels were developed and subjected to physicochemical experiments on rat skin, comprising rheological tests, dispersion coefficient tests, mucoadhesive strength tests, in vitro degradation tests, and ex vivo releasing tests. The test formulations were put through in vitro testing to determine the rate and duration of drug release from Emulgel.

REFERENCES

[1]. Ansel, H.C., Allen Jr, L.V., Popovich, N.G., 1999. Pharmaceutical Dosage Forms and Drug Delivery Systems, 7th ed. Lippincott Williams and Wilkins, New York. Bonacucina, G., Cespi, M., Palmieri, G.F., 2009.

[2]. Characterization and stability of emulsion gels based on acrylamide/sodium acryloyldimethyl taurate copolymer. AAPS PharmSciTech. 2, 10.

[3]. Choi, H.G., Yong, C.S., Sah, H., Jahng, Y., Chang, H.W., Son, J.K., Lee, S.H., Jeong, T.C., Rhee, J.D., Baek, S.H., et al., 2003.

[4]. Physiochemical characterization of diclofenac sodium loaded poloxamer gels as a rectal delivery system with fast absorption. Drug Dev. Ind. Pharm. 29, 545–553.

[5]. Crunkhorn, P., Mencock, S.C., 1971. Mediators of inflammation induced in rat paw carregeenan. Br. J. Pharmacol. 42, 371–402. Gennaro, AR. (Ed.), 1995.

[6]. Remington: the Science and Practice of Pharmacy, 19th ed. Mack Publishing Company, Easton. Gupta, G.D., Gaud, R.S., 2005.

[7]. Release rate of tenoxicam from acrypol gels. Ind. Pharm., 69–76. Gupta, A., Mishra, A.K., Singh, A.K., Gupta, V., Bansal, P., 2010.

[8]. Formulation and evaluation of topical gel of diclofenac sodium using different polymers. Drug Invention Today 2, 250–253.

[9]. ICH Harmonized Tripartite Guidelines, Stability Testing of New Drug Substances and Products. ICH Committee 2003; 8

[10]. . Jain, A., Deveda, P., Vyas, N., Chauhan, J., et al., 2011. Development of antifungal

emulsion based gel for topical fungal infection(s). IJPRD 2 (03).

[11]. Junping, K., Yun, N., Wang, N., Liang, L., Zhi-Hong, H., 2005. Analgesic and anti-inflammatory activities of total extract and individual fractions of Chinese medicinal plants Polyrhachis lamellidens. Bio. Pharm. Bull. 23, 176–180.

[12]. Kakkar, A.P., Gupta, A., 1992. Gelatin based transdermal therapeutic system. Ind. Drugs 29, 308–312.

[13]. Kasliwal, N., Derle, D., Negi, J., Gohil, J., 2008. Effect of permeation enhancers on the release and permeationkinetics of meloxicam gel formulations through rat skin. Asian J. Pharm. Sci. 3 (5), 193–199.

[14]. Kumar, L., Verma, R., 2010. In vitro evaluation of topical gel prepared using natural polymer. International Journal of Drug Delivery 2, 58–63.

[15]. Lionberger, D.R., Brennan, M.J., 2010. Topical nonsteroidal antiinflammatory drugs for the treatment of pain due to soft tissue injury: diclofenac epolamine topical patch. J Pain Research 3, 223– 233.

[16]. Mohamed, M.I., 2004. Optimization of chlorphenesin emulgel formulation. AAPS J. 6 (3). Murty, S.N., Hiremath, S.R.R., 2001.

[17]. Physical and chemical enhancers in transdermal delivery of terbutaline sulphate. AAPS Pharm. Sci. Tech. 2, 1–5. Schreier, H., Bouwstra, J.A., 1985.

[18]. Liposomes and Niosomes as topical drug carriers: Dermal and Transdermal delivery. J. Contr. Rel. 30, 863–868. Stanos, S.P., 2007.

[19]. Topical agents for the management of musculoskeletal pain. J. Pain Sympt. Manage. 33. Topical Emulsion, Gel Composition Comprising Diclofenac Sodium. Patent no. WO/2004/017998).

[20]. An overview on preparation of emulsion-filled gels and emulsion particulate gels., Taktam Farjami, Ashkan Madadluo, Trends in food science & Technology, volume 86, 2019.

[21]. Overview: Application of Carbapol 940 in Gel, Fenny Indah Safitri, Desy Nawangsari, Advances in Health Sciences Research, vol.34, pg.80.

[22]. Patch tests, Rosana Lazzarini, Ida Duarte, Continuing Medical Educaton, An Bras Dermatol, 2013;88(6):879-88.

[23]. Test methods of bioadhesive system, Prajapati Twinkle Kantibhai, Kauhika S. Patel, world journal of pharmaceutical research, vol.7, issue 2, 267-278.

[24]. An overview on Emulgel, Sreevidya V.S., International Journal of Pharmaceutical and Phytopharmacological Research, February 2019, Volume 9, Issue 1, Page 92-97.

[25]. In vitro and ex vivo correlation of drug release, Yan Wang, Bryan Newman, HHS Public access, e. 2018 April 28; 276: 93–101.