

Formulation And Evaluation Of Oxaprozin Emulgel

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Abstract: Emulgel have emerged as a extensively used drug delivery system for the delivery of hydrophobic drugs. The objective of the study was to formulate and evaluate emu gel of oxaprozin, NSAIDs using a gelling agent i.e. carbapol 940 . To enhance the permeability , mentha oil and clove oil were used . Separately, emulsion and gel were prepared & mixed together to provide emulgel formulations. The viscosity, spreading coefficient, bioadhesion, skin irritation tests and in vitro drug release tests of emulgel were evaluated. Formulation F2 & F4 found comparable analgesic and anti inflammatory activity with marketed ibuprofen gel. So emu gel of oxaprozin can be posses an effective anti inflammatory and analgesic activity.

Keywords:- Oxaprozin, emulgel, NSAIDs,

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I. Introductions

There are various topical preparations of non-steroidal anti inflammatory drugs in the markets like gels, creams, lotions, ointments, emulgels etc. NSAIDs are one of the most prescribed drugs because NSAIDs exhibit antiinflammatory, analgesic and antipyretic properties. (Dr. salette Reis et. Al.) But these drugs are famous for multiple adverse effects like gastrointestinal bleeding, cardiovascular side effects as well as hepatotoxicity and nephrotoxicity (S.wongrakpanich et.al.). According to American Health Association, 2007 the use of NSAIDs can lead to severe cardiovascular diseases (Natalia Schellack et.al.) Oxaprozin (C₁₈H₁₅NO₃/4,5-DIPHENYL-2-OXAZOLE-PROPIONIC ACID) is a newer NSAIDs drug & it acts like prostaglandin synthetase inhibitor. (Searle company, FDA). It is most effective against inflammatory process. In presence of pathogens, toxic molecules, tissue injuries, or any other harmful conditions, the inflammatory process is the innate immune response. There are some symptoms like redness, pain, swelling, heat and disturbance of function which characterized the inflammatory process. NSAIDs like oxaprozin , are one the most prescribed medicine to treat these conditions. To overcome from adverse effects of NSAIDs drugs, topical drug delivery system is safe option (Rachit khullar et.al.) . Topical delivery system have many advantages like greater contact time , mean resident time & bypassing the first pass metabolism. (Habeeba Basheer et.al.) . Emulgel is a type of newer topical preparation and has emerged as most beneficial in the field of pharmaceutics. emulgel is composed of gel and emulsion & gel offer rapid drug release as well as emulsion is one of the best approach for hydrophilic drugs (Verma Sachin et.al.) The emulgel of oxaprozin is not available in the market till date.

II. Material And Method

2.1. Materials

Oxaprozin was obtained as a gift sample from Amneal pharmaceuticals pvt.ltd. Ahmadabad 382213 India, Carbopol 940 was obtained from Cipla pharmaceuticals Mumbai (India). Dialysis membrane was produced from Hi media Mumbai. All other chemicals used were of analytical grade & were used without any further chemical modification.

2.2. Methods

2.2.1. Gel preparation

The preparation of carbapol gel was carried out by dispersing carbapol 940 in purified water & after it provide continuous stirring at moderate speed. The pH was adjusted in the range of 6.5 to 6.7 with the help of tri ethanol amine (TEA)

2.2.2 Emulsion preparation

Dissolution of span 20 in liquid paraffin forms the oil phase of emulsion & heated up to 70 to 80⁰C . Then mentha oil and clove oil was mixed with above prepared oil phase. oxaprozin drug , tween 20 dissolved in ethanol to make aqueous phase & maintain temperature at 70 to 80⁰C. Addition of preservatives like methyl paraben and propyl paraben into propylene glycol and then mixed this mixture to the aqueous phase. Finally, to

make emulsion, the oil phase was poured slowly into the aqueous phase with continuous stirring gently and allowed it to cool at room temperature.

2.2.3. Emulgel preparation

Emulgel was prepared by mixing already prepared emulsion with gel base at moderate stirring to get oxaprozin emulgel.

| Ingredients | F1 | F2 | F3 | F4 |
|------------------|------|------|------|------|
| Oxaprozin | 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 | 1 |
| Ethanol | 2.5 | 2.5 | 2.5 | 2.5 |
| Methyl paraben | 0.03 | 0.03 | 0.03 | 0.03 |
| Ethyl paraben | 0.01 | 0.01 | 0.01 | 0.01 |
| Clove oil | - | - | - | - |
| Mentha oil | 4 | 6 | - | - |
| Water | q.s | q.s | q.s | q.s |

2.3 Evaluation of emulgel

2.3.1 Physical examination

Visually, the prepared emulgel formulation were examined for their organoleptic properties like their color, appearance and their consistency (Rachit Khullar et.al.).

2.4. Rheological study

A cone and plate viscometer with spindle was used to determine the viscosity of all formulated batches. At 25^oC, a thermostatically controlled water bath was attached to the assembly. A beaker covered with thermostatic jacket contained the formulation whose viscosity was to be determined . Spindle was permitted to move freely into the emulgel and reading was noted.

2.5. Spreading coefficient

Multimer was used to determine the spreadability of formulations. It contains a wooden part connected to a pulley at one end. The Slip & Drag characteristics of emugel can was lead to measurement of spreading coefficient. Emulgel was fixed between ground slide, provided with the hook having same dimensions as that of the connected ground slide. 500mg emulgel was placed on the top of two slides for 5 mints. to remove out the air & offered a uniform film between two slides. On the pan connected to the pulley, placed a measured quantity of weight with the help of hook. To cover a distance of 5cm ,the required time(in seconds) by top slide was noted. The spreadability is inversely proportional to the time interval. (Vivek Chandra et.al.)

2.6. Skin irritation test (patch test)

Skin irritation test was performed on the set of 8 rats. In this test, the emulgel was applied on the skin of rats after proper shaving. Noted the undesirable changes like changes in color, in skin morphology for a period of 24 hours.(Murty et.al.)

2.7. Bioadhesive strength measurement

Bioadhesive strength was measured by using a modified method & this apparatus contain two arm balance . Both the ends are tied to glass plates using strings. One side contain two glass plates, other side contains single glass plate for keeping weight. By adding extra weight on the left hand pan, the right and left pans were balanced. The balance was remained in this position for 5 min. Accurately weighed 1gm emulgel was placed between these two slides containing hairless fresh rat skin piece & extra weight from the left pan was removed to fixed the two slides of glass and some pressure was applied to removed the present air & remained this balance for 5 mins. Weight was added slowly at 200mg/min to the left hand pan until two glass slides got detached from each other. This weight which required to detach the emulgel from slides gave the measure of Biodhesive strength. (Rachit Khullar et.al.) The bioadhesive strength is calculated using following formula:-

$$\text{Bioadhesive strength} = \text{weight required (in gm)}/\text{Area (cm}^2\text{)}$$

2.8. In vitro release studies

The franz diffusion (FD) cell was use to carry out in vitro release studies. The dialysis membrane was placed between the donor and acceptor compartment of the diffusion cell & applied the formulation on membrane. To maintain the pH & used as dissolution media, phosphate buffer was used (7.4). Maintain the temperature at 37°C by circulating water jacket. Whole assembly was putted on a magnetic stirrer to provide continuous stirring using magnetic blend. A similar blank set was run simultaneously as a control. 5ml sample was withdrawn at a suitable time interval & using equal amount of dissolution media to replaced it. At 285 range, the sample were analyzed spectrometrically & the cumulative % drug release was calculated. (Kakkar & Gupta 1992)

2.9. Stability studies

Aluminium collapsible tubes was used for packing of the prepared emulgel and after then, subjected to stability studies at 5°C, 25°C/60% RH, 30°C/65% RH and 40°C/75% RH for 3 months. Samples were withdrawn at 15 days time intervals and evaluated for physical appearance, pH, viscosity and drug contents. (Harmonized Tripartite Guidelines,2003)

III. Results And Discussion

3.1. Physical appearance

The formulations of emu gel were yellowish white viscous creamy preparation with a glossy appearance and smooth homogenous texture. Results have been discussed in table2:-

| Table2- Physical parameters of formulation batches | | | | |
|--|-------------|-------------|-------------|------------------|
| Formulations | Color | Homogeneity | Consistency | Phase separation |
| F1 | White | Excellent | Excellent | None |
| F2 | White | Excellent | Excellent | None |
| F3 | Pale yellow | Excellent | Excellent | None |
| F4 | Yellow | Excellent | Excellent | None |

3.2. Rheological studies

The test was performed at 100 round per minutes sped for 10 minutes. Results are discussed in following fig.1:-

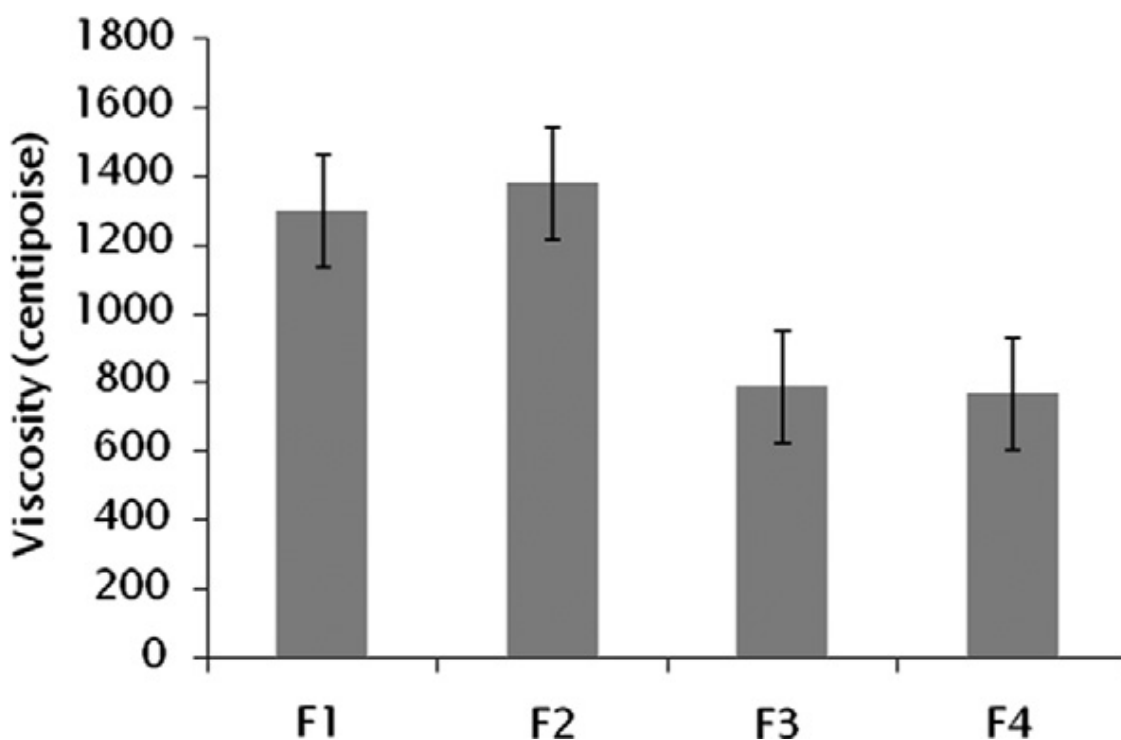


Figure 1 Viscosity of the formulations F1-F4 (mean± SD).

3.3. Spreading coefficient

The spreading coefficient of various emulgel formulations are given below fig2:-

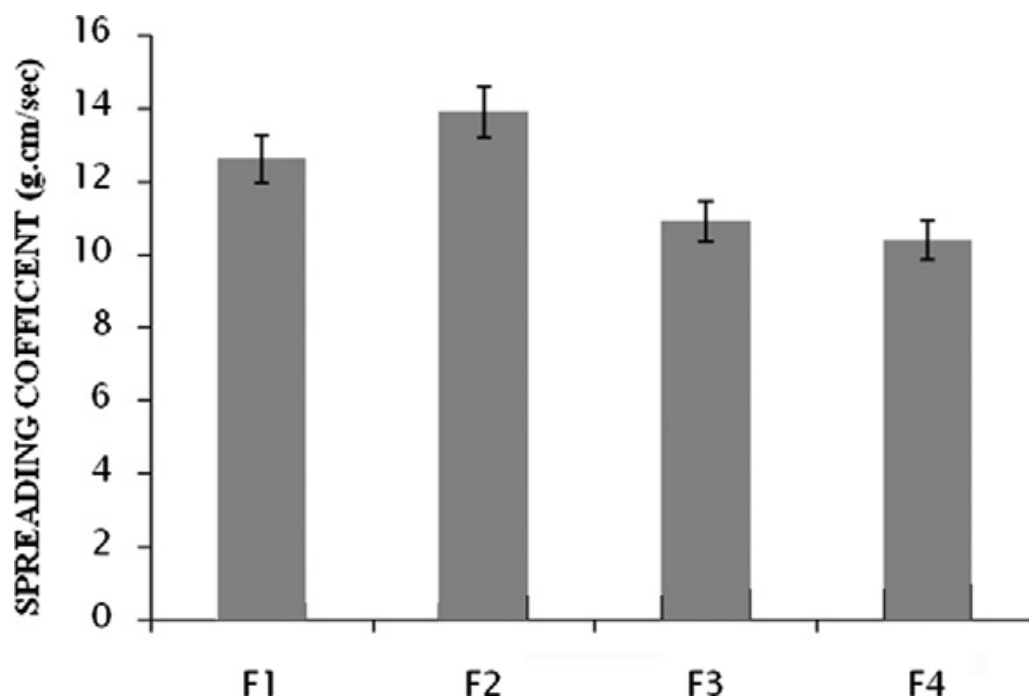


Figure 2 Spreading coefficient of the formulation F1–F4 (mean± SD).

3.4. Skin irritation test

Allergic symptoms like inflammation, itching, redness, swelling and irritation were not appeared on rats up to 24 hour

3.5. Bioadhesive strength measurement

The bioadhesive strength of various emu gel formulation have been shown in fig3:-

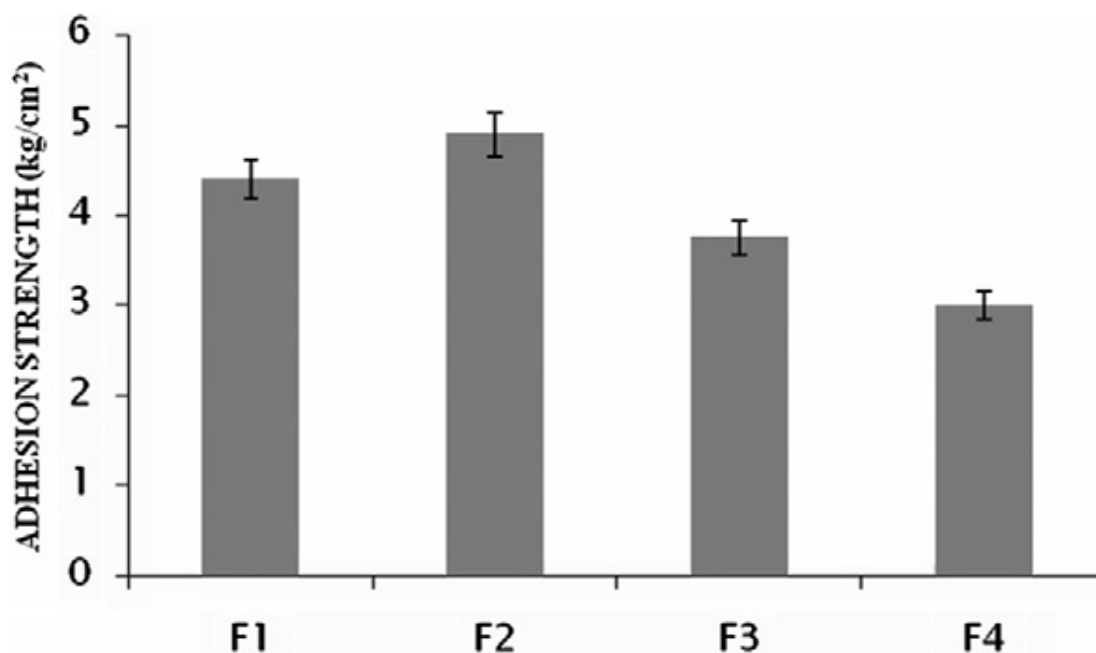


Fig3:- Bioadhesive strength of formulations F1–F4 (mean ±SD).

3.6. In vitro release study

The in vitro drug release study provide the result about the release of drug from emulgel formulations can be situated in following descending order.(fig4,table3)
 F4(56.04%)>F2(53.46%)>F1(52.13%)>F3(51.34%)

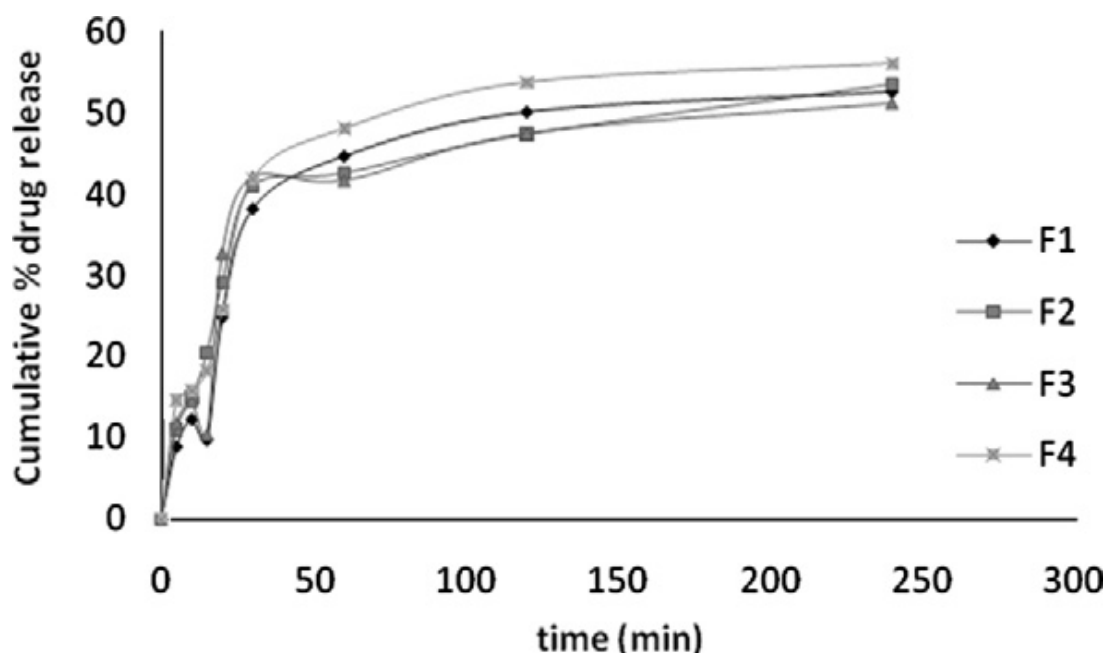


Fig4:-In vitro cumulative % drug release of formulation F1-F4.

Table3:- Data for in vitro cumulative % drug release data of formulations F1-F4

| Time | F1 | F2 | F3 | F4 |
|------|-------------|-------------|-------------|-------------|
| 0 | 0.00+0.00 | 0.00+0.00 | 0.00+0.00 | 0.00+0.00 |
| 5 | 08.90+0.010 | 11.20+8.65 | 11.82+6.83 | 14.55+30.44 |
| 10 | 12.20+0.09 | 11.40+9.45 | 11.85+6.97 | 14.59+20.79 |
| 15 | 0.98+1.34 | 14.92+4.76 | 14.54+13.30 | 15.78+10.30 |
| 20 | 24.65+4.42 | 16.98+7.98 | 17.65+9.80 | 17.96+10.90 |
| 25 | 38.10+31.67 | 29.47+6.89 | 32.75+6.03 | 35.87+7.31 |
| 30 | 44.60+31.70 | 40.95+29.90 | 41.69+7.55 | 45.98+8.12 |
| 60 | 50.00+7.55 | 42.56+3.10 | 51.80+0.98 | 53.89+2.88 |
| 120 | 52.23+7.55 | 53.48+2.31 | 51.25+0.44 | 53.41+3.21 |
| 240 | 52.13+9.88 | 53.46+8.78 | 51.34+6.77 | 56.04+0.99 |

3.7. Stability study

All the prepared emulgel formulations were found to be unchanged upon the storage for 3 months, no change was developed in their physical appearance ,pH, viscosity and drug contents.

IV. Conclusion

In the future , drug delivery via emu gel will be used extensively to maintain greater patient compliance . Emulgel provide better spreadability, adhesion and viscosity & this become famous soon. Moreover, they will become a solution gel bases for loading hydrophobic drugs for long term stability. Similarly in the study, emulgel of oxaprozin were formulated and subjected to physiochemical studies like spreading coefficient studies, rheological studies and bioadhesion strength and in vitro drug release test. To determine drug release rate from emulgel, in vitro release tests were performed. From in vitro studies formulation F4 showed maximum release 56.04% in 240 minutes. The formulations F2&F4 were comparable with marketed ibuprofen topical gel. So oxaprozin emu gel can be used as anti inflammatory analgesic agents for topical drug delivery.

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