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DESIGN AND DEVELOPMENT OF PIROXICAM EMULGEL USING GALANGAL OIL AS PERMEATION ENHANCER

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ABSTRACT

The current research work is undertaken with the aim to formulate and evaluate piroxicam emulgel using Galangal oil which increases the permeation of the drug through the skin. Four different formulations were primped and distinguished physically in the matter of physical appearance like colour, odour, texture, Spreadability, pH, drug content, extrudability and viscoelastic properties. The pH of the prepared formulations was found in between 6.35 to 6.37 which lies in the normal pH range of the skin. The spectra of the pure drug and excipients are determined by **ATR-FTIR** model. It concludes that the final product is safe and effective and compatible with each other without causing any negative adverse effects and compatible with each other. *In-vitro* drug release studies was performed and evaluated using Franz diffusion cell. From the obtained results it was concluded that F_3 was optimized as it has shown higher drug release and maximum drug content of 93%. *In-vivo* study was performed to assess the anti-inflammatory effect using a carrageenan-induced rat paw oedema model. It was concluded that inflammation of rat paw was reduced as compared to marketed formulation. The prepared piroxicam emulgel has better anti- inflammatory activity than marketed formulation of diclofenac emulgel.Since emulgels had appeared as a novel technique for topical drug delivery,it can be very efficient for hydrophobic drugs.

Keywords: Piroxicam,Emulgel,Galangal oil,Topical drug delivery

INTRODUCTION:

The current goal of the research is to develop an emulgel with a safe, effective, and stable dosage form **[1]**. Emulgels can be employed as superior topical drug administration methods than current systems because of the action being potentiated by numerous permeation-enhancing substances **[2]**. The nonsteroidal anti-inflammatory medication (NSAID) piroxicam is a member of the oxicam class and is used to treat the symptoms of painful inflammatory disorders including arthritis. Piroxicam acts by inhibiting the synthesis of endogenous prostaglandins, which are implicated in the mediation of pain, stiffness, soreness and oedema **[3]**. It is a well-known approach to administering hydrophobic NSAIDs **[4]**. Due to NSAIDs' potent anti-inflammatory and analgesic properties, the4 widely employed in rheumatology. NSAIDs are frequently applied in the symptomatic therapy of different rheumatic disorders characterised by chronic musculoskeletal pain and various forms of acute pain, along with their usage in treating rheumatoid arthritis (RA) and osteoarthritis (OA) **[5]**. Comparing equivalent oral dosage to topical treatment, the bioavailability and maximum plasma NSAID levels are typically less than 5 and 15%, respectively. NSAIDs applied topically enter gradually and in modest amounts entering the systemic circulation **[6]**. Piroxicam belongs to BCS class-II which has the property of low solubility and high permeability **[7]**. Piroxicam is a non-steroidal anti-inflammatory drug with analgesic and antipyretic properties that is used to treat rheumatoid arthritis, osteoarthritis, and severe contusions. It is well absorbed after oral administration, but in addition to damaging the gastric mucosa, its use has also been linked to a number of unfavourable adverse effects based on the kidneys and the stomach. Dermal delivery is an alternative method, but it requires a formulation that guarantees deep skin penetration, enabling therapeutic effect at a localised site. Although piroxicam is not readily taken after topical administration, some studies have been done to forecast the percutaneous absorption of piroxicam using various substances as permeation enhancers like galangal essential used in the formulation **[8]**. It acts as permeation enhancer and increases the absorption of drug and shows its anti-inflammatory property **[9]**.

MATERIALS AND METHODS:

Materials:

Piroxicam was obtained as a gift sample from Aurobindo Pharma Limited, Hyderabad, Galangal essential oil was purchased from Avi naturals, New Delhi, Liquid paraffin, Tween20, Span20, Propylene glycol, Methyl paraben, Propyl paraben, Ethanol, Carbopol 940,

Triethanolamine were analytical grade ingredients available in our institution.

Method: [10]

Preparation of emulgel includes three steps:

Step 1: Formulation of gel base: Required quantity of carbopol940 was taken and soaked in distilled water overnight. Gel was prepared by using carbopol940 and the pH was adjusted to 6.6 using triethanolamine

Step 2: Formulation of o/w emulsion: Aqueous phase was prepared by dissolving methyl paraben and propyl paraben in propylene glycol, tween 20 was added to the propylene glycol mixture. Oily phase of the emulsion was prepared by mixing span 20 with liquid paraffin. Both the oily phase and aqueous phases are separately heated to 70-80˚C and then slowly oily phase is added to aqueous phase in a motor by constant stirring and finally O/W emulsion was formed. The drug was dissolved in ethanol and added to the emulsion.

Step 3: Incorporated emulsion into gel base in 1:1 ratio with constant stirring, and the emulgel is formed.

FORMULATION OF INGREDIENTS FOR EMULGEL USING CARBOPOL 940: (Table 1)

Table 1: Formulation of Ingredients For Emulgel

S. No	Composition	F1	F2	F3	F4
1	Piroxicam	0.15	0.15	0.15	0.15
2	Liquid paraffin	7.5	7.5	7.5	7.5
3	Tween 20	0.5	0.5	0.5	0.5
4	Span 20	1	1	1	1
5	Propylene glycol	5	5	5	5
6	Ethanol	2.5	2.5	2.5	2.5
7	Methyl paraben	0.03	0.03	0.03	0.03
8	Propyl paraben	0.01	0.01	0.01	0.01
9	Galangal oil	0.25	0.50	0.75	1.0
10	Carbopol 940	0.15	0.15	0.15	0.15
11	Triethanolamine	q.s to adjust the pH to 6 - 6.5			
12	Distilled water	q. s	q. s	q. s	q. s

EVALUATION PARAMETERS [11]

Physical Appearance

Visual examination of the created emulgel formulations was done to check for colour, homogeneity, consistency, and pH.

pH

This gel's pH was measured using a pH metre. It was determined and noted in a beaker what pH the gel had.

Rheological Study

The viscosity of the different emulgel formulations was measured using a Brookfield viscometer with spindle 52 at 25°C.

Drug Content Determination

By using a UV spectrophotometer, the drug content of the emulgel was determined. Using phosphate buffer 7.4, one millilitre of emulgel was diluted to 20 millilitres in methanol. To create a piroxicam solution

with a 10 µg/ml concentration, 2 ml of this solution were further diluted.

Drug content = (concentration × dilution factor × volume taken) × conversion factor

Spreadability

A 1cm-diameter circle containing 1g of emulgel was premarketed on a glass plate, which was then covered with another glass plate. Five minutes were given for a 500g weight to lay on the upper glass plate. The formula revealed the diameter increase brought on by the emulgel spreading:

$$S = M.L/T$$

Where, S= Spreadability (gm.cm/sec)

M= Mass placed on the pan

L= Length of the slide (cm)

T= Time (sec) required to move the upper slide

Extrudability

In order to conduct this test, a clean, collapsible tube with a 1 cm diameter opening must contain produced gel. The weight of gel ejected from the tube when finger pressure is applied while holding the tubes in the hands is used to gauge the extrudability.

FTIR

The ATR-FTIR model is used to determine the spectra of the pure medication and excipients. A wide variety of sample types, including liquids, solids, powders, semisolids, and pastes, can be measured fast and accurately by the ATR-FTIR model. A little drop of the sample is deposited onto the ATR crystal to measure liquids, pastes, and semisolids. The sample is placed onto the ATR crystal and forced down using the swivel press to ensure the best contact for powers, thin films, or other semisolid samples. The measurement is then taken and recorded.

Drug release *in vitro* research employing a Franz diffusion cell

Gellified Emulsion (500 mg) was evenly placed on the egg membrane, which was positioned on top of the diffusion cell's donor and receptor chambers. For the drug release experiments, a Franz diffusion cell (15.5 ml cell volume, 37± 0.5ºC, speed 50 rpm, effective diffusion area 3.14 cm2) was utilised. To solubilize the medication, newly prepared PBS solution (pH 7.4) was injected into the receptor chamber. Magnetic stirrer was used to stir the receptor chamber. At appropriate times, samples (1.0 ml aliquots) were collected. After the proper dilutions, samples were examined for drug content using a UV/VIS visual spectrophotometer. With respect to time, the total amount of medication released across the egg membrane was calculated.

***In-vivo* studies [12]**

White male albino rats weighting between (1 70 and 200 gm) were selected for evaluation of the anti-

inflammatory activity by measurement of o edema size results from carrageenan injection in the right hind paw region of the body. Animals were housed 4 per cage in standardised condition at animal house in

the Chalapathi institution of pharmaceutical sciences. All animals were acclimatized and kept under constant temperature(25±2˚C) and 12-hour light or dark cycle for atleast two weeks prior the experiments. All the experiments were performed in accordance with IAEC guidelines. Each animal was allowed free access to standard food pellets and water. The IAEC approval number was 20/IAEC/CLPT/2022-23.

Treatment

The animals were divided into four groups, consisting of (four animals per each).

Group 1: - Control group treated with non-medicated gel base.

Group 2: - Treated with carrageenan 1%w/v (0.1ml)

Group 3:- Treated with standard (marketed diclofenac emulgel)

Group 4: - Treated with formulation-3

Paw oedema size induced by carrageenan injection

On the right hind paw of the rats, 100 mg of the examined gel base was topically administered. Bandages were used to cover the application area lightly, and it was left in place for two hours. The left-over gel on the skin's surface was then removed by removing the dressing and wiping it off with a piece of cotton. The volume of the paw was measured immediately prior to the injection of carrageenan and treated as zero time. Then, 0.1ml of a freshly made, sterile carrageenan solution in saline was injected into the rats' right hind paw's sub-plantar region. Equal amounts of saline were administered to the opposite paw. A digital Plethysmometer was used to measure the thickness of the right hind paw from ventral to dorsal surfaces at intervals of 0, 5, 15, 30, 60, and 120 minutes following the sub-plantar injection of carrageenan. Following carrageenan injection, the extent of the oedema was quantified as a percentage change in paw thickness (mm) from the control (pre-drug, zero time).

RESULTS AND DISCUSSION:

FT-IR (Figure 1)

The compatibility of the excipients and essential oil present in the end product with the API and excipients has been established through observation, analysis, and interpretation of the FTIR results of the API and excipients used in the formulation and comparison with the FTIR results of the final product. The declares that the finished product is risk-free and efficient without having any unfavourable side effects.

Physical appearance

All formulation batches were found to be homogenous yellowish milky emulsions while emulgels were found to be yellowish white viscous creamy preparation **(Table 2)**. The drug releases from the produced emulgel were visible at 0, 5, 10, 15, 30, 60, 120, and 240 minutes. It was noted the dosage release percentage. Better release was seen when formulation F_3 consistently

released the medication throughout time. The rate of release of a drug from its pharmaceutical dosage form, which is primarily governed by viscosity, has a significant impact on the therapeutic effectiveness of the drug. Because F3 was the most viscous formulation.

Optimization:

Based on the above performed evaluation tests it was concluded that F_3 formulation was optimized as it is showing better results compared to other formulations, and it was opted for *in-vivo* studies to determine anti-inflammatory activity.

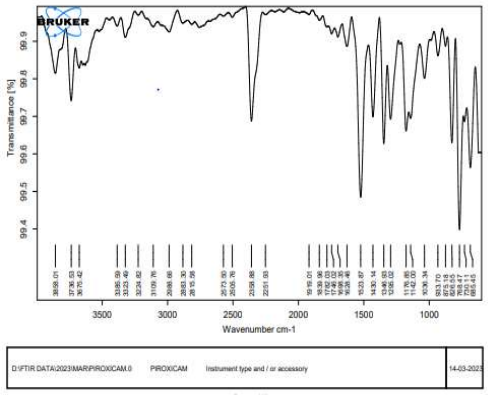
***In-vitro* diffusion studies: (Table 3)**

***In-vivo* studies: (Table 4)**

Discussion of paw oedema size induced by carrageenan injection

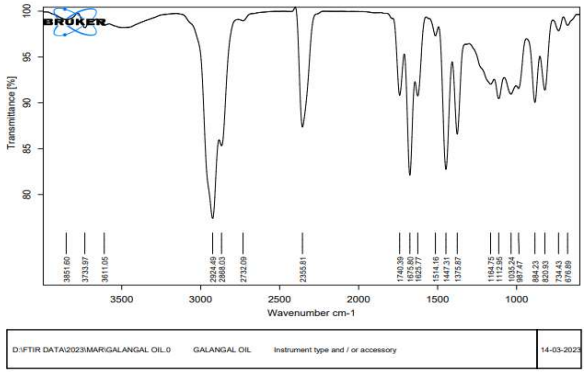
Topical treatment of the rats with piroxicam significantly inhibits the oedema size induced by carregenan injection into the sub-plantar area of the right hind paw for each rat. It is observed from figure that the groups treated with piroxicam emulgel formulae exhibit a maximum percent oedema inhibition after 1 hour which is lower than that of diclofenac emulgel after 1 hour **(Figure 2)**.

Piroxicam



Formulation-1

Galangal oil



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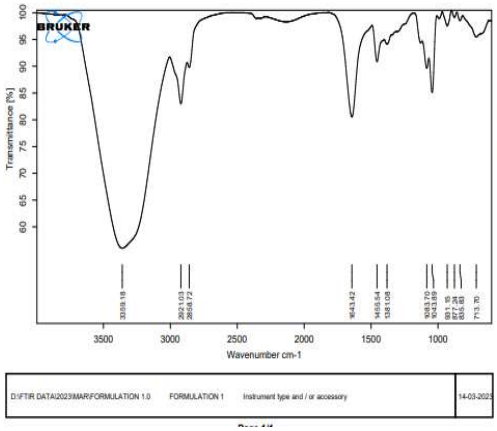

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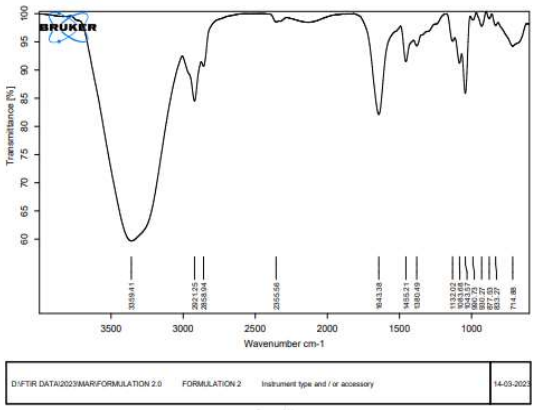

Formulation-4

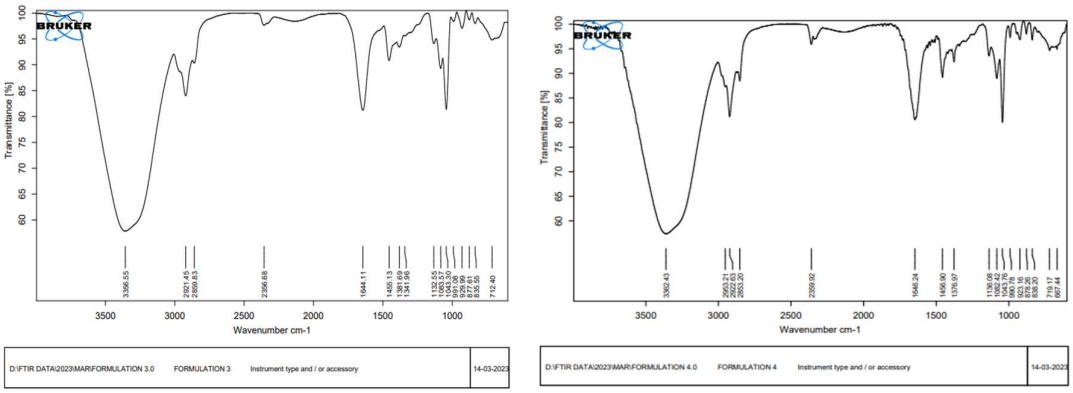

Figure 1: FTIR

Table 2: Physical appearance

Formulation	pH	Viscosity (Cp)	Drug content (%)	Spreadability (gm.cm/sec)	Extrudability(gm)
F_1	6.36	32	77	1.16	0.61
F_2	6.35	20	84	1.30	0.73
F_3	6.36	18	93	1.46	1.18
F_4	6.37	15	90	1.56	1.20

Table 3: *In-vitro* diffusion studies

Time(min)	F_1(%)	F_2(%)	F_3(%)	F_4(%)
5	5.28	4.8	19.68	16.32
10	5.76	5.76	27.84	21.8
15	9.84	7.2	30.48	24.48
30	16.8	25.92	36.72	27.84
60	19.2	42.96	38.8	31.2
120	26.4	54.04	65.2	37.92
240	30	59.02	68.8	38.64

Table 4: *In-vivo* studies

Paw volume (ml)				
Time (min)	Control	Carrageenan 1%w/v 0.1 ml	Standard (Diclofenac emulgel 100mg/kg)	Test (F_3)
0	1.475±0.048	1.525±0.048	1.600±0.041	1.475±0.048
5	1.700±0.041	1.975±0.048	1.875±0.085	1.700±0.041
15	1.650±0.065	2.375±0.063	2.075±0.085	1.950±0.065
30	1.725±0.048	2.775±0.085	1.975±0.085	2.125±0.075
60	1.700±0.041	3.075±0.095	1.925±0.048	2.025±0.063

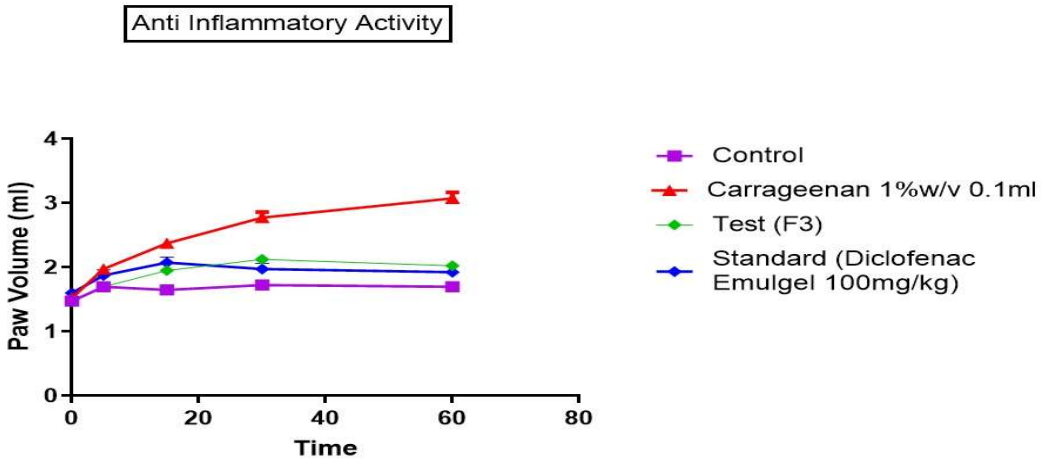

Figure 2: Anti Inflamatory Activity

DISCUSSION:

While emulgels were discovered to be homogenous yellowish-milky emulsions, all formulation batches were discovered to be yellowish-white viscous creamy preparations. The pH range of the developed formulations, which corresponds to the typical pH range of the skin, is 6.35 to 6.37. The excipients and essential oil present in the finished product are compatible with one another and don't have any negative side effects, as shown by observation, analysis, and interpretation of the FTIR results of API and excipients used in the formulation and comparison with FTIR results of formulation. Galangal oil has 1,8 cineole and -Terpineol components, according to analysis of its FTIR spectrum. Franz diffusion cell was used to carry out and assess *in-vitro* drug release patterns. F_3 was determined to be the most optimised formulation out of all. Using a carrageenan-induced rat paw oedema model, we had conducted an *in-vivo* investigation for the optimised formulation to evaluate the anti-inflammatory activity.

CONCLUSION:

Piroxicam emulgel was formulated in order to increase the drug's skin penetration using penetration enhancers like galangal oil which we included in our formulation. In order to determine and compare the penetration activity, we conducted 4 formulation studies. Based on the outcomes of *in-vitro* testing and other evaluation criteria, including drug content, Spreadability, extrudability, we found that F_3 was the most effective formulation. According to in-vivo tests, F_3 penetrates the skin more deeply and reduces inflammation over the course of the studies. The F_3 formulation has demonstrated efficient penetration and anti-inflammatory effects when compared to the other three formulations. So, it can be concluded that topical emulgel containing galangal oil has good permeation through skin and piroxicam posses an effective anti-inflammatory activity.

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