LORNOXICAM AND FRANKINCENSE OIL TRANSDERMAL GEL: A POTENTIAL FORMULATION FOR MANAGEMENT OF INFLAMMATION

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Keywords:
NSAIDs, natural oil, skin permeation enhancer, in-vitro evaluation, ex-vivo study, carrageenan induced rat paw edema

ABSTRACT: Inflammation is usually accompanied by pain. The pathogenesis of pain involves not only nociception i.e. the aspect related to sensation of pain but also the emotional aspect involving the pain related fear and stress. Lornoxicam is a non-steroidal anti-inflammatory drug of oxicam class. Frankincense oil, used commonly in aromatherapy, has been known to have calming and grounding effect on emotions. The aim of this study was to provide a formulation for topical application which has a potential as an effective alternative for better management of inflammation. Gel formulation of lornoxicam, 0.5%w/w, was optimized. Lornoxicam gel formulation containing frankincense oil was prepared. The effect of addition of frankincense oil on physical properties of the gel and drug permeation was studied. Anti-inflammatory activity of the developed lornoxicam gel containing frankincense oil was demonstrated. The in-vitro diffusion studies showed a higher and faster release of lornoxicam from the gel containing frankincense oil than that from the gel without frankincense oil. The flux obtained for lornoxicam in ex-vivo permeation studies was higher for the formulation containing frankincense oil (17.47µg/cm²/hr) than that for the formulation without frankincense oil (6.7 µg/cm²/hr). The enhancement ratio calculated was 3.8. Lornoxicam gel containing frankincense oil showed significantly higher inhibition of edema than the gel without frankincense oil and the marketed preparation in in-vivo study. Frankincense oil exhibited enhanced permeation of lornoxicam from gel formulation. The study indicates that transdermal gel containing lornoxicam and frankincense oil has a potential as an effective medication for management of inflammation.

INTRODUCTION: Inflammation is usually accompanied by pain. Chronic inflammatory pain, a frequent symptom in clinical practice, is still considered a poorly controlled condition and difficult to treat. The pathogenesis of pain involves not only nociception i.e. the aspect related to sensation of pain but also the emotional aspect involving the pain related fear and the probable depression that follows.

It also involves behavioral aspects involving pain catastrophizing, hypervigilance and somatic awareness. From the perspective of patients suffering from inflammatory conditions like arthritis, application of medicament directly at the site of inflammation or soreness stands an advantage due to convenience of administration. Most of the commonly used nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with severe gastrointestinal adverse effects when administered orally. A desire to avoid systemic side effects of pain killers, particularly of the NSAIDs, has led to interest in delivery of these drugs through the skin. However, the stratum corneum layer of the skin poses a major barrier to passage of drugs across the skin. Penetration enhancers are therefore used in formulations to increase the flux...
of drugs through stratum corneum. They may i) fluidize the intracellular lipids thereby enhancing the drug diffusion, ii) disrupt the lipid structure and enhance the drug partitioning into the stratum corneum. The action of penetration enhancer should be reversible. The compounds used as penetration enhancers in topical formulations should be pharmacologically inert, non toxic and non-irritating apart from having compatibility with drugs and other excipients of the formulation. Hence natural penetration enhancers have attracted interest of the researchers as an alternative to synthetic chemical enhancers.

Frankincense oleo gum-resin known as salai guggul in ayurvedic medicine is obtained from bark of several species of *Boswellia*. *Boswellia* has long been used and extensively studied for its anti-inflammatory properties. Extract of *Boswellia* contains boswellic acids which impart anti-inflammatory properties to the extract. However boswellia oil, also known as frankincense oil (FO), which is steam distilled from the oleogum resin, is not extensively reported to possess significant anti-inflammatory activity. Mikhael BR *et al.* have reported immunomodulatory activity for FO.

Though the constituents of FO differ according to climate, harvest conditions and its geographical source, terpenes are major constituents of the oil. These terpenes provide a characteristic soothing fragrance to FO due to which it is used commonly in aromatherapy. Frankincense has been known to have calming and grounding effect on emotions. Hence the essential oil of frankincense is often used in massage oil blends for pain relief.

It was therefore deemed to be of interest to study the effect of presence of FO in a topical anti-inflammatory formulation. The prime objective of this study was to carry out preliminary evaluation of the feasibility of a formulation containing NSAID and FO and thus assess potential of such a formulation as an effective medication for management of inflammation. Lornoxicam (LRN), (Chlortenoxicam) (CAS number: 70374-39-9) (PubChem CID: 54690031) was taken as a model NSAID in the study. LRN is an NSAID of the oxicam class with analgesic and anti-inflammatory activity. The dose of LRN is low, 4mg to 8mg and like other NSAIDs, its oral administration may be associated with serious systemic adverse effects, particularly gastrointestinal disorders. Effect of various penetration enhancers on gel formulation of LRN has been studied in literature. The present work involves formulation and *in-vitro* and *in-vivo* evaluation of a gel containing LRN and FO to be applied to the skin at the site of inflammation which also may possess potential to deal with the nociceptive and emotional aspects of inflammatory pain, hence likely to result in better treatment acceptability by the patients.

A carbopel gel of LRN containing FO was optimized and studied with respect to viscosity, spreadability, *in-vitro* and *ex-vivo* drug release and *in-vivo* effect on carrageenan induced rat paw edema.

### MATERIALS AND METHODS:

**Materials:**
LRN was a generous gift sample from Abbott Healthcare Pvt. Ltd., Mumbai, India. Carbopol® 980 NF (CRB) was a gift sample from Lubrizol, Mumbai, India. Frankincense oil was purchased from M/s. Falcon, Bangalore, India. Propylene glycol, Polyethylene glycol 400 and Triethanolamine was purchased from Fisher Scientific, India. Methyl paraben and Propyl paraben were obtained as gift samples from M/s. Encube Ethicals, Mumbai, India. Acetonitrile (HPLC grade) was purchased from S.D. Fine Chemicals, Mumbai, India. All other chemicals used were of analytical grade.

**METHODS:**

**Development of gel formulations:**

**Formulation of LRN gels:**
Gel containing 0.5 % w/w LRN was formulated. CRB was used as a gelling polymer. Quantity of solvent for the gel and the gelling polymer was optimized based on the capacity of the solvent co-solvent system to give a visually clear gel with desired consistency. The compositions of various formulation trials are given in Table 1.
TABLE 1: % COMPOSITION OF FEASIBILITY TRIALS FOR LRN GEL.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
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<tbody>
<tr>
<td>LRN</td>
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<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
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<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
</tr>
<tr>
<td>CRB</td>
<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
<td>0.50</td>
<td>0.75</td>
<td>0.75</td>
<td>0.75</td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td>PG</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>20</td>
</tr>
<tr>
<td>PEG 400</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td>60</td>
<td>60</td>
<td>30</td>
<td>30</td>
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<td>30</td>
</tr>
<tr>
<td>Ethanol</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.20</td>
<td>0.20</td>
<td>0.20</td>
<td>0.20</td>
<td>0.20</td>
<td>0.20</td>
</tr>
<tr>
<td>Methyl paraben</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Propyl paraben</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Purified Water</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TEA</td>
<td>q.s.</td>
<td>q.s.</td>
<td>q.s.</td>
<td>q.s.</td>
<td>q.s.</td>
<td>q.s.</td>
<td>q.s.</td>
<td>q.s.</td>
<td>q.s.</td>
</tr>
</tbody>
</table>

(RLN- Lornoxicam, CRB- Carbopol® 980 NF, PG- Propylene glycol, PEG 400-Polyethylene glycol 400, TEA- Triethanolamine, q.s. – Quantity sufficient)

To prepare gels, weighed amount of methyl paraben and propyl paraben was dissolved in the selected solvent. LRN was dispersed in it under stirring. CRB was separately allowed to hydrate in a calculated amount of water. LRN dispersion was then added to the hydrated carbopol dispersion under stirring. This mixture was then neutralized with required amount of triethanolamine to a pH of 7-7.2. The resulting gels were visually observed for clarity.

**Preparation of LRN gel with FO:**
0.5%w/w LRN gels were prepared with 2%w/w, 3%w/w and 5%w/w FO as given in Table 2.

TABLE 2: % COMPOSITIONS OF FORMULATIONS FOR OPTIMIZATION OF QUANTITY OF FO.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>F10</th>
<th>F11</th>
<th>F12</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRN</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>CRB</td>
<td>0.75</td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td>PG</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>PEG 400</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>FO</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Methyl paraben</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Propyl paraben</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Purified water</td>
<td>q.s.</td>
<td>q.s.</td>
<td>q.s.</td>
</tr>
<tr>
<td>Triethanolamine</td>
<td>q.s for pH adjustment</td>
<td>q.s for pH adjustment</td>
<td>q.s for pH adjustment</td>
</tr>
</tbody>
</table>

(LRN- Lornoxicam, CRB- Carbopol® 980 NF, PG- Propylene glycol, FO- Frankincense oil, PEG 400-Polyethylene glycol 400, q.s. – quantity sufficient)

Weighed amount of methyl paraben and propyl paraben was dissolved in a mixture of polyethylene glycol 400 and propylene glycol (3:2) for preparing the gel. LRN was dispersed in it. CRB was allowed to hydrate in calculated amount of water. FO was added to it and mixed uniformly under stirring. LRN dispersion was then added under stirring to the hydrated CRB containing FO. This mixture was then neutralized with required amount of triethanolamine to a pH of 7.0 to 7.2.

**Texture analysis:**
The gels in absence of FO, F9, and in presence of FO, F10, were studied for their texture in terms of the adhesion force recorded on a texture analyzer (Wet Tack Analyzer, Rohit instruments, India, Courtesy: Pidilite Industries, India). About 1g sample was placed on the base platform of the texture analyzer. A one inch aluminum probe experiencing a constant load of 0.500 kg was made to travel downwards through the gel and return back upwards. The force required to detach the probe from the surface of the gel during return movement was recorded as the adhesion strength. An average of three determinations was calculated.

**Evaluation of the gels:**

**Viscosity:**
Viscosity of the optimized LRN gels with FO (F10) and without FO (F9), was determined on a Brookfield DV-III viscometer.
Spreadability: Spreadability was checked for F9 and F10. 0.5g sample was spread evenly on the edge of a glass slide which was in turn placed on a measuring scale. Another glass slide was placed over the sample which was in turn attached to a fixed load of 10 g (M) and on this was placed a weight of 100 g for 1 minute. The weight was then taken off and the upper glass slide was made to travel under the 10g load till it completely slides off. Distance travelled by the gel (L) and time taken was recorded. Spreadability was calculated using the formula:

\[ \text{Spreadability} = \frac{ML}{T} \]

M is the load applied to the upper glass slide
L is the distance travelled by the gel sample
T is the time taken to travel distance L

Drug content: Drug content was determined for F9 and F10. About 200 mg gel was accurately weighed. To this 2ml methanol was added. Sonication was carried out for 20 minutes and volume was made to 10ml with phosphate buffer pH 7.5. The solution was filtered and the filtrate was analyzed by HPLC. HPLC analysis was carried out on Agilent (1220 Infinity) auto sampler HPLC using BDS hypersil (4.6 mm x 250 mm, 5µ, Thermoscientific) column. Mixture of acetonitrile: trisodium acetate buffer (0.02 M)(45:55) constituted the mobile phase. The retention time was found to be 4.3 min ± 0.2 min at a mobile phase flow rate of 1ml/min and a detection wavelength of 377 nm.

Drug penetration experiments: In-vitro diffusion study: LRN gels F9 and F10 were studied for in-vitro drug release. In-vitro drug release through dialysis membrane (Dialysis membrane-150, Hi-media) was studied using a vertical diffusion cell. Phosphate buffer pH 7.5 was used in the recipient compartment. About 0.2g accurately weighed amount of gel was then spread uniformly on the skin in the donor compartment over an effective permeation area of 3.8cm². The recipient compartment was continuously stirred uniformly and 1ml aliquot was withdrawn at 30 min, 2 h, 4 h, 6 h and 8 h time points. The aliquots were replaced by adding equal amount of pH 7.5 buffer to the recipient compartment to maintain sink conditions. Absorbance of the aliquots, appropriately diluted, was taken on ultraviolet spectrophotometer at a detection wavelength of 377 nm. Cumulative amount of LRN permeated was calculated and plotted against time. The slope of the straight line portion of the graph divided by the permeation area gave the flux of LRN through the skin per unit area per hour.

Ex-vivo permeation study: Penetration of LRN was studied through porcine ear skin from 0.5%w/w LRN gels with and without FO. The porcine ear skin was cleared of hair and the fatty layer and stored in normal saline at -20°C and used for study within a week.

Aliquots were suitably diluted and absorbance read on a uv spectrophotometer at detection wavelength of 377 nm. Cumulative amount of LRN released was calculated and plotted against time. The slope of the straight line portion of the graph divided by the diffusion area gave the flux of LRN through dialysis membrane per unit area per hour.

Skin Irritation study: The skin irritation study was carried out for gel with FO, F10, with appropriate permission from ethics committee of...
SVKM’s NMIMS. Skin surface of 4 cm$^2$ area was shaved on both sides of the dorsal surface of abdominal region of six Sprague Dawely rats with the help of electric clippers. The test formulation was applied on one side while the other side was untreated and considered as control. The treated and untreated areas were observed after 24h, 48h and 72 h for any erythema, reddening or inflammation. After 24 h, one animal was sacrificed and the skin samples were excised from untreated (control) and treated areas. Each specimen was stored in 10% formalin solution and subjected to histopathological study.

**In-vivo study: Carrageenan-induced paw edema in rat.**

**Selection of animals:** All procedures for in-vivo experiments were approved by the Ethics Committee of SVKM’s NMIMS, Mumbai. Female Sprague-Dawley rats (200-250 g) were obtained from Bharat Serum, Thane, India. The animals were kept in polyacrylic cages maintained under 24 °C –27°C. The animals were allowed free access to standard laboratory feed and water. The animals were divided into five groups, with six animals in each group. Each group was placed in a separate cage. The groups were treated as follows:

<table>
<thead>
<tr>
<th>Groups</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>Disease control.</td>
<td>Placebo gel(without lornoxicam) containing FO</td>
<td>F9 (0.5% LRN gel without FO)</td>
<td>F10 (0.5%LRN gel with FO)</td>
<td>Marketed 0.5%w/w piroxicam gel</td>
</tr>
</tbody>
</table>

**Study protocol:**
Paw edema was induced by injecting 100 μl of 1% carrageenan (M/s. Sigma) solution in the left hind foot pad of the animals. In case of control group, Paw volume (ml) were determined using a water plethysmometer (IITC Life Sciences, Woodland Hills, CA) before carrageenan injection and at 0.5, 1, 2, 3, 4 and 5 h after the injection. The paw volume readings obtained before carrageenan injection served as baseline reading for comparison. The paw was initially marked in order to minimize variation in measurement with plethysmometer. In case of the test groups, about 0.5g of the test gel sample was applied to the left hind paw after the baseline reading. The gel was made to stay in place with the aid of a loose adhesive bandage. 1h after the gel application, the bandage was removed, the excess gel was wiped off from the paw and edema was induced in the paw by injecting 100 μl of 1% carrageenan solution. Paw volumes were measured at 0.5, 1, 2, 3, 4 and 5 h after the injection. The increase in paw volume was calculated based on the difference in paw volumes between the baseline paw volume and paw volumes measured after carrageenan injection at the time points mentioned earlier.

**Statistical analysis:**
The data obtained in the in-vivo study was subjected to statistical analysis with the help of Graph Pad Prism 5. Student’s $t$-test was used for comparison between two samples. Probability value less than 0.05 (p<0.05) was considered statistically significant. One way ANOVA was used to compare different groups.

**RESULTS AND DISCUSSION:**
Selection of an appropriate solvent is an essential aspect of formulation development as choice of vehicle influences drug penetration properties. For a gel formulation it is essential that the drug dissolves in the solvent and no insoluble particles remain in the gel. Further in case of drugs having pH dependent solubility the solvent should be selected such that pH of the formulation is in the range that the skin can tolerate without any irritation as well as clarity of the formulation is maintained. LRN has a pH dependent solubility. The LRN solubility increases as pH increases. Formulation trials were designed with an aim to obtain a clear gel using process that has scale up feasibility. Adjustment of pH to 7 and above gave gels of acceptable clarity. Table 1 gives composition of various trials taken for optimization of formulation. Methyl paraben and propyl paraben were used for their antimicrobial preservative action. A gel formulation should have optimum viscosity for convenient handling. It should not be too fluid that it flows out of the tube, at the same time should not adversely affect the release of drug from the gel. The gelling polymer concentration
was selected based on the consistency of the gels observed in feasibility trials. Formulation F7 was visually clear on keeping for a week at pH of 7.2. It also exhibited consistency suitable for handling. F8 and F9 were prepared to assess the reproducibility of F7 with respect to process and clarity.

The formulation was reproducible and hence this formulation was considered as optimum formulation for further studies and referred to as F9 in this text. Formulations containing 2%, 3% and 5% FO (F10, F11 and F12 respectively) were prepared by addition of the calculated amount of FO to F9. It was observed that F12 with 5% FO was a loose flowable gel not suitable for handling and application. F11 and F12 imparted a tacky resinous feel on the skin which may be attributed to FO. F10 containing 2% FO had acceptable consistency and feel on application to the skin. Further studies were therefore carried out with F10. The viscosity of F9 was found to be 5800 centipoise while F10 was 3155 centipoise. The lower viscosity of F10 than F9 may be attributed to the presence of frankincense oil in F10. F10, however, was convenient for application and handling. Texture analyzer was used to determine the adhesion strength of the developed gels. The adhesion strength for F9 was 0.85 kg (± 4%) and that for F10 was 0.7 kg (± 2%). Fig. 1A and 1B are representative texture analysis plots of F9 and F10.

![Texture Analysis Graphs](image)

**FIG. 1: TEXTURE ANALYSIS GRAPHS. A. TEXTURE ANALYSIS GRAPH OF F9, AVERAGE ADHESION STRENGTH 0.85 KG. B. TEXTURE ANALYSIS GRAPH OF F10, AVERAGE ADHESION STRENGTH 0.7 KG.**

Good spreadability is a desirable characteristic of any topical formulation. A formulation that spreads uniformly with least effort during application has good patient compliance.
Fig. 2 depicts the spreadability test results. Spreadability was better for F10 than F9. The results of spreadability test correlate with the results obtained in texture analysis. Lower adhesion strength resulted in a good spreadability of F10 than F9.

Average drug content of F9 was found to be 97.7% (±1%) while that of F10 was 99.2% (±1%). This indicates that there is no degradation of the API during the process of preparation of the gels.

In-vitro drug diffusion studies through dialysis membrane showed significantly higher diffusion of LRN into the receptor compartment in case of F10 as compared to F9 (p<0.05). Fig.3 depicts the comparative in-vitro release profile of LRN from F9 and F10.

The in-vitro flux obtained for F9 was 55.97µg/cm²/hr while that obtained for F10 was 77.35µg/cm²/hr. Thus it was observed that in presence of 2% FO, penetration of LRN through dialysis membrane was enhanced. The results of ex-vivo studies through porcine ear skin are depicted in Fig. 4.

Fig. 4 shows the cumulative amount of LRN permeated ex-vivo from F9 and F10.

F10 exhibited significantly higher and faster penetration of LRN through the biological membrane than F9 (p<0.05). Flux obtained for F9 was 6.7µg/cm²/h while that for F10 was 17.47µg/cm²/h. The enhancement ratio calculated was 2.6. This indicates that presence of 2% FO enhances the flux of LRN from the gel through porcine ear skin. Since F10 exhibited better results in drug permeation studies than F9, it was studied for skin irritation potential. The images obtained for histopathological samples in skin irritation studies are depicted in Fig.5.

Fig. 5 shows the histopathological images of treated (A) and control (B) skin sections studied for skin irritation potential of F10.

The section of the skin sample to which F10 was applied did not exhibit any abnormality with respect to: scab formation, hemorrhage, break in length of epithelium, infiltration of neutrophils, inflammatory cells, infiltration of mononuclear cells (MNC) /PMN, giant cells, hyperkeratinization, re-epithelisation and new hair follicle formation, and a minimal change for
fibrosis. There were no visual signs of irritation or lesions on the treated skin after 24h, 48h, 72h and at intermittent time intervals up to 14 days. F10 treated skin was comparable to the control sample which was untreated. Thus, formulation F10 is not expected to possess any skin irritation potential.

Carrageenan-induced rat paw edema is a widely used convenient procedure for assessing anti-inflammatory activity in the development process of drugs including the non-steroidal anti-inflammatory drugs and selective COX-2 inhibitors.\(^{32}\) Fig. 6 depicts the results of the inhibition of carrageenan-induced rat paw edema study for F9 and F10.

Since no dermal formulation of LRN presently is available, marketed preparation of piroxicam 0.5%w/w gel was taken for comparison. Placebo gel containing FO was included in the study to find out if FO contributes to any anti-inflammatory activity. It was observed that the increase in paw volume and hence the edema was maximum in the group-1 which received only carrageenan injection and no treatment. There was significant difference between the extent of swelling in group treated with F9 and that treated with F10 (p<0.05). The increase in paw volume was least for group-4 indicating that the group which received treatment with F10, that is LRN gel containing FO, exhibited maximum inhibition of edema. The edema inhibition exhibited by F10 was significantly higher than the marketed piroxicam gel 0.5%w/w (p<0.05). There was no significant difference between the group treated with F9 and group treated with marketed piroxicam gel 0.5%w/w (p>0.05). F10 was thus more effective than F9 and marketed preparation of piroxicam in reducing edema. The placebo gel containing FO exhibited no inhibition of edema however the onset of edema development was slower than exhibited by group-1.

There was no significant difference between the results of group treated with placebo gel with FO and the disease control group which received only carrageenan injection (p>0.05). Statistical analysis using the one-way ANOVA indicated that there was a significant difference between groups (p<0.01). These results indicate that F10 has higher potential to control inflammation among the studied formulations and this may be attributed to enhanced skin permeation of LRN in presence of FO.

It is seen from the in-vitro and ex-vivo studies that presence of FO enhances the permeation of LRN. The results of in-vitro and ex-vivo studies are in-line with the observed significant decrease in extent of edema formation in the in-vivo study on carrageenan-induced rat paw edema model.

**CONCLUSION:** Transdermal gel containing lornoxicam and frankincense oil is a potential promising alternative for management of inflammation. From the results obtained in this work, we can also conclude that frankincense oil has a potential as a skin permeation enhancer. It would be worth investigating this effect on various categories of drugs. Confirmatory studies on human subjects are essential to substantiate the results obtained in in-vitro and in-vivo studies in this work. The effect of presence of frankincense oil in the formulation on emotional aspect of pain resulting from inflammation forms future scope of this work.

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