INTRODUCTION
In the early 1990s, researchers sought out a new carrier system beyond liposomes, emulsions, and polymeric nanoparticles; they came up with solid lipid nanoparticles. SLNs can be derived from either natural or synthetic sources and consist of biocompatible lipids and well-tolerated excipients. SLNs are appealing for their capacity to enhance the performance of nutraceuticals, medicines, and other materials due to their unique qualities, which include a micro size, a bigger area, and interaction of phases.1-3

SLNs’ solid lipid core matrix, supported by surfactants, allows them to dissolve compounds with lipophilic properties. The excipients used to construct solid lipid-type drug delivery systems are typically well-tolerated and classified as GRAS. When making SLNs, a variety of lipids are utilized, such as triglycerides, partial glycerides, fatty acids, steroids, and waxes. Triglycerides and hard fats are lipids that fall into this category. In order for the SLNs to maintain a solid matrix when stored, the chosen lipid must have a melting point greater than 45°C. The application of lipids, which are known to have low cytotoxicity, could be an advantage of SLNs because it reduces the risk of acute and chronic toxicity. Numerous emulsifiers, each with a distinct charge and molecular weight, have been used to stabilize the aqueous lipid dispersion.4-6

Among the lornoxicam derivatives, lornoxicam is a non-steroidal anti-inflammatory medicine with a pKa of 4.7 and a log P of 1.8. As compared to other non-steroidal anti-inflammatory drugs, it is a seriously powerful medicine. For various inflammatory and unpleasant situations, it is used. Some have compared its analgesic effects to opioids. Previously, it was thought that LRX prevented cyclooxygenase isoenzymes from causing arachidonic acid to produce prostaglandins. Inhibiting stomach acid release is a key function of prostaglandins in mucosal care of the GI tract. Consequently, dyspepsia, ulceration, and bleeding are common gastrointestinal adverse effects of prostaglandin inhibition. Though it has better tolerance than other NSAIDs, LRX has a number of estimated gastrointestinal adverse effects. When used orally, it might cause problems with the kidneys and blood.7-9

To avoid gastrointestinal adverse effects, another option for NSAIDs, including LRX, is to apply them topically. To distribute medications through many routes, including topical treatment, nanoparticles derived from lipophilic materials, such as waxes or lipids, seem to be reactive colloidal carrier systems. Compared to more conventional delivery methods, they provide a number of benefits. When it comes to drug delivery and other positive skin effects, solid lipid nanoparticles and nanostructure lipid carriers shine. Through occlusion,
they enhance skin hydration and offer a moisturizing effect. Because they are composed of harmless lipids, they are ideal for use on skin that is injured or irritated. Many studies have detailed the advantages of SLN and NLC as colloidal carrier systems and how they were able to successfully incorporate active chemicals.8-10

One promising method for drug administration through the skin is nanoemulsion. For the SLN/NLC/NE formulations loaded with LRX and the placebo, there was no need to employ the hot high-pressure homogenization process. To find out if formulas 10–12 were physically stable, tests were carried out. The rate of drug penetration through the rats’ full-thickness skin was investigated in this study. An LRX gel was also made for ex-vivo and in-vitro comparisons with SLN, NLC, and NE.

MATERIALS AND METHODS

The lornoxicam was kindly procured from the business sector. We sourced all of the remaining excipients from Merck and Sigma-Aldrich, respectively. A sample of xanthan gum was received as a gift. The remaining compounds were all of analytical quality.

Formulation of SLN

Using a high pressure homogenization process set at 90, the placebo SLN formulations were created. The lipid was melted and then mixed with a hot aqueous surfactant solution using an UltraTurrax at 20,000 rpm for 1-minute. In order to homogenize the generated coarse emulsion, a double-staged APV-two thousand high-pressure homogenizer was used, with the first stage operating at 5 × 10⁴ Pa and the second stage at 15 × 10⁴ Pa. Three cycles of homogenization were used. Sealed vials made of silanized transparent material were filled with hot pre-emulsion. In order to facilitate the creation of nanoparticles, the vials were promptly chilled to 25°C. SLN1 and SLN2 were produced by adding LRX in lipophilic phases.9-11

Efficiency of Entrapment and Solubility of Nanoparticles

The receptor phase in both in-vitro and ex-vitro tests was a phosphate buffer solution. We tested LRX’s solubility at a pH of 7.4. Each of four 25 mL flasks was filled with 15 mL of PBS with a pH of 7.4. Each flask was filled with LRX at a concentration higher than what was anticipated to mix in the receptor phase. The flask sealed firmly. In a water bath maintained at 25 ± 10°C, all flasks were immersed. For 24 hours, the apparatus was subjected to continuous agitation at 200 rpm. Later, S&S5893’s blue ribbon filter paper was used to filter the combination.

A specific amount of the transparent liquid was taken out and diluted. The receptor phase solubility of LRX was examined at a wavelength of 376 nm. The dispersion medium’s free drug concentration was used to calculate the NP’s EE and LC. Water was added to the nanoparticle dispersion at specific intervals. For 40 minutes, it was spun at 11,148 × g in a centrifuge. The supernatant was diluted to 10 mL using pH 7.4 PBS, according to the correct volume. Spectrophotometric analysis was performed on the solution at 376 nm.11-13

FTIR Study

The LRX and other formulation constituents’ chemical interactions were determined using FTIR. To do this, nanoparticle dispersions were periodically diluted with water. Various dilutions underwent 40 minutes of centrifugation at 11,148 × g. To remove the watery component, the residues were placed on separate glass plates and heated to 500°C for the night. Thereafter, FTIR analysis was performed on the samples. A Perkin Elmer 100 FTIR instrument, equipped with the Perkin Elmer Spectrum Version 6.0.2 Software, was used to scan powdered samples and pure LRX over a wavenumber range of 4000 to 650 cm⁻¹ with a resolution of 4 cm⁻¹. To guarantee redevelop contact among the sample and crystal for scanning, its necessary to consistently apply the same force while placing the sample on the sample stage. It was transmission mode that the system was running on.

DSC Study

Using DSC, we were able to learn about drug-lipid interactions, polymorphism, crystal ordering, and the melting and crystallization behavior of solid lipids in NPs. This process was executed on nanoparticles, pure lipids, and pure pharmaceuticals. After being weighed into standard sealed aluminum pans, 20 µL samples with a solid content of 3 to 4 mg were heated at a rate of 10 K min⁻¹ while being flushed with 20 mL N2 min⁻¹ from 20 to 90°C. The DSC 204 F1 program was used to determine melting points and enthalpies. The crystallization index, as determined by the following equation, proved that the medication in formulations was in a crystallized condition.12-14

Measurements of Particle and Droplet Sizes

The use of a Mastersizer 2000 laser diffractometer coupled with a Hydro 2000MU wet sample dispersion unit allowed for the determination of the particle and droplet size distribution of both drug-loaded and placebo NPs, as well as NE. All measurements were done in triplicate at 25°C after samples were diluted with water at specific intervals for this purpose. The measuring medium utilized was water, which has a refractive index of 1.33. The results were evaluated by calculating the particle size distribution by volume output included particle size distribution profiles, as well as D10, D50, and D90.13-15

Release of Drugs In-vitro

We used the dialysis bag diffusion method to find out how much LRX each formulation released. Prior to the experiment, the dialysis bags were immersed in PBS with a pH of 7.4 for the night. The bags were sealed after being filled with half a gram of the mixture. Each was placed in a conical flask with 200 mL of pH 7.4 PBS. To maintain a constant temperature of 37 ± 0.5°C, flasks were put in a water bath. The experiments were conducted for 48 hours with continuous agitation at 60 rpm. At regular intervals, samples were collected. A condition of sink was given. After samples were appropriately diluted, their spectro photometric release at 376 nm was measured.14-16
Drug Penetration Study
The DETAE group at Turkey’s Istanbul University Institute of Experimental Medicine supplied the 18 male Wistar albino rats used in the study. The animals were kept in plastic cages that were controlled by a 12-hour light-dark cycle and maintained at constant temperature and humidity. They were provided with tap water and a standard laboratory diet. At least 7 days before the experiments, the rats were brought inside the lab to become used to it. After that, rats were sacrificed by separating their cervical spines. We measured the permeability of lipid nanocarrier-entrapped LRX and the action potentials of lipid NPs in the full-thickness skin of Wistar albino rats.17-19

RESULTS AND DISCUSSION

Analyzing Nanoparticle Solubility and Entrapment Effectiveness
In pH 7.4 PBS, the solubility of LRX was found to be 0.303 ± 0.008 mg mL. Utilizing Compritol 888 ATO, Lanette O, and oleic acid, LRX was effectively loaded into SLN and NLC. Since LRX dissolves more easily in liquid lipids than in solid ones, adding liquid lipids to the lipid phase improved the EE (Table 1) and LC, making the lipid phase an ideal solvent for the hot homogenization process. By imparting a unique structure that allows for more effective medication accommodation in the nanoparticle, liquid lipids affect the crystallization behavior and structure of solid lipids as well.18-20

FTIR Study
In our article, we went into great detail on the LRX FTIR data (Figures 1 and 2). The medication and excipients were found to be compatible using FTIR analysis at 4, 25, and 40°C for a duration of 6 months. The primary bands of LRX, which are specified by other components, had larger peaks and lower intensity. The aliphatic ester structure of triglycerides induced the C=O stretching bands, which showed strong peaks at 1736.05 to 1710.54 cm⁻¹. Triglyceride stretching bands at 3269.71 to 2848.36 cm⁻¹ were found to be more numerous than LRX’s bands at C-H and O-H.20-22

DSC Study
With a melting enthalpy of 125.89 J g⁻¹, the pure Compritol 888 ATO was found to have a melting point of 75.90°C. The addition of surfactant to the dispersion caused the Placebo Compritol 888 ATO nanoparticles to have a wider melting peak at 74.29°C with a melting enthalpy of 15.45 J g⁻¹. A CI of 70.1% was determined. One possible explanation for the drop in onset and peak temperatures observed with nanoparticles is the tiny size effect, which the Thomson equation can describe. Less organized crystals or an amorphous form may be associated with a greater melting range when contrasted with bulk lipids. The amount of energy needed to melt this substance is lower than that required to melt a perfectly crystalline substance, which must overcome the lattice forces. Thus, it was deduced that a lower-ordered lattice structure was the consequence of melting enthalpy values that were lower than those of bulk solid lipids and vice-versa. The presence of liquid lipids as a quest

Table 1: Entrapment efficiency of nanoparticles

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulations</th>
<th>Percent (%) EE</th>
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</thead>
<tbody>
<tr>
<td>1.</td>
<td>Batch I</td>
<td>92.12 ± 0.34</td>
</tr>
<tr>
<td>2.</td>
<td>Batch I</td>
<td>98.13 ± 0.85</td>
</tr>
<tr>
<td>3.</td>
<td>Batch I</td>
<td>93.47 ± 0.12</td>
</tr>
<tr>
<td>4.</td>
<td>Batch I</td>
<td>98.90 ± 0.13</td>
</tr>
</tbody>
</table>

ingredient was thought to be responsible for the significantly less organized organization in NLC formulations. DSC curve of pure drug represented in Figure 3.22-24

Size Distribution of Nanoparticles and Droplets
Both nanoparticles and NEs showed very narrow size distributions in the LD analysis. Various formulations were produced with diameters ranging from 100 to 400 µm. The addition of liquid oil to the lipophilic phase was shown to reduce particle size, whilst the addition of drugs did not produce any discernible effect. So, unsurprisingly, NEs exhibited the smallest droplet size. The NLC and NE formulations had smaller particles and droplets than the SLN formulations because the heat homogenization process reduced the size of the lipophilic phase (Figure 4), which is responsible for its lower viscosity.24,25

In-vitro Study
Each and every one of the nanoformulations showed controlled drug release. LRX gel facilitated the fastest release of medicine, with 100% occurring after 24 hours, followed by 97.7% for NE after 48 hours, 73.7 for batch II, 64.2% after batch III, 54.6% following batch IV, and 49.2% following batch IV.
The identical solid lipids were employed in both the NLC and SLN formulations, although the former’s release rates were substantially higher. The release rate of LRX rose as CI and the overall crystalline state of nanoparticles decreased, despite the fact that there was no discernible difference in the formulations of SLN and NLC.

Liquid lipids made medication diffusion easier. The incorporation of Lanette O-based liquid lipid into SLN exposed other flaws. The kinetic evaluation of different formulations is represented in Table 2.

### Drug Penetration Study

For transdermal medication delivery, drug delivery in the skin might be a sign of drug penetration in the skin. When tested against LRX gel, SLN and NLC dispersions had a higher penetration rate. All three batches (I, II, and III) achieved statistically identical penetration profiles. Different formulations achieved different steady-state fluxes for medication penetration. Furthermore, NE disrupted the deeper horny layer’s lipid architecture, which enhanced the drug’s penetration into the dermis. Because nanoscale range particle size of formulations, the penetration characteristics through the skin of SLN and NLC were employed by spontaneous exclusivity. Following this, the medication was better able to penetrate the skin. The nanometer range in particle size allowed SLN and NLC to penetrate deeper layers of skin. The physicochemical features of nanoparticles, such as their solid state at body temperature and high lipid permeability, allowed them to exhibit reservoir action and prolonged drug release.

### Table 2: Pharmacological formulation kinetic evaluation

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Zero-order</th>
<th>First-order</th>
<th>Higuchi model</th>
<th>Korsmeyer-Peppas model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Batch I</td>
<td>0.9262</td>
<td>0.8248</td>
<td>0.9941</td>
<td>0.9941</td>
</tr>
<tr>
<td>Batch II</td>
<td>0.9325</td>
<td>0.8357</td>
<td>0.9914</td>
<td>0.9945</td>
</tr>
<tr>
<td>Batch III</td>
<td>0.9412</td>
<td>0.8624</td>
<td>0.9830</td>
<td>0.9966</td>
</tr>
<tr>
<td>Batch IV</td>
<td>0.9565</td>
<td>0.8147</td>
<td>0.9851</td>
<td>0.9957</td>
</tr>
</tbody>
</table>

The research concluded that the medication was released from the nanoparticles as they penetrated the skin due to polymorphic transitions in the solid lipid.25

### CONCLUSION

Using Compritol 888 ATO, Lanette O, and oleic acid as solid and liquid lipids, SLN and NLC of LRX were effectively produced with a large drug payload. After six months in storage, stability tests showed that the drugs and excipients were physically stable and compatible. They acted as a depot to give continuous drug absorption in the skin, increasing the skin penetration rate of the drug by three to four times compared to a typical LRX gel formulation. Therefore, it was determined that SLN and NLC of LRX have anti-inflammatory and analgesic properties when applied topically, with fewer side effects than when taken orally.

### REFERENCES

12. Thombe NA, Niphade PS, Ahire ED, Kshirsagar SJ. Formation