Lornoxicam is a nonsteroidal anti-inflammatory drug of the oxicam class with analgesic, anti-inflammatory, and antipyretic properties. Lornoxicam microsponges were prepared by the quasi-emulsion solvent diffusion technique using different concentrations of polymers such as Eudragit RS 100 and Eudragit RSPO. Microsponges were evaluated for their particle size, percentage yield, entrapment efficiency, scanning electron microscopy (SEM), and in vitro drug release studies.

Results: The percentage yield, entrapment efficiency, average particle size, and in vitro drug release for optimized formulation F12 were found to be 70.23% w/w, 81.34% w/w, 172.72 μm, and 96.64% up to 8 h, respectively. From SEM, it was observed that microsponges were found to be spherical in shape with rough surface texture. The formulation F12 shows zero-order release kinetics with an r value of 0.961 and the value of Korsmeyer–Peppas model was found to be 0.792, it follows super case II non-Fickian diffusion. The in vitro drug release studies showed that formulations comprised varying concentrations of Eudragit RSPO in higher proportion exhibited much retarded drug release as compared to formulations comprised a higher proportion of varying concentrations of Eudragit RS 100.

Conclusion: Among all the formulations F12 shows better results, which are released more than 80% of the drug release within 8 h; hence, it is optimized. These developed microsponges are releasing the drug for a longer period, which will be effective for osteoarthritis, rheumatoid arthritis, and acute lumbar sciatica therapy.

Keywords: Lornoxicam, Microsponges, Quasi-emulsion solvent diffusion method, Eudragit RS 100, Eudragit RSPO.
**Methods**

**Procedure for drug and excipients compatibility by Fourier-transform infrared (FTIR) studies**

FTIR spectra of lornoxicam, Eudragit RS 100, Eudragit RSPO, Eudragit RS PO and drug, Eudragit RS 100 and Eudragit RS PO were recorded by using FTIR spectrometer. Spectra between 4000 and 400 cm⁻¹ of the drug, a before mentioned polymers and for drug-polymer powder mixtures were recorded using FTIR spectrophotometer (Bruker, ATR, version1.2.4) using KBr pellet technique. In this ATR sampling technique, solid samples to be analyzed should be free from moisture. Samples were dried by placing in the oven for 20 min at 40°C. One spatula of dried sample placed into mortar and pestle and properly grained. The prepared sample was placed on the crystal of ATR for recording spectrum [10].

**Formulation of lornoxicam microsponges**

All the formulations were prepared by the quasi-emulsion solvent diffusion technique using the polymers Eudragit RS 100 and Eudragit RS PO and plasticizers polyethylene glycol 400 and propylene glycol. Drug, polymer, and plasticizer were dissolved in a mixture of ethanol and dichloromethane and then sonicated for 10 min. This solution was poured drop by drop with a syringe into 1000 ml beaker containing 0.75% w/v PVA solution, maintained at a temperature of 30–40°C with stirring at 1000–1200 rpm speed for 5 h to allow the volatile solvent for evaporation. The formulated microsponges were filtered, washed with distilled water and dried at 40°C [5,6,11]. The various formulations prepared using different polymers and plasticizers with different ratios are shown in Table 1.

**Evaluation of lornoxicam microsponges**

**Scanning electron microscopy (SEM) studies**

The lornoxicam microsponges were observed under a SEM. The instrument used in this study was Hitachi S-3700N, Japan. The microsponges were mounted directly on the SEM sample stub, using double-sided sticking tape and coated with a gold film (thickness 180–200 nm) under reduced pressure.

**Particle size analysis**

The particle size was measured using an optical microscope, and the mean particle size was calculated by measuring 100 particles with the help of a calibrated ocular micrometer. The slide containing microsponges were mounted on the stage of the microscope and diameter of at least 100 particles was measured using a calibrated optical micrometer.

**Percentage production yield**

The production yield of the microsponges was determined by calculating accurately the initial weight of raw materials and the last weight of microsponges obtained, and their percentage yield (w/w) was determined using below equation [12].

\[
\text{Yield}(\%) = \frac{\text{Actual weight of the product}}{\text{Total weight of excipient and drug}} \times 100
\]

**Percentage of unentrapped drug**

Formulated microsponges were filtered from PVA solution. Filtered microsponges were washed thoroughly with 0.75% w/v PVA solution, and washings were added to the above filtrate. 5 ml was taken from this mixture of filtrate and washings, and centrifuged for 10 min and filtered. Filtered sample was suitably diluted with 0.75% w/v PVA solution and analyzed spectrophotometrically at 354 nm using ultraviolet (UV)-Vis spectrophotometer. Percentage of the unentrapped drug was calculated [13].

\[
\text{Percentage of unentrapped drug(%) = \frac{\text{Amount of drug present in filtrate}}{\text{Total amount of drug used for microsponges}} \times 100}
\]

**Entrapment efficiency**

Microsponges equivalent to 16 mg of pure drug was crushed, powdered and was taken in 100 ml volumetric flask. To this, 80 ml of methanol was added and shaken for 1 h on a mechanical shaker and then sonicated for 5 min to complete removal of lornoxicam from microspheres. After sonication, volume was made up to the mark with methanol. This solution was centrifuged and filtered. Filtered sample was suitably diluted with methanol and analyzed spectrophotometrically at 353 nm using UV-VIS spectrophotometer. Entrapment efficiency was calculated as follows [14,15].

\[
\text{Entrapment efficiency(%) = \frac{\text{Amount of drug present in filtrate}}{\text{Total amount of drug used for microsponges}} \times 100}
\]

**In vitro drug release studies**

**Procedure**

In vitro, drug release studies were carried out using USP type II apparatus at 100 rpm. Microsponges equivalent to 16 mg of pure drug was added to 900 ml of pH 6.8 phosphate buffer which is used as the dissolution medium. The temperature of the dissolution medium maintained at 37±0.5°C. An aliquot (5 ml) of dissolution medium was withdrawn at specific time intervals up to 12 h, filtered and suitably diluted before spectrophotometric analysis. Sink conditions were maintained by replenishing the medium with an equal amount (5 ml) of pH 6.8 phosphate buffer. The absorbance of the sample was measured at 357 nm by UV-Visible spectrophotometer [16]. The concentration of lornoxicam in test samples was calculated using calibration curve. Six samples were run for each formulation in pH 6.8 phosphate buffer.

### Table 1: Formula of lornoxicam microsponges

| Ingredients         | F1     | F2     | F3     | F4     | F5     | F6     | F7     | F8     | F9     | F10    | F11    | F12    |
|---------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Drug: polymer ratio | 1:1    | 1:0.75 | 1:0.5  | 1:0.5  | 1:0.5  | 1:0.5  | 1:1    | 1:0.75 | 1:0.5  | 1:0.5  | 1:0.5  | 1:0.5  |
| Lornoxicam (mg)     | 500    | 500    | 500    | 500    | 500    | 500    | 500    | 500    | 500    | 500    | 500    | 500    |
| Eudragit RS 100 (mg)| -      | -      | -      | -      | -      | -      | 500    | 325    | 250    | 250    | 250    | 250    |
| Eudragit RSPO (mg)  | 500    | 325    | 250    | 250    | 250    | -      | -      | -      | -      | -      | -      | -      |
| PEG plasticizer (ml)| 0.5    | 0.5    | 0.25   | 0.25   | 0.25   | 0.5    | 0.5    | 0.5    | 0.5    | 0.5    | 0.5    | 0.5    |
| PG plasticizer (ml)| -      | 0.25   | -      | 0.25   | -      | 0.25   | 0.25   | 0.5    | -      | 0.25   | -      | 0.5    |
| 0.75% w/v PVA solution (ml)| 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 |
| Ethanol (ml)        | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     |
| Dichloromethane (ml)| 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     | 10     |

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RESULTS AND DISCUSSION

Drug and excipient compatibility studies by FTIR
FTIR spectrum of lornoxicam was recorded, and spectral interpretation was done. The characteristic IR absorption peaks of lornoxicam: C=O amide stretching at 1641.30 cm⁻¹, N-H 2° amide stretching at 3122.62 cm⁻¹, C-Cl aromatic stretching at 670.15 cm⁻¹, Thiazide SO₂ at 1354.60 cm⁻¹, C-H aromatic stretching at 3068.73 cm⁻¹, and O-H stretching at 3393.35 cm⁻¹ were there in drug sample spectrum, which confirmed the purity of lornoxicam.

Compatibility study using FTIR was carried out to ensure any possible interaction between drug and Eudragit RS100 and Eudragit RSPO used. FTIR spectroscopic study results revealed no any new peak appearance or disappearance of existing peaks, discarding any chemical interaction probability among drug and polymers used. The characteristic C=O 1° amide stretching vibration at 1640.91 cm⁻¹, N-H 2° amide stretching at 3123.29, C-Cl aromatic stretching at 670.05 cm⁻¹, Thiazide SO₂ at 1354.71 cm⁻¹, C-H aromatic stretching at 3068.71 cm⁻¹, and O-H stretching at 3393.53 cm⁻¹ peaks of lornoxicam were present in the physical mixture of drug and polymers. Thus, FTIR spectroscopy results showed that lornoxicam was compatible with selected polymers (Fig. 2).

SEM
Morphology of prepared microsponges was discovered by SEM analysis. SEM image of optimized formulation (F12) of lornoxicam microsponges shown in Fig. 3. SEM results indicated that microsponges formed were highly porous, spherical in shape with rough surface texture and tiny particles are adhered on the porous outer surface. Pores were induced by diffusion of solvent from the surface of microsponges.

Percentage yield, percentage of unentrapped drug, percentage entrapment efficiency, and particle size studies of lornoxicam microsponges
The percentage yield of all formulations was carried out and was found within the range between 69.58% and 75.35%. Percentage of the unentrapped drug was found to be 24.06%–30.35%. Entrapment efficiency was found to be 62.24%–70.34%. The mean particle size of the microsponges significantly increased with increase in polymer concentration. The reason may be due to the viscosity of medium which increases as the polymer concentration increases. This may be resulting in the formation of larger particles. The particle size of prepared microsponges was observed in the range of 172.72–234.44 µm. The sizes of microsponges affect the encapsulation efficiency and the release rate of the drug. It was observed that as the ratio of drug to polymer was increased, the encapsulation efficiency was decreased. This could probably be due to the fact that in high drug to polymer ratio, the amount of polymer available per microsponge was comparatively less. Probably in high drug-polymer ratios less polymer amounts surround the drug and reducing the thickness of polymer wall and microsponges with smaller size were obtained (Table 2).

In vitro drug release
In vitro, drug release studies were performed in pH 6.8 phosphate buffer for 12 h. The cumulative percentage of drug release of prepared formulations was found to be in the following order: F12> F11> F6> F5> F10> F9> F4> F3> F8> F7> F2> F1. The percentage drug release of formulations F1, F2, F3, F4, F5, F6, F7, F8, F9, and F10 was found to be 61.21%, 65.61%, 80.68%, 83.25%, 92.57%, 95.09%, 73.46%, 86.65%, and 89.17%, in 12 h respectively. The percentage drug release of formulation F11 was found to be 95.47% in 10 h. Formulation F12 showed high release, 95.47% in 8 h. This could be due to smaller microsponges are formed at a lower polymer concentration and have a large surface area exposed to dissolution medium, giving rise to faster drug release. Hence, it is considered as an optimized formulation.

Results indicate that proportion of polymers in the formulation was the key factor governing the release of drug from microsponges. As the concentration of polymer increased, there was an increase in particle size and diffusional path length. This may decrease the overall drug release from the polymer matrix. Formulations comprised Eudragit RSPO in higher proportion exhibited much-retarded drug release as compared to formulations comprised Eudragit RS 100 in higher proportion. The drug release profile from microsponges for all the formulations is shown in Figs. 4-7 and Table 3.

Release of lornoxicam from the microsponges for the optimized formulation F12 was found to follow zero-order kinetics (correlation
coefficient, \( r^2 \) value 0.961). Higuchi plot showed an \( r^2 \) value of 0.971 for optimized formulation F12 suggesting that the diffusion plays an important role in the controlled release. The data were fitted to Korsmeyer–Peppas equation; the value of diffusion exponent “n” for optimized formulation F12 is 1.731, indicated that the drug release follows super case II diffusion.

**CONCLUSION**

Microsponges of lornoxicam were prepared by the quasi-emulsion solvent diffusion method using polymers such as Eudragit RS 100 and Eudragit RSPO. As the polymer concentration is increasing, the particle size of microsponges was increased, and the drug release was decreased. Among all the formulations, F12 shows better results, which are released more than 80% of the drug release within 8 h. Hence, lornoxicam loaded microsponges prepared by this quasi-emulsion solvent diffusion method are potential for prolong the release of the drug, which will be effective for osteoarthritis, rheumatoid arthritis, and acute lumbar sciatica therapy.

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AUTHOR’S CONTRIBUTIONS
The first author carried out the experimental part of the work. The second author guided and monitored the experimental design, data compilation, critical revision of the article, and corrected the manuscript and third author data analysis, interpretation, and drafting the article.

CONFLICTS OF INTEREST
All the authors hereby declare that there are no conflicts of interest.

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