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RESEARCH ARTICLE

# DEVELOPMENT AND EVALUATION OF TRANSDERMAL GEL OF LORNOXICAM

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## Abstract

**Objective:** Transdermal drug delivery systems deliver the drug through the skin at controlled rate to the systemic circulation. It maintains the blood concentration of the drug within the therapeutic system window ensuring that drug levels neither fall below the minimum effective concentration nor exceed the minimum toxic dose. The objective of the present work was to formulate transdermal gel of Lornoxicam. It is a COX-1 and COX-2 inhibitor used in the treatment of inflammation, pain and edema, rheumatoid arthritis.
**Methods:** Transdermal gel of Lornoxicam was formulated using triethanolamine as solvent, HPMC K100 and EC as polymers. Formulated gel was evaluated with respect to different physiochemical parameters such as pH, viscosity, spreadability. *In-vitro* release study was performed for 10 hrs. Selected formulation was subjected to stability testing at different temperatures.
**Results:** There was good homogeneity in all formulations and no lumps were present. The pH of the gel formulations was in the range of 6.77 to 7.14. Viscosity of various formulated gels was found in the range of 2176.5 to 3468.4 centipoises. The cumulative percent drug release after 10 hrs in between 50.3 to 82.11%. Accelerated stability studies for 12 weeks revealed that the transdermal gel formulation were stable at up to 45°C.
**Conclusion:** Study concludes Lornoxicam can be delivered in the form of transdermal gel in an efficient way. On the basis of drug content, particle size morphology, *in-vitro* release and stability studies, it can be concluded that formulation LTG4 was an optimum formulation.
**Keywords:** *In-vitro* release, Lornoxicam, pH, spreadability, stability studies, transdermal gel, viscosity.

## INTRODUCTION

Transdermal drug delivery system successfully delivers precise amount of drug through the skin for systemic action[1]. It has been accepted as potential non-invasive route of drug administration, with advantages of prolonged therapeutic effect, reduced side effects, improved bioavailability, better patient compliance and easy termination of drug therapy. Transdermal delivery offers a better route of delivery, it have better patient compliance by frequency of administration of the drug[2]. Skin is the outermost tissue of the human body. The skin basically consists of three anatomical layers epidermis, dermis, subcutaneous. For a drug penetrating across the skin the greatest resistance is met in the stratum corneum, viable epidermis and dermis[3]. The term 'gel' was introduced in the later 1800 to name some semisolid material according to pharmacological, rather than molecular criteria. Gels are transparent or translucent semisolid formulations and is colloid that is typically 99% weight liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from small amount of a gelating substances present. When dispersed in an appropriate solvent, gelling agents merge or entangle to form a three dimensional colloidal network structure, which limits fluid by entrapment and immobilization of the solvent molecules[4]. Transdermal application of gels at pathological sites offer great advantage in a faster release of drug directly to the site of action, independent of water solubility of drug as compared to creams and ointments[5]. Lornoxicam is a potent non-steroidal anti-inflammatory drug, used for the variety of inflammatory conditions. The mechanism of action includes inhibition of prostaglandin synthesis through the inhibition of cyclooxygenase enzymes[6]. Lornoxicam is one of the newer and potent NSAIDs that inhibit the

prostaglandin synthetase cyclo-oxygenase and act as useful anti-inflammatory agent to control rheumatoid arthritis and other related conditions[7]. Lornoxicam was selected as a candidate for the drug delivery because of many drawbacks like non-compliance due to frequent dosing and various side effects like gastro-intestinal irritation and ulcerogenicity. Additionally, Lornoxicam is having molecular weight, partition coefficient, and daily dose which make it an ideal candidate for transdermal drug delivery systems[8].

To avoid invasive drug therapy such as injections and to eliminate frequent dosing regimen with oral administration, a transdermal drug delivery system of Lornoxicam has been studied as an alternative dosage form.

## MATERIALS AND METHODS

Lornoxicam was obtained from Olex pharmaceuticals, Nigeria as gift sample. HPMC K100 was obtained from Juneng Nigeria Ltd and ethyl cellulose from Neildek Trading company, Aba. All other chemicals were of analytical grade.

**Development of Lornoxicam transdermal gel**

Different Lornoxicam transdermal gel formulations were prepared by adding different ingredients as shown in Table 1 by means of a magnetic stirrer with continuous mixing until a homogenous gel was formed. The solution was then neutralized and made viscous by addition of triethanolamine. Final weight was made up to 100 g with distilled water. The gel was set aside for few minutes until the bubbles disappeared. All the samples were allowed to equilibrate for at least 24 hours at room temperature prior to performing rheological measurements. The gels were kept in plastic well-closed containers and stored at room temperature until the time of analysis[9].

**Evaluation of formulations**

**Physical appearance and homogeneity**

The physical appearance and homogeneity of the prepared Lornoxicam transdermal gels were tested by visual observations after the gels have been set in the container. They were tested for their appearance and presence of any aggregates[10].

**Table 1: Compositions of the Lornoxicam transdermal gel formulations.**

| S. N. | Ingredients | LTG1 | LTG2 | LTG3 | LTG4 |
|---|---|---|---|---|---|
| 1. | Lornoxicam (gms) | 0.06 | 0.06 | 0.06 | 0.06 |
| 2. | HPMC K100 | 0.3 | - | 0.6 | - |
| 3. | EC | - | 0.3 | - | 0.6 |
| 4. | Methyl Paraben (gms) | 0.75 | 0.75 | 0.75 | 0.75 |
| 5. | Triethanolamine (ml) | 0.3 | 0.3 | 0.3 | 0.3 |

**Clarity**

The clarity of various formulations was determined by visual inspection under black and white background and it was graded as follows; turbid: +, clear: ++, very clear (glassy):+++[11].

**Drug content**

A specific quantity (100mg) of Lornoxicam transdermal gel of different formulations was taken and dissolved in 100ml of phosphate buffer of pH 7.4. The volumetric flask containing gel solution was shaken for 2hr on mechanical shaker in order to get complete solubility of drug. This solution was filtered and estimated spectrophotometrically at 380 nm using phosphate buffer (pH 7.4) as blank[12].

**Viscosity study**

The viscosity of the Lornoxicam transdermal gel formulation was determined using a Ostwald viscometer. The gel formulations were placed in the sample holder of the viscometer and allowed to settle for 5 min and the viscosity measured at a rotating speed of 50 rpm at room temperature (25–27$^0$C)[13].

**Measurement of pH**

The pH of various gel formulations was determined by using digital pH meter. One gram of Lornoxicam transdermal gel formulation was dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average values were calculated[14].

**Extrudability**

The extrusion of the gel from the tube is an important during its application and in patient acceptance. This study is useful in explaining whether the gel is removing from the collapsible tube during application in proper manner or not. Gels with high consistency may not extrude from the tube whereas, low viscous gels may flow quickly, and hence suitable consistency is required in order to extrude the gel from the tube. The formulations were filled into collapsible aluminum tubes. The tubes were pressed to extrude the 0.5 cm ribbon of the gel in 10 second and the extrudability of formulations was checked[15].

More quantity extruded better was extrudability. The extrudability was then calculated by using the following formula:

$$\text{Extrudability} = \frac{\text{Applied weight to extrude gel from tube (in gm)}}{\text{Area}}$$

***In-vitro* drug release**

The *in vitro* drug release from different Lornoxicam transdermal gel formulations was studied across cellophane membranes using modified Keshery Chien diffusion cell. The receptor compartment was filled with the mixture of phosphate buffer of pH 7.4 and polyethylene glycol 400 and maintained at 37±0.5$^o$C with constant magnetic stirring. Accurately weighed quantity of gel was placed on the donor compartment. The samples (1ml) was collected from the receptor compartment at predetermined time interval and replaced by equal volume of fresh receptor solution to maintain constant volume allowing sink condition throughout the experiment. The amounts of drug in the sample were assayed spectrometrically at 322 nm against appropriate blank[16].

**Stability study**

Stability studies carried out by storing the prepared transdermal gel of batch TG12 at various temperature conditions like refrigeration (2-8$^{o}$C) room temperature (25±0.5$^{o}$C) and elevated temperature (45±0.5$^{o}$C) for a period of 12 weeks. Drug content and variation in the average vesicle diameter were periodically monitored. ICH (International Conference on Harmonisation) guidelines were followed[17].

**Statistical analysis**

Experimental results were expressed as mean±SD. Student's *t*-test and one-way analysis of variance (ANOVA) were applied to check significant differences in drug release from different formulations. Differences were considered to be statistically significant at $p<0.05$.

## RESULTS AND DISCUSSION

Four transdermal gel formulations of Lornoxicam were prepared by using different polymers i.e. HPMC, EC in different ratio. Stability of the transdermal gel is crucial both during storage and *in-vivo* application. The amount of drug retained within the vesicles under defined conditions ultimately governs the shelf life of the drug. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under influence of a variety of environmental factors such as temperature, humidity and light, and enables recommended storage conditions. Accelerated stability studies for 12 weeks revealed that the transdermal gel formulation were stable at up to 45$^{o}$C. The results showed that transdermal gel formulation was quite stable at refrigeration and room temperatures as not much leakage of drug was found at these temperatures. Therefore, the selected transdermal gel formulations can be stored at either refrigeration or room temperature. The pure drug shows sensitivity to light and moisture.

**Table 2: Properties of Lornoxicam transdermal gel formulations.**

| Formulation Code | Homogeneity | pH[a] | Viscosity[a] (Centipoise) | % Drug Content[a] | Extrudability |
|---|---|---|---|---|---|
| LTG1 | +++ | 6.77±0.33 | 3290.5±0.14 | 97.28±0.58 | ++ |
| LTG2 | ++ | 7.14±0.22 | 2176.5±0.42 | 98.54±0.74 | + |
| LTG3 | + | 6.93±0.15 | 3463.7±0.15 | 98.26±0.32 | + |
| LTG4 | ++ | 6.84±0.45 | 3468.4±0.45 | 98.72±0.47 | ++ |

a- Average ±SD of three determination has been reported, +: Satisfactory, ++: Good, +++: Excellent

The physical appearance and homogeneity of the prepared Lornoxicam transdermal gels were tested by visual observations after the gels have been set in the container.

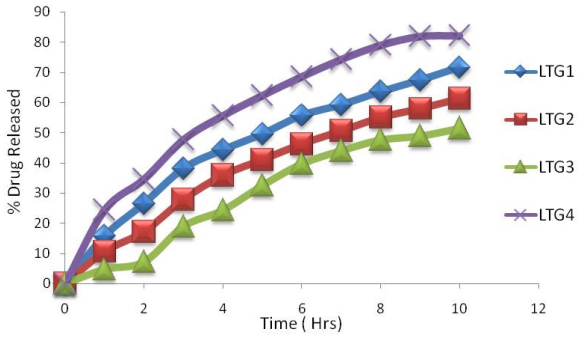


**Figure 1: Percentage of drug released from Lornoxicam transdermal gel formulations.**

The drug content of the gel formulations shows content uniformity in all formulations. All transdermal gel formulations were found to be transparent and were free from presence of particles. The extrudability of formulations was found to be satisfactory and good. The *in-vitro* permeation of Lornoxicam transdermal gels formulation was studied using locally fabricated Franz diffusion cell. The cumulative percent drug release after 10 hrs in between 50.3 to 82.11%. Rapid drug leakage was observed during the initial phase. However, after that a slow release occurred. It was also observed that the drug release generally decreased as the polymer ratio increased. The release of the drug was retarded due to the hydrophobic and insoluble nature of the polymers used. There was good homogeneity in all formulations and no lumps were present. The pH of the gel formulations was in the range of 6.77 to 7.14, which lies in the normal pH range of the skin and would not produce any skin irritation. Viscosity of various formulated gels was found in the range of 2176.5 to 3468.4 centipoises.


**Figure 2: Stability study of Lornoxicam transdermal gel of batch LTG4 at different temperature.**

## CONCLUSIONS

At present scenario transdermal application of gels at pathological sites offer great advantage in a faster release of drug directly to the site of action, independent of water solubility of drug as compared to creams and ointments. The present study has been a satisfactory attempt to formulate Lornoxicam

transdermal gel formulations with a view of improving its oral bioavailability and giving a prolonged release of drug. It has been observed that optimized batch produces the gel with good consistency, homogeneity, spreadibility. All transdermal gel formulations were found to be transparent and were free from presence of particles. The stability study of the optimized formulation showed satisfactory characteristics without being drastically influenced. On basis of drug content, particle size morphology, *in-vitro* release and stability studies, it can be concluded that formulation LTG4 was an optimum formulation. However there is need *in-vivo* study to justify the development of transdermal gel of Lornoxicam.

## AUTHOR'S CONTRIBUTION

**Umar S:** writing original draft, conceptualization, methodology, investigation. **Onyekachi MK:** writing, review, and editing, supervision, resources.

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## DATA AVAILABILITY

The data supporting the findings of this study are not currently available in a public repository but can be made available upon request to the corresponding author.

## CONFLICT OF INTERESTS

None to declare.

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