Available online on 15.3.2017 at <http://ujpr.org>
Universal Journal of Pharmaceutical Research
 An International Peer Reviewed Journal

Open access to Pharmaceutical research
 This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial Share Alike 4.0 License which permits unrestricted non commercial use, provided the original work is properly cited

Volume 2, Issue 1, 2017

Open Access

RESEARCH ARTICLE

DEVELOPMENT AND EVALUATION OF TRANSDERMAL GEL OF LORNOXICAM

Saifullahi Umar¹, Moh Kingsley Onyekachi²

¹Department of Pharmacognosy and Drug Development, Bayero University Kano, Nigeria.

²Ahmadu Bello University, Zaria, Nigeria.

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 physicochemical 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 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.

Article Info: Received 7 January 2017; Revised 4 February; Accepted 6 March, Available online 15 March 2017

Cite this article-

Umar S, Onyekachi MK. Development and evaluation of transdermal gel of Lornoxicam. Universal Journal of Pharmaceutical Research 2017; 2(1): 15-18

DOI: <http://doi.org/10.22270/ujpr.v2i1.R4>

Address for Correspondence:

Saifullahi Umar, Department of Pharmacognosy and Drug Development, Bayero University Kano, Nigeria, E-mail: saifullahiumar.su@gmail.com

INTRODUCTION

Transdermal drug delivery system successfully delivers precise amount of drug through the skin for systemic action¹. 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 drug². 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 dermis³. 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 molecules⁴. 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 ointments⁵. 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 enzymes⁶. 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 conditions⁷. 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 systems⁸.

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

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

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 aggregates¹⁰.

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 blank¹².

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°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 calculated¹⁴.

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 analysis⁹.

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 checked¹⁵.

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°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 spectrophotometrically at 322 nm against appropriate blank¹⁶.

Stability study

Stability studies carried out by storing the prepared transdermal gel of batch TG12 at various temperature conditions like refrigeration (2-8°C) room temperature (25±0.5°C) and elevated temperature (45±0.5°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 followed¹⁷.

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°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.

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

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. 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.

CONCLUSION

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, spreadability. 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

The manuscript was carried out, written, and approved in collaboration with all authors.

ACKNOWLEDGEMENTS

The authors extend their thanks and appreciation to the Bayero University Kano, Nigeria to provide necessary facilities for this work.

CONFLICT OF INTERESTS

No conflict of interests is associated with this work.

REFERENCES

1. Kavitha K, More Mangesh R. Design and evaluation of transdermal films of Lornoxicam. *Int J of Pharm and Bio Sci* 2011; 2(2):54-62. <https://doi.org/10.1.1.641.4577>
2. Venna D. Formulation and evaluation of transdermal patch of an Antihypertensive drug. *As J Pharm Life Sci* 2013; 3(1):22-31.
3. Murthy TEG, Kishore VS. Effect of casting solvent on permeability of antihypertensive drugs through ethyl cellulose films. *J Scient Ind Res* 2008; 67:147-150.
4. Silvia S, Guterres M, Alves P. Human skin penetration and distribution of Nimesulide from hydrophilic gels containing nanocarriers. *Int J Pharmaceutics* 2007; 341: 215-220. <https://doi.org/10.1016/j.ijpharm.2007.03.031>
5. Gohel MC, Jani GK, Amin A, Bajaj S, Dave BS. Application of simplex lattice design for the development of transdermal gels of diclofenac sodium. *J Pharm Sci* 2000; 62(2): 108-14.
6. Balfour JA, Fitton A, Barradell LB. Lornoxicam. A review of its pharmacology and therapeutic potential in the management of painful and inflammatory conditions. *Drugs* 1996; 51(4): 639-57. <https://doi.org/10.2165/00003495-199651040-00008>
7. Frizziero L, Focherini MC, Valentini M, Reta M, Rocchi P. Long term study on the efficacy and safety of lornoxicam in rheumatoid arthritis. *Minerva Med* 2002; 93(4): 315-20. <https://doi.org/10.1186/s13075-019-2046-0>
8. Stationwala R, Patidar A, Main P, Choukse R Agrawal S. Transdermal delivery of lornoxicam from pluronic lecithin organogel. *Int J of Chem Pharm Sci* 2011; 2 (2): 32– 37.
9. Dash S, Murthy PM, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. *Acta Poloniae Pharmaceutica-Drug Research* 2010; 67 suppl 3: 217-223.
10. Herkenne C. Effect of propylene glycol on ibuprofen absorption into human skin *in vivo*. *J Pharm Sci* 2008; 97: 185-197. <https://doi.org/10.1002/jps.20829>
11. Bradley JD, Brandt KD, Katz BP, Kalasinski LA, Ryan SI. Comparison of an anti inflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee. *New Engl J Med* 1991; 325: 87-91. <https://doi.org/10.1056/NEJM199107113250203>
12. Nair R, Sevukarajan M, Mohammed B and Kumar J. Formulation of microemulsion based vaginal gel- *in vitro* and *in vivo* evaluation. *Der Pharmacia Lettre* 2010; 2 (6): 99-105.
13. Somashekhara CN, Gowthamarajan K, Gowda DV, Rajesh N, Siddaramaiah. Formulation and evaluation of ketoprofen loaded transdermal drug delivery. *Int J Pharma Res* 2009 1, 40-47.
14. Silvia S, Marta P. Alves. Human skin penetration and distribution of Nimesulide from hydrophilic gels containing nanocarriers. *Int J Pharmaceutics* 2007; 341: 215-220. <https://doi.org/10.1016/j.ijpharm.2007.03.031>
15. Sanjay, Jain BD, Padsalg A, Patel K, Mokale V, Formulation, development and evaluation of Fluconazole gel in various polymer bases. *Asi J Pharm* 2007; 1:63-68.
16. Cordero JA, Alarcon L, Escribano E, Obach R, Domenech J. A comparative study of the transdermal penetration of a series of nonsteroidal antiinflammatory drugs. *J Pharm Sci* 1997; 86(4), 503-508. <https://doi.org/10.1021/js950346l>
17. Finnin BC, Morgan TM. Transdermal penetration: application, limitation and potential. *J Pharm Sci* 1999; 88: 955–958.