FORMULATION AND EVALUATION OF PLURONIC LECITHIN ORGANOGEL OF FLURIBRUFEN

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Abstract

Fluribrufen, organogel were prepared for transdermal drug delivery system. The purpose of this research is to formulate and evaluate the suitability of pluronic lecithin organogels containing flurbiprofen for topical application. Four formulations were developed using flurbiprofen, lecithin, Pluronic F127, isopropyl palmitate, water, sorbic acid and potassium sorbate were coded as FL1, FL2, FL3 and FL4. All the formulations carried 30% w/w of lecithin phase and 70% w/w of Pluronic phase. The formulated organogels were evaluated for appearance and feel psychorheologically, in vitro diffusion study, drug content, viscosity and pH. Release of flurbiprofen from all formulations was monitored via dialysis membrane-70 and Wistar rat skin as a semipermeable membrane into phosphate buffer saline (0.2 M, pH 7.4) using Keshary-Chien diffusion cell. The viscosities of different formulations were determined by using Brookfield Viscometer at 25°. An attempt has been made to explore the potential of pluronic lecithin organogels for topical delivery of flurbiprofen. It was observed that the system with optimized concentration of plasticizers was a promising controlled release transdermal drug delivery system for Fluribrufen.

Keywords: Fluribrufen, organogel, FTIR, Drug release

INTRODUCTION:

Organogels:

Organogels are semi-solid systems, in which an organic liquid phase is immobilized by a three-dimensional network composed of self assembled, intertwined gelator fibers. Despite their majoritarily liquid composition, these systems demonstrate the appearance and rheological behaviour of solids. Organogels can be distinguished from hydrogels by their predominantly organic continuous phase and can then be further subdivided based on the nature of the gelling molecule: polymeric or low molecular weight (LMW) organogelators.

Lecithin Organogel:

The topical delivery has been attempted and made successful using several lipid-based systems viz vesicular systems, lipid microspheres, lipid nanoparticles, lipid-microemulsions, and polymeric gels. In a recent development, phospholipids in conjunction with some other additives have been shown to provide a very promising topical drug delivery vehicle known as lecithin organogels (LOs). LOs are thermodynamically stable, clear, viscoelastic, biocompatible, and isotropic gels composed of phospholipids (lecithin), appropriate organic solvent, and a polar solvent. LOs, the jelly-like phases, consist of a 3-dimensional network of entangled reverse cylindrical (polymer-like) micelles, which immobilizes the continuous or macroscopic external organic phase, thus turning a liquid into a gel. These systems are currently of interest to the pharmaceutical scientist because of their structural and functional benefits. Several therapeutic agents have been formulated as LOs for their facilitated transport through topical route (for dermal or transdermal effect), with some very encouraging results. The improved topical drug delivery has mainly been attributed to the biphasic drug solubility, the desired drug partitioning, and the modification of skin barrier function by the organogel components. Being thermodynamically stable, LOs are prepared by spontaneous emulsification and therefore possess prolonged shelf life. The utility of this novel matrix as a topical vehicle has further increased owing to its very low skin irritancy potential.

Materials and Methods:

Materials:

Lornoxicam,pH7.4buffer,potassiumdihydrogenphosphate, sodiumhydroxide,disodiumhydrogen phosphate, sodium hydroxide, n-octanol, Pluronic F-127,

ecithin, isopropylmyristate, Sodiumsorbate, Sodium

Benzoate, distilledwater, ethanol,methanol, and acetone.

Methods: Preformulationstudies

Determinationofsolubility

Qualitativesolubility

Qualitativesolubilityanalysisofdrugsweredonebydissolving5mgofdrugin 5 ml of distilled water and different solvents such as HCl (0.1N), NaOH (0.05N), Saline phosphate buffer (pH 7.4), Phosphate buffer(pH 9), Phosphate buffer(pH 4), phosphate buffer (pH 2), ethanol, methanol, acetone and chloroform wereused to determinethesolubilityofdrug.

Table 5 Dataforstandardcurveof flurbiprofeninethanol

S.No.	Concentration(µg/ ml)	Absorbance
1.	0	0
2.	2	0.098
3.	4	0.185
4.	6	0.368
5.	8	0.467
6.	10	0.599
7.	12	0.743
8.	14	0.879

Fig 2.Standardcurveofflurbiprofen in ethanol

7. EVALUATION

7.1 Methodsforevaluationstudiesfortransdermalgel

1) Measurementof pH

The pH of various gel formulations was determined by using digital pH meter.The measurement of pH of each formulation was done in triplicates and averagevalueswerecalculated.

2) Rheological studiesa.)Viscositystudy

Brookfielddigitalviscometer(modelDV-I+,BrookfieldEngineeringLaboratory, INC., USA) was used to measure the viscosity (in poise) of the preparedgelformulations.Thespindle(T-D) was rotated at 10rpm.
Theviscosityofformulationswasmorecorrectwhichwasnear to100%torque.Samplesweremeasured at 30 ± 1° C. Reading was detected 30 sec after measurement was made,whenthelevel was stabilized.

b.)Spreadability

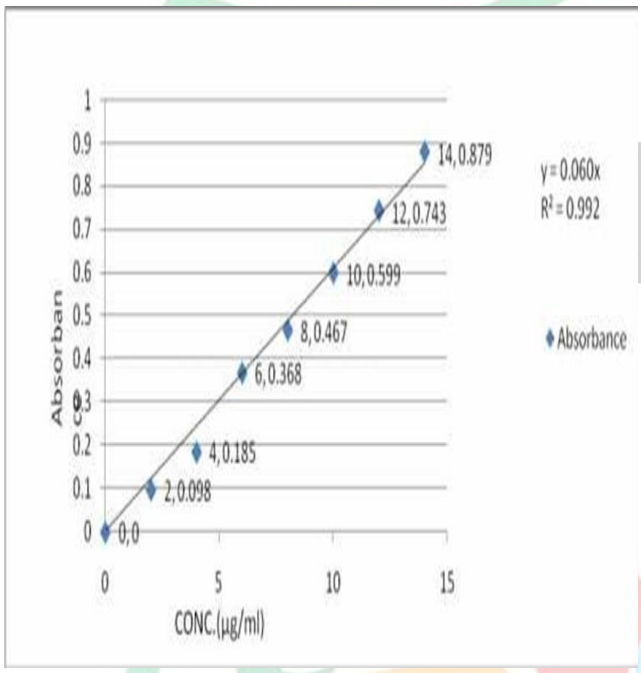
Concentric circles of different radii were drawn on a graph paper and a glass plateof 100 ± 5 g was fixed on it. Weighed amount of gel (1g) was transferred to thecentre of the plate and allowed to spread over an area of 2 cm diameter. The otherglass plate of 100 ± 5 g was placed gently on the spreaded gel. Again the gel wasallowedtospreadandthespreaddiameterwasrecordedafter1minute.Thensubsequent glass plates were added one by one and the spread diameter of the gel wasrecordedafter1 minuteofeachaddition.

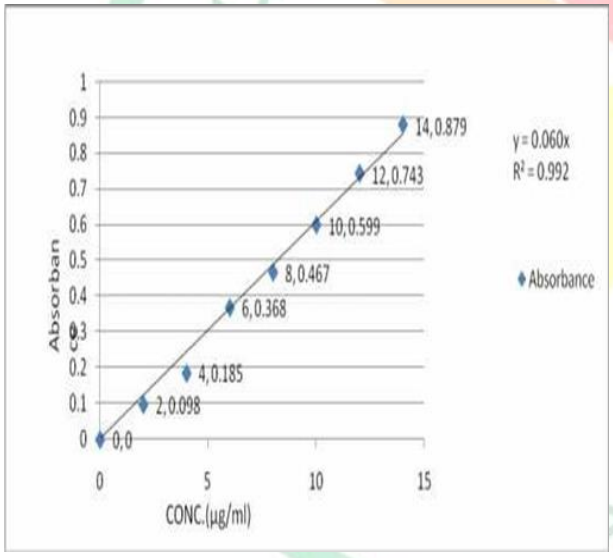
3) Drug content

1 g of the prepared gel was dissolved in 100ml of ethanol. 1 ml of the solutionprepared was further diluted to 100ml. Then absorbance was measured at λ max. Drugcontent was calculated using the equation, which was obtained by linear regressionanalysisofcalibration curveofdrugs.

4) Invitro Diffusion studies

Phosphate buffer of pH 7.4 was used for in vitro release as a receptor medium. Theegg membrane was used in franz-diffusion cell. The 1g of gel sample was applied onthemembrane and thenfixed inbetweendonorandreceptorcompartmentofdiffusion





cell.Thereceptorcompartmentcontain edphosphatebufferofpH7.4.Thetempe rature of diffusion medium was thermostatically controlled at 37±1ºC and themedium was stirred by magnetic stirrer at 100 rpm. The sample at predeterminedintervals were withdrawn and replaced by equal volume of fresh fluid. The samples withdrawn were spectrophotometrically estimated using phosphate buffer pH as 7.4 ablankat λmax.

Stability off ormulations

The optimized formulations from all the ten formulations were selected andsubjected to the stability testing for 90 days. Formulations were kept at 40^0C, 25^0C &roomtemperaturefor90days&evaluatedforfollowingparameters:

i) Physicalstability: Thegelformulationswereevaluatedintermsofphysicalcharacter like phase separation & rheological parameters. Physical stability testingwasdonebyvisual inspection oftheformulationat 15 days interval for3 months.

ii) Chemicalstability: Thegelformulationswereevaluatedfor%drugcontent.The

%drugcontentof the formulations weredetermined at15 daysinterval for 3 months.

From the Evaluation studies results reported in chapter 7, two formulationswere selected as optimized PLO formulations. They were than subjected to 90 daysstability studies. The optimized gel formulations were evaluated in terms of physicalcharacter & chemical character like phase separation, rheological parameters, pH & %drugcontent.

B) Flurbiprofen

1) Measurementof pH

The pH of various gel formulations were determined by using digital pH meterasmentioned. TheResults areshown in table7.4.

Table 10pH,viscositiyand%drugcontentofdifferentformulation of

S.No.	Formulations	pH	Viscosity(cps)	% Drugcontent
	F1	5.46	2982	94.66
	F2	6.01	3013	97.48
	F3	6.04	3145	97.25
	F4	5.89	3144	96.51
	F5	5.94	3098	95.98
	F6	6.03	3318	96.22
	F7	6.03	3372	97.67
	F8	5.86	3460	96.87

ThepHofskinisaround6

7.Theabovetable7.4showsthatpHofall theformulations were found to be in the range of 5.4 to 6.2, which is around to the pH ofskin.It shows that formulationsarefit fortransdermal use.

The viscosity of all the formulation was found to be in the range of 2959 to3460 poise given in above table 7.4. The increase in viscosity with increase in lecithinconcentrationis dueto formation ofcomplexnetwork.

All the gel formulations showed drug content in the range of 93 to 98% asgiven in above Table 7.4 indicating uniform distribution of drug throughout the baseand high uptake capacity of drug in the base. Results also reveal that PLO gels havehigh%drugcontent.

Conclusion:

The transdermal anti-inflammatory gels containing Flurbiprofen and different polymers(lecithin and pluronic), were prepared and evaluated for different parameters.. All eight formulations were evaluated for In-vitro release study. Study was carried for 8 hrs for all formulation and results reported shows that, the Formulation F2 and F4 shows good cumulative % Release profile of Flurbiprofen in 8 hr. But the linear curve shown was obtained from F2(3% lecithin) formulation. This indicates that PLO Gel has increased drug permeation across the membrane.

This study reveals that 3% of lecithin would enhance the penetration of drug (Flurbiprofen). The formulation of organogel using 3% lecithin and 20% pluronic andFlurbiprofen is favorable for use as a transdermal delivery, as it provides optimum drug penetration.

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