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Formulation and Evaluation of Lornoxicam Matrix Based Topical Gel

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ABSTRACT

The formulation and evaluation of pluronic lecithin organogel containing nonsteroidal anti-inflammatory drugs for topical usage. The Four pluronic lecithin organogel formulations were developed and evaluated. All the formulated organogel were evaluated with different parameters like such as the appearance of gel, *in-vitro* diffusion study, drug content, viscosity, and pH. In general, the organogel was thermodynamically stable and has been explored as a matrix system for the delivery of bioactive agents. In the current study, many were attempts have made to estimate the properties of organogels, various types of organogelators, and some applications of the organogels in a controlled delivery.

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INTRODUCTION

In general, a topical gel is a gel substance, which often contains some form of medicine and is applied to the skin or the mucus membranes. Many people prefer gel forms when they are applying topical medications, especially over lotions or ointments. In most cases a topical gel is clear and it tends to be more readily absorbed by the skin than is a lotion or ointment. Methods of Preparation of gels include fusion method, cold method, and dispersion method.

Gel:

A gel is defined as "a semisolid system consisting of dispersion made up of either small inorganic particles or large organic molecules enclosing and interpenetrated by liquid". Gels are also defined as a semi-rigid system in which the movement of dispersing medium is restricted by an interlacing three-dimensional network of particles or solvated macromolecules of the dispersed phase. A high degree of physical or chemical cross-linking may be involved. A gel may consist of twisted matted strands often wound together by stronger types of Van der Waals forces to form crystalline and amorphous regions throughout the system.33

Characteristics of Gel:

The gel should exhibit little viscosity change under the temperature variation of normal use and storage. A topical gel should not be taken to a higher concentration of gel former may produce a gel difficult to dispense or apply.

Swelling can be looked at as the initial phase of dissolution, solvent penetrates the gel matrix, gel interactions are replaced by gel solvent interactions. Limited swelling is usually the result of some degree of crosslinking in the gel matrix that prevents total dissolution, such gels swell when the solvent mixture possesses a solubility parameter comparable to that of the gallant.34

Many gel systems undergo contraction upon standing. The interstitial liquid is expressed; collecting at the surface of the gel this process is referred to as "syneresis". The mechanism of contraction has been related to the relaxation of the elastic stresses developed during the setting of the gel. As these stresses are relieved, the interstitial space available for the solvent is reduced, forcing the expression of fluid. 34

Inorganic particles are capable of gelling a vehicle due to the formation of a "house of cards" structure. Clay such as bentonite or kaolin possesses a lamellar structure that can be extensively hydrated. The flat surfaces of bentonite particles are negatively charged while the edges are positively charged. The attraction of phase to the edge of these colloidal lamellae creates a three-dimensional network of particles throughout the liquid, immobilizing the solvent.

Molecular weight is an important consideration in gel formation, very long polymers can entangle to a greater extent, leading to higher viscosity at a given concentration. Thus, a lower concentration of higher molecular weight polymer may be required to gel the solvent. A solution of gelling agent and dispersions of flocculated solids are typically pseudoplastic, exhibiting a non-Newtonian flow behavior characterized by a decreasing viscosity with increasing shear rate.35

Types of Gels:

Single-phase gels are the gels in which macromolecules are uniformly distributed throughout the liquid with no apparent boundaries between the dispersed macromolecules and the liquid. Two-phase gels are the gels in which the gel consists of floccules of small distinct particles, a two-phase gel system often referred to as Magma.

Classification of Gels:

Hydrogels-Hydrogel (also called Aqua gel) is a network of polymer chains that are water-insoluble, sometimes found as a colloidal gel in which water is the dispersion medium. Common ingredients are e.g. polyvinyl alcohol, sodium polyacrylate, acrylate polymers, and copolymers with an abundance of hydrophilic groups. **Organogels**-An organogel is a non-crystalline, non-glassy thermoreversible (thermoplastic) solid material composed of a liquid organic phase entrapped in a three-dimensionally cross-linked network. The liquid can be for example an organic solvent, mineral oil, or vegetable oil. The solubility and particle dimensions of the structurant are important characteristics for the elastic properties and firmness of the organogel. Often, these systems are based on the self-assembly of the structurant molecules. **Xerogels**-A xerogel is a solid formed from a gel by drying with unhindered shrinkage. Xerogels usually retain high porosity (25%) and enormous surface area (150–900 m^2/g), along with a very small pore size (1-10 nm). When solvent removal

occurs under hypercritical (supercritical) conditions, the network does not shrink and a highly porous, low-density material is known as an aerogel is produced. Heat treatment of a xerogel at elevated temperature produces viscous sintering (shrinkage of the xerogel due to a small amount of viscous flow) and effectively transforms the porous gel into a dense glass.

General Method of Preparation for Gel:

To prepare uniform gels it is necessary to disperse the gelling agent in such a manner that it does not form clumps upon the addition of water. Some technique intends small quantity of dispersing agents such as alcohol or glycerine, propyl gallate, and hydroxypropyl cellulose may be used to enhance gel formation and triturate. Because of the high attraction between the disperse phase and the aqueous phase gels, these preparations remain fairly uniform.37

Another technique is to sprinkle the gelling agent into a vortex of stirred water. If there are several other powders the gelling powder is followed by the addition of water shaking material in a bottle, mixing in a mortar with a pestle, or using a mechanical stirrer. Appropriate preservative depending upon use and the gelling agent; include the paraben at about 0.2%, benzoic acid 0.2%, and chlorocresol 0.1%.38

Stability of Gels:

A gel formulation that is unstable or not suitable for marketing under normal circumstances would exhibit some irreversible change in its rheological properties of sufficient magnitude to cause it to be unacceptable in final use. Examples of unstable gels include gels that “set-up” during storage and can no longer be expressed from a tube, gels that undergo a separation of phases either of the liquid (as in synergetic) or of the solid (as in particle sedimentation); and gels that suffer a progressive loss of consistency, of changing from semisolid to viscous liquids.39

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 behavior 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. Formation of a three-dimensional network of reverse cylindrical micelles in lecithin organogel, involving hydrogen bonding between lecithin and polar solvent molecules.

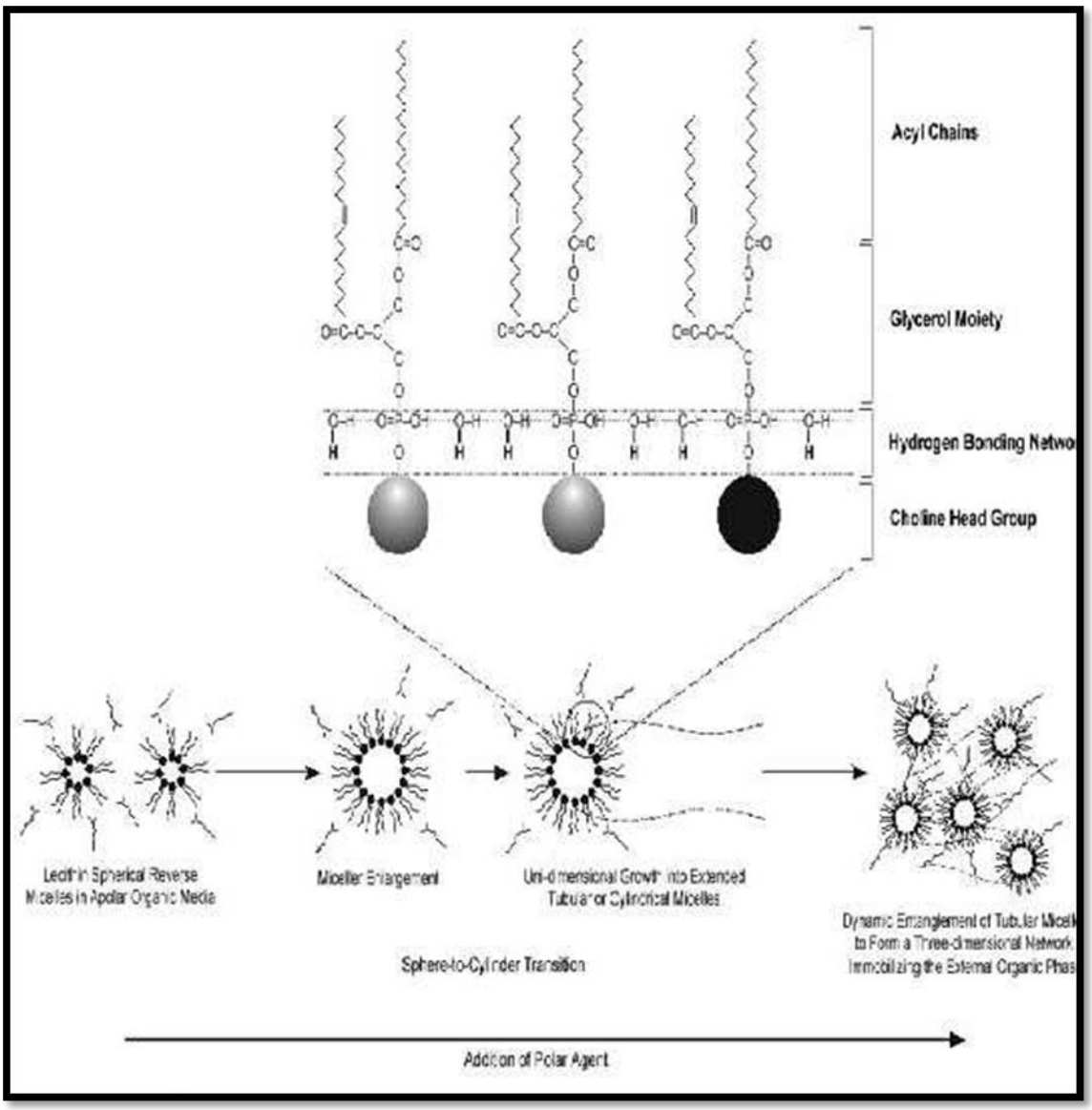

Figure No. 1: Schematic diagram of Formation of Organogel

Criteria for Selection of Drug:

A wide range of drugs has been incorporated within PLO for transdermal delivery. The skin is, however, a good barrier to drug permeation, and drug flux is known below. Drug absorption following application to the skin is so low that only a few drugs have been

formulated for transdermal delivery.

An ideal drug for transdermal delivery is:

- A potent chemical with a daily dose of a few milligrams.
- A small molecule.
- One that has a high lipid solubility and reasonable water solubility.
- Non-irritating and non-sensitizing to the skin.
- Drugs having a short half-life.
- The drugs should not be metabolized in the skin itself while permeating through it.

Topical and Dermal applications

Analgesic/Anti-inflammatory drugs

Authors have suggested PF-127 gels as potential topical drug delivery systems having advantages over traditional bases in terms of ease of application, and drug release characteristics. Interestingly, many studies have focused on the development of topical/dermal formulations containing analgesic or anti-inflammatory drugs because the possibility of delivering these drugs through the skin for local pain and inflammations at low doses is attractive. However, in many cases, penetration enhancers may be present in the topical/dermal formulations because otherwise, only small amounts of drugs pass through the skin. Thermally reversible gels of PF-127 as vehicles for the percutaneous administration of indomethacin.

MATERIALS AND METHODS

Materials

Chemicals: Lornoxicam, Flurbiprofen, Aceclofenac, Piroxicam, pH 7.4 buffer, potassium dihydrogen phosphate, sodium hydroxide, disodium hydrogen phosphate, sodium hydroxide, n-octanol, Pluronic F-127, lecithin, isopropyl myristate, Sodium sorbate, Sodium Benzoate, distilled water, ethanol, methanol, and acetone.

Preparation of standard curve

A. Lornoxicam

a. Standard curve of lornoxicam in 0.05 N NaOH

A standard stock solution of Lornoxicam was prepared by dissolving 100 mg drug in 100 ml 0.05 N NaOH (i.e.1000µg/ml). An aliquot of this solution is further prepared by taking10 ml of the above solution and diluting it up to100 ml (i.e.100µg/ml). From the above solution, further dilutions are prepared in the range of 5-35 µg/ml. Absorbances were taken on a UV spectrophotometer at 376 nm against 0.05 N NaOH as a blank. From these absorbances, the standard curve is plotted. Standard curve equation and regression value are obtained. The absorptivity coefficient of the drug at desired wavelengths was determined.

b. Standard curve of lornoxicam in 7.4 PBS

A standard stock solution of Lornoxicam was prepared by dissolving 10 mg drug in 10 ml 7.4 PBS (i.e.1000 µg/ml) containing 12 mg of Tromethamine. This solution was then sonicated till the complete dissolution of the drug. An aliquot of this solution is further prepared by taking 10 ml of the above solution and diluting it up to 100 ml (i.e.100 µg/ml). From the above solution, further dilutions are prepared in the range of 4-24 µg/ml. Absorbances were taken in a UV spectrophotometer at 376 nm against 7.4 PBS as a blank. From these absorbances, the standard curve is plotted. Standard curve equation and regression value are obtained. The absorptivity coefficient of the drug at desired wavelengths was determined.

B. Flurbiprofen

a. Standard curve of Flurbiprofen in ethanol

100 mg of Flurbiprofen was accurately weighed and dissolved in ethanol in a 100 ml volumetric flask and the volume was made up to the mark with ethanol. The above-prepared solution of Flurbiprofen was subsequently diluted with ethanol to get 2, 4, 6, 8, 10, 12 µg per ml of the final solution. Then the absorbance was measured by spectrophotometer at 248 nm using ethanol as blank. An average of triplicate readings was taken.

b. Standard curve of flurbiprofen in 7.4 PBS

A standard stock solution of Flurbiprofen was prepared by dissolving 10 mg drug in 10 ml

7.4 PBS (i.e.1000 µg/ml). The aliquot of 10 ml solution is further taking 10 ml of diluted up to 100 ml (i.e. 100 µg/ml). The above solution is prepared in the range of 10-90 µg/ml. Absorbances were taken on a UV spectrophotometer at 248 nm against 7.4 PBS as a blank. From these absorbances, the standard curve is plotted. Standard curve equation and regression value are obtained.

C. Aceclofenac

a. Standard curve of Aceclofenac in PBS

A stock solution containing 1 mg/mL of the pure drug was prepared by dissolving 50 mg of Aceclofenac in sufficient PBS to produce 50 mL solution in a volumetric flask. Aliquot of 10 ml diluted up to 100 ml (i.e. 100 µg/ml). The above solution is prepared in the range of 10-90 µ g/ml. Absorbances were taken on a UV spectrophotometer at 273 nm against 7.4 PBS as a blank. From these absorbances, the standard curve is plotted. Standard curve equation and regression value are obtained.

D. Piroxicam

a. Standard curve in 0.1N HCl

A standard stock solution of piroxicam was prepared by dissolving 100 mg drug in 100 ml 0.1N HCL (i.e. 1000 µg/ml). From the stock solution, 10 ml was taken and diluted up to 100 ml (i.e. 100 in 0.1N HCL. Again 0.2, 0.4, 0.6, 0.8, 1, 1.2, 1.4, 1.6, 1.8 and 2 ml solution was taken from this solution and diluted up to 10 ml with 0.1N HCL to get the desired concentration range (2-20 µg/ml). The absorbance of the drug was measured at λmax 333 nm on a UV spectrophotometer.

RESULTS AND DISCUSSION:-

Table No. 1: Organoleptic properties of Lornoxicam

Organoleptic properties	**Results**
Colour	Orange to Yellow powder
Crystallinity	Amorphous in nature
Taste	Slightly bitter
Odour	Odourless

Table No. 2: Qualitative Solubility of the drug in different solvents

Solvents (5 ml)	Solubility Properties of the drug (5 mg)
Distilled Water	+
0.1N HCl	+++
3.6 pH Buffer	++
7.4 pH Buffer	+++
9.2 pH Buffer	+++
Ethanol	++
Methanol	++
Chloroform	++
Acetone	+++
Hexane	+
0.05 N NaOH	++++

\+ Insoluble

++ Poorlysoluble

+++ Slightlysoluble

++++ Freely soluble

The results were showed that Lornoxicam is insoluble in distilled water & hexane and very little solubility in organic solvents like ethanol, methanol, chloroform & acetone but the drug was freely soluble in alkaline solvents like 7.4 pH buffer and buffer. The drug showed high solubility in 0.05 N NaOH, which indicates the acidic nature of the drug.

Table No. 3: Quantitative Solubility of the drug in different solvents

Solvent	Concentration of drug in a solvent
0.05 N NaOH	6.306 mg of drug was present in 1ml of 0.05 N NaOH
0.1N HCl	0.664 mg of drug was present in 1 ml of 0.1N HCl
3.6 pH Buffer	0.732 mg of drug was present in 1 ml of 3.6 pH buffer
7.4 pH Buffer	0.92 mg of drug was present in 1 ml of 7.4 pH buffer
9.2 pH Buffer	1.224 mg of drug was present in 1 ml of 9.2 pH buffer

Standard Curve

The standard curve of the drug in 0.05 N NaOH and 7.4 PBS was prepared by the method reported by Nemutlu et al (2005). The absorbances were taken out at 376nm. Standard curve of lornoxicam in 0.05 N NaOH.Absorbances of the drug at 376 nm in 0.05 N NaOH is given.

Table No. 4: Absorbances of Lornoxicam at 376 nm in 0.05 N NaOH

Sr. No.	Concentration (µg/ml)	Absorbance
1	5	0.076
2	10	0.147
3	15	0.216
4	20	0.298
5	25	0.367
6	30	0.438
7	35	0.513

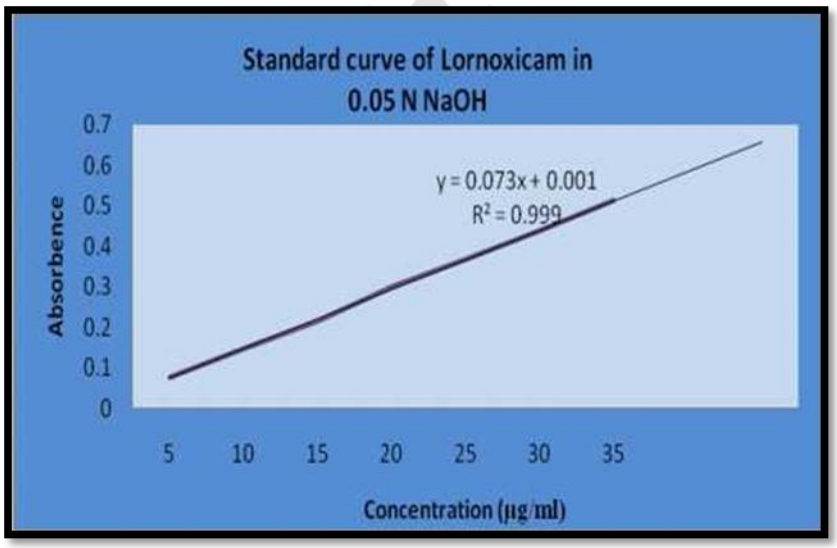

Figure No. 2: Standard curve of Lornoxicam in 0.05 N NaOH at 376 nm

a. Standard curve of lornoxicam in PBS 7.4:

Absorbances of the drug at 376 nm in PBS 7.4 are given below in Table No. 5.

Table No. 5: Absorbances of Lornoxicam at 376 nm in PBS 7.4

Sr. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	4	0.1672
3	8	0.3354
4	12	0.4885
5	16	0.6515
6	20	0.8225
7	24	0.9663

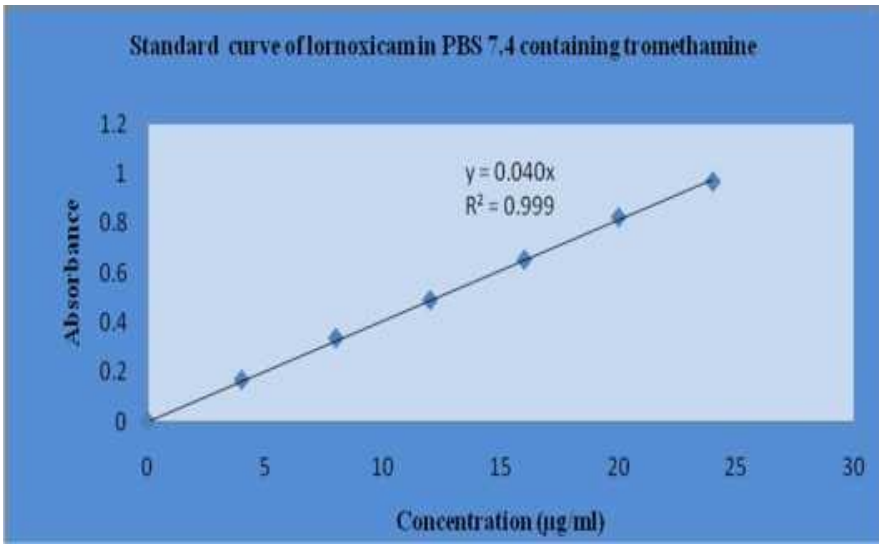

Figure No. 3: Standard curve of lornoxicam in PBS 7.4

The standard Curve of Lornoxicam in 7.4 PBS showed linearity in the range of 5-35 µg/ml and 4-24 µ g/ml with regression coefficients of 0.9997 & 0.9996 respectively. It shows that the drug follows Beer's Lambert Law in these ranges.

ParticleSize

The results of the Microscopic evaluation for the measurement of particle size of the drug particles are given in Table No. 6.

Table No. 6: The particle size distribution of Lornoxicam

Sr. No.	Size Range	MidPoint (M. P.)	No. of Particles (N)	M. P. ×N	M. P. × N × L. C. (d)
1.	0-1	0.5	06	03	5.82
2.	1-2	1.5	09	13.5	12.15
3.	2-3	2.5	11	27.5	53.35
4.	3-4	3.5	27	94.5	183.33
5.	4-5	4.5	23	103.5	200.79
6.	5-6	5.5	24	132	256.06
			∑n=100		**∑d=714.5**

Least Count (L. C.) = 1.94

The particle size was found to be 7.145 µm. The particle size distribution pattern depicted in Figure No. 4 shows that drug particles are distributed in a range of 1-6 µm and the maximum number of particles are present in a size range of 4-6 µm. This distribution pattern also indicates that the drug is amorphous.

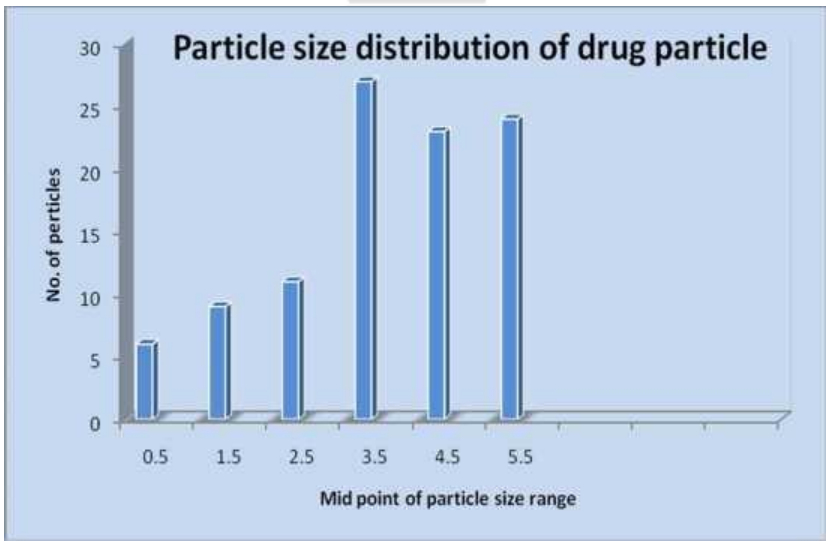

Figure No. 4: Particle Size Distribution of Drug (Lornoxicam)

1) Melting point:

The melting point of flurbiprofen was obtained by Thiel's melting point apparatus. The melting point was observed from 110-112^{0}C which is approximately the same as I.P.1996.

2) Drug- Excipient compatibility studies:-

Table No. 7: Drug-Excipient Compatibility Observations

Sr.No.	Additives (50 mg each) with drug	Observation at 60°C for 2weeks	Observation at 40°C for 2month	Remarks
1.	Drug (flurbiprofen)	No change	No change	Accepted
2.	Drug + pluronic F-127	No change	No change	Accepted
3.	Drug + lecithin	No change	No change	Accepted
4.	Drug + isopropyl myristate	No change	No change	Accepted
5.	Drug + PEG 400	No change	No change	Accepted
6.	Drug + Sodium sorbate	No change	No change	Accepted
7.	Drug + Sodium Benzoate	No change	No change	Accepted
8.	Drug + Oleic acid	No change	No change	Accepted
9.	Drug + Ethanol	No change	No change	Accepted

It is concluded that there is no interaction between excipients and drugs. The drug and excipient are compatible with each other and can be used for the formulation of gel.

Formulation and optimization of a transdermal gel

Method of preparation of pluronic lecithin organogel

The ten formulations of pluronic lecithin organogel with different drugs were developed with different composition as given in Table No.8.

Pluronic Lecithin Organogel (PLO) is a microemulsion based gel. It is made up of 2 phases, an oil phase, and an aqueous phase. Ten PLO formulations were prepared by altering the concentration of Lecithin and Pluronic while keeping the concentration of other excipient and drug unchanged.

Oil Phase was prepared by mixing soya lecithin (different amount of lecithin from 1 – 9 gm in different formulations) and Sodium Benzoate (0.2 gm) in an appropriate quantity of isopropyl myristate (quantity sufficient to 100 ml). The mixture was kept overnight at room temperature to dissolve its constituents completely.

The aqueous phase was prepared by dispersing the weighed amount of pluronic F-127 (from

5 – 30 gm in different formulations) and Sodium Sorbate (0.2 gm) in cold water (quantity sufficient to 100 ml). The dispersion was stored in a refrigerator for effective dissolution of Pluronic F-127.

The next day, the active ingredient (0.5 gm) was dissolved in Polyethylene glycol- 400 (15 ml) and mixed with the prepared oil phase. Polyethylene glycol-400 was used for the solubilization of drugs. Finally, the aqueous phase (70%) was slowly added to the oil phase (30%) with stirring using a mechanical stirrer.

Method of preparation of carbopol gel:

For the preparation of Carbopol gel, Carbopol 934 was finely dispersed in 50:50 propylene glycol: water and stirred continuously at 300 rpm for 3 hrs. Then, the active ingredient (0.5 gm) was finely dispersed in propylene glycol (15 ml) and then added to the carbopol mixture and mixed for 1hr. The dispersion was then neutralized and made viscous by the addition of triethanolamine.

A. Lornoxicam

Table No. 8: Composition of Pluronic Lecithin organogel of Lornoxicam

CONTENT		L-1	L-2	L-3	L-4	L-5	L-6	L-7	L-8	L-9	L-10
DRUG	Lornoxicam (gm)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
	PEG 400 (ml)	20	20	20	20	20	20	20	20	20	20
OIL PHASE (%)	Soya Lecithin (gm)	1	3	5	7	9	3	3	3	3	3
	Sodium Benzoate (gm)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	02
	Isopropyl Myristate q.s. (ml)	100	100	100	100	100	100	100	100	100	100
AQUEOUS PHASE (%)	Pluronic F-127 (gm)	20	20	20	20	20	5	10	15	30	25
	Sodium Sorbate (gm)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
	Distilled water q.s. (ml)	100	100	100	100	100	100	100	100	100	100

Table No. 9: Composition of Carbopol gel of Lornoxicam

Sr. No.	Ingredients %	Formulation
1.	Lornoxicam	0.5 gm
2.	Carbopol 934	3 gm
3.	Oleic acid	2.5 ml
4.	Ethanol	30 ml
5.	Propylene glycol	20 ml
6.	Triethanolamine	0.5 ml
7.	Distilled water	100 ml q. s.

EVALUATION

Result of evaluation studies of a transdermal gel

A. Lornoxicam

1) Measurement of pH

The pH of the skin is around 6.8. The results are given in Table No. 10 show that the pH of all the formulations was found to be in the range of 5.6 to 6.4, which is around the pH of the skin. This shows that formulations are fit for transdermal use.

2) Viscosity

The viscosity of all the formulations was found in the range of 2953 to 3276 poise given in Table No. 10. The results show that with the increase in polymer concentration i.e. lecithin and pluronic there is an increase in viscosity of the Pluronic lecithin organogel. This increase in viscosity is due to the formation of complex and stabilized because of the synergistic contribution of both phospholipids and polymeric co-surfactant molecules, in their respective hydrated state (strong hydrogen bonding with water). The viscosity of L-11 formulation, which is a carbopol gel, is less than Pluronic lecithin organogels, due to the weak hydrogen bonding between carbopol and water/polar solvent in carbopol gel as compare to lecithin and pluronic with water in Pluronic lecithin organogel.

3) Percentage drugcontent

For calculation of drug content, 1 gm of the prepared gel was dissolved in 100 ml of 0.05 N NaOH. One ml of the solution was further diluted to 100 ml. The absorbance was measured at 376 nm in a UV spectrophotometer against 0.05 N NaOH as a blank. The results are in Table No. 10.

The gel formulations were showed that drug content in the range of 95 to 99%, indicating a uniform distribution of drug throughout the base. Results also reveal that PLO gels have a higher % drug content than Carbopol gel, which indicates the superiority of the former on later.

Table No. 10: P^H, Viscosity, and % drug content of different formulation of gel

Sr. No.	Formulations	pH	Viscosity (cps)	% Drug content
1.	L1	5.7	3165	99.23
2.	L2	6.2	3045	99.54
3.	L3	6.1	3242	96.92
4.	L4	6.27	2953	99.51
5.	L5	5.93	3178	99.29
6.	L6	6.4	3028	96.86
7.	L7	6.3	3276	98.85
8.	L8	5.9	2953	97.46
9.	L9	6.16	3143	97.32
10.	L10	6.06	3162	98.15
11.	L11	6.1	2999	95.67

Spreadability

Quantity of gel was taken in 1 gm and initial diameter was taken measurement. The observations are recorded.

Table No. 11: Formulations?

			Different gel formulations(cm)									
Sr. No.	**No. of plates placed on gel**	**L1**	**L2**	**L3**	**L4**	**L5**	**L6**	**L7**	**L8**	**L9**	**L10**	**L11**
1.	1	2.2	2.1	2.4	2.5	2.3	2.22	2.4	2.4	2.6	2.2	2.0
2.	2	2.4	2.56	2.4	2.7	2.7	2.24	2.5	2.38	2.7	2.4	2.5
3.	3	2.52	2.74	2.6	3.04	2.9	2.28	2.6	2.45	2.72	2.7	2.7
4.	4	2.6	2.83	2.7	3.21	3.1	2.38	2.7	2.56	2.79	2.8	2.86
5.	5	2.88	3.1	3.1	3.33	3.22	2.42	2.96	2.66	2.8	2.9	2.98
6.	6	2.91	3.18	3.1	3.33	3.25	2.47	3.0	2.75	2.83	3.0	3.08
7.	7	2.90	3.26	3.2	3.39	3.27	2.54	3.06	2.8	2.85	3.2	3.12
8.	8	2.91	3.34	3.3	3.40	3.27	3.36	3.15	2.84	2.86	3.34	3.14
9.	9	2.92	3.45	3.4	3.41	3.27	3.55	3.18	2.84	2.87	3.36	3.14

The spreadability of all formulations was found in the range of 2.1 to 3.55 cm (in diameter). Spreadability is significantly influenced by the structural stability and rheological behavior of organogel, which in turn depends upon the type of organic solvent, the concentration of gelators or cosurfactants, or type and amount of polar solvents. The results show that the spreadability of L2, L3, L4, L5, L6, L7 & L10 were found good, which might be due to the optimized amount of cosurfactant, organic and polar solvents. The spreadability of Carbopol gel was also found good, this shows structural stability and good rheological behavior of Carbopol gel.

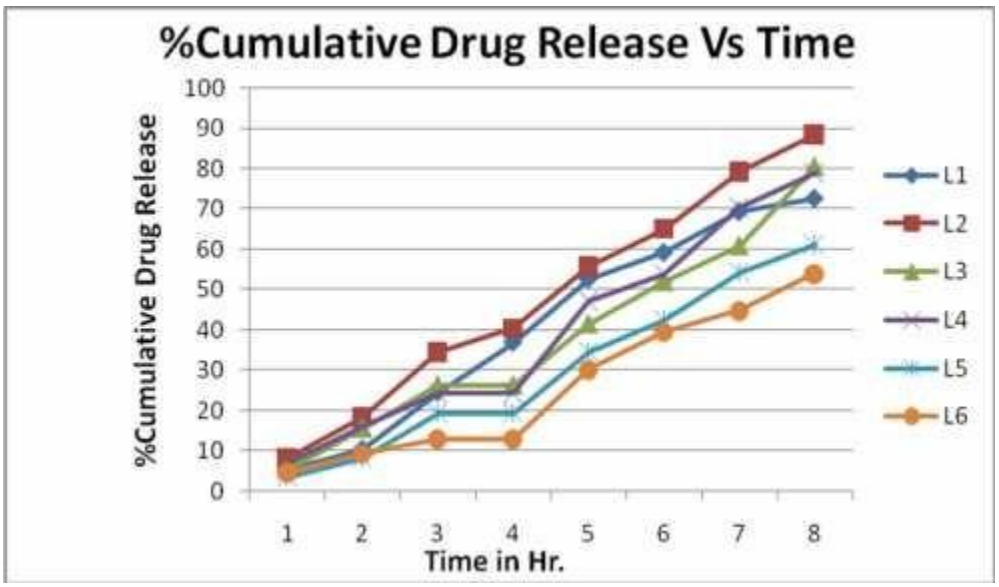

Figure No. 5: % Cumulative drug release profile of formulation L-1 to L-6

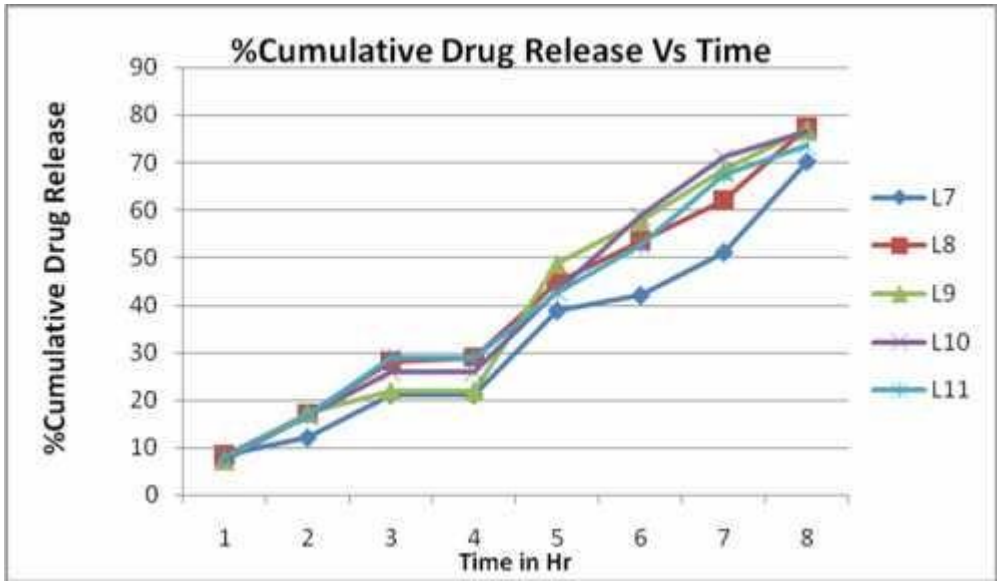

Figure No. 6: % Cumulative drug release profile of formulation L-7 to L-11

SUMMARY AND CONCLUSION

The transdermal drug delivery is one of the promising routes of the drug delivery system, since it bypasses the first-pass metabolism, avoids inactivation of drugs by pH effects and enzymes present in the GI tract. It provides a continuous mode of administration at rates approaching zero-order similar to that provided by an intravenous infusion, bioavailability of the drug is increased. The delivery is non-invasive, no hospitalization is required, and improves patient compliance.

Any drug for its permeation through the skin should be thermodynamically active, must be lipophilic as well as hydrophilic in nature having a favorable partition coefficient. The preformulation study for the drug was conducted.

LORNOXICAM: The λmax of Lornoxicam was found at 376 nm, which is comparatively the same as given in Merck Index. This shows that the drug is pure. By the determination of organoleptic properties, it was observed that the Lornoxicam is orange to yellow colored amorphous powder, bitter in taste, and odorless drug. Results of qualitative solubility studies show that the Lornoxicam is more soluble in alkaline solvents and insoluble in water. This indicates the acidic nature of the drug. Results of quantitative solubility show that Lornoxicam has the highest solubility in 0.05N NaOH and solubility of Lornoxicam increases

with the increase of pH, which indicates that the ionization of the drug increases with the elevating pH.

The partition coefficient was found to be 1.7, which is suitable for transdermal drug delivery, the obtained value of the partition coefficient of Lornoxicam was more than 1 which showed that the Lornoxicam is lipophilic. The average particle size of Lornoxicam was measured by microscopy method was found to be 7.145 micrometers. The melting point was observed at 225-227 ^{0}C and this range is nearly the same as reported in Merck Index, it shows the drug is amorphous. The standard curve of Lornoxicam was prepared in phosphate buffer 7.4 and in 0.05N NaOH, the r^2 values were obtained 0.999 and 0.999 respectively, which shows the linearity of absorbance between the range of 5-35 ug /ml. The preformulation study of Lornoxicam showed satisfactory results to select the drug for the transdermal drug delivery system. The transdermal anti-inflammatory gels containing Lornoxicam& different polymers were prepared and evaluated for different parameters like pH, drug content & rheological properties like viscosity and spreadability, and the results found were all satisfactory. The Results indicate that PLO gel shows better results than Carbopol Gel.

All eleven formulations were also evaluated for the *In-vitro* drug release study. The study was carried for 8 hrs for all formulations and the results reported in table 7.3 show that the Formulation L-2 and L-4 showed a good cumulative % Drug Release profile of Lornoxicam in 8 hr. But the linear curve is shown in fig. 7.1 was obtained from an F-2 formulation. The cumulative amount permeated from Carbopol gel through the membrane was found to be 65% which was less than PLO Gel formulations. This indicates that PLO Gel has more drug permeation across the membrane than carbopol gel.

REFERENCES

1. Willis-Goulet, H.S., Schmidt, B.A., Nicklin, C.F., Marsella, R., Kunkle, G.A., Tebbett, I.R.,2003. Comparison of serum dexamethasone concentrations in cats after oral or transdermal administration using pluronic lecithin organogel (PLO): a pilot study. Vet sDermatol. 14(2),83-9.
2. Murdan, S., 2005, A Review of pluronic lecithin organogel as a topical and transdermal drug delivery system. Hospital pharmacist. 12,267-279.
3. Katzang G. Bertram, Master B. Susan and Trevor J., 2009, Anthony,"Basic and clinical pharmacology", edition Published by Tata McGraw-Hill education private limited New Delhi,624-625.
4. Belgamwar, V.S., Pandey, M.S., Chauk, D.S, Surana, S.J., 2008, Pluronic lecithin organogel. Asian journal of pharmaceutics.134-138.
5. Ansel, H. C., Allen V. L., Popovich G. N., 2001, Pharmaceutical Dosage Forms and Drug Delivery Systems. 4, 376–380.
6. Sinko. J. Patrick, Martins "Physical pharmacy and Pharmaceutical science" Fifth edition distributed by B.I. Publication PVT Ltd., 232.

7. Loganathan, V., Jaswanth, A., Sulaiman, A., Rajaseskaran, A., Manimaran, S. and Kumar Senthil, B., 2008, the effects of polymers and permeation enhancers on release of flurbiprofen from gel formulation. Indian J. Pharm. Science. 200-204.
8. Kumar,R.,Katare,O.P.,2005.Lecithinorganogelsasapotentialphospholipid-structured system for topical drug delivery: a review. A. A. P. S. Pharm. Sci. Tech. 6(2), E298-3
9. Tripathi, K.D., In: "Essentials of medical pharmacology", 2008, 6thedition. JAYPEE Brothers Medical publishers Ltd. New Delhi,194.
10. SinghHarikishanandKapoorV.K.,1996,"Medicinalandpharmaceuticalchemistry",First edition, pub. By M.K. Jain for vallabhprakashan, 279.
11. www.rxlist.com (as cited on21/01/2012).
12. www.drug.com (as cited on21/01/2012).
13. http://www.drugbank.ca/drugs/DB00966 (as cited on19/01/2012).
14. http://www.drugbank.ca/drugs/DB00381 (as cited on19/01/2012).
15. Ardente, A.J., Barlow, B.M., Burns, P., Goldman, R., Baynes, R.E., 2008, Vehicle effects on in vitro transdermal absorption of sevoflurane in the bullfrog, Ranacatesbeiana. Environmental Toxicology and Pharmacology. 25,373– 379.
16. Lachman L., Lieberman H. A., 1990, The Theory And Practice of Industrial Pharmacy. 3, 534.
17. Preformulation A need for Dosage Form DesignPharmainfo_net.mht
18. Remington. The Science and Practice of Pharmacy. 20, 745 –747.
19. Ali Javed, Khar R.K. and Ahuja Alka, 2009, "Dosage form Design", IV edition, Birla publication PVT. LTD. Delhi.1-3
20. "Indian Pharmacopoeia", 1996, Vol. II Govt. of India published by the controller of publication, Delhi, A-90.
21. Jain N.K., "Pharmaceutical product development", 2006, First edition, published by satishkumarjain and produced by V.K.Jain for CBS Publisher and Distributers Pvt. Ltd, New Delhi,61-111.
22. Arpad Pardutz*et al*., 2010, NSAIDs in the Acute Treatment of Migraine: A Review of Clinical and Experimental Data *Pharmaceuticals*, *3*,1966-1987.
23. Allen V.L., Popovich G. N., Ansel, H. C., 2007. Pharmaceutical Dosage Forms and Drug Delivery Systems.8,96-125.
24. Atiyeh B.S., 2007, Nonsurgical management of hypertrophic scars: Evidence-based therapies, standard practices, and emerging methods. AesthetPlast Surg., 31:468-492.
25. Amlalo R.N.O.T., 2005, In-vitro release of ketoprofen from propreitry and extemporaneously manufactured gels, Rhodes university, Grahmstown,1-222.
26. Alster T.S., Tanzi E.L., 2003, Hypertrophic scars and keloids: etiology and management, Am J ClinDermatol., 4:235-243.
27. Arora P., Mukherjee B., 2002, Design, development, physicochemical and in-vitro, in- vivo evaluation of transdermal patches containing diclofenac diethyl ammonium salt, J. pharm Sci. Vol. 91(9),2078-2088.