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ORGANOGELS- A REVIEW

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INTRODUCTION:

Topical dosage forms are those which are applied to the skin. These preparations are applied to the skin for their physical effects that is for their ability to act as skin protectants, lubricants, emollients, drying agents, etc or for their specific effect of medicinal agents present. Preparations sold over the counter frequently contain mixtures of medicinal substance used in the preparation of such condition as minor skin infections, itching, bruise, acne, psoriasis and eczema. Skin application, which require a prescription, generally contain a single medicinal agent intended to counter a specific diagnosed condition.

ADVANTAGES OF TOPICAL SYSTEMS:

1. Though least therapeutic interest but of practical relevance is a patient compliance. The systems are easy to apply and remove. It avoids risk and inconveniences associated with intravenous therapy.
2. They eliminate the variables, which influences gastrointestinal absorption such as food intake, stomach emptying, intestinal motility and transit time.
3. Produces sustained and controlled level of drug in plasma thus reduces the chance of over or under dosing.
4. Reduces frequency of drug dosing.
5. Topical systems are easily retractable thereby termination of drug input, if toxic effects are observed.
6. Offers an alternative route when oral therapy is not possible as in case of nausea and vomiting.

7. Helps in achievement of more constant blood levels with lower dosage of drug by continuous drug input and by by-passing hepatic first metabolism and consequent degradation.
8. In certain circumstances, enzymatic may be used to improve permeability of certain hydrophilic drugs when applied to the skin in the form of pro drug.

LIMITATIONS OF TOPICAL SYSTEMS:

1. Drugs with reasonable partition coefficient and possessing solubility both in oil and water are most ideal, as drug must diffuse through lipophilic stratum- corneum and hydrophilic viable epidermis to reach the systemic circulation. Only drugs, which are effectively absorbed by the percutanoeus routes or by using penetration promoters, can be considered.
2. The route is not suitable for drugs that irritate or sensitize the skin.
3. The route is restricted by the surface area of delivery system and the dose that needs to be administered in the chronic state of disease.
4. Topical drug delivery systems rare relatively expensive compared to conventional dosage forms. They may contain a large amount of drug, of which only a small percentage may be used during the application period.

Apart from these limitations other problems include pharmacokinetics and pharmacodynamics restrictions. Thus clinical need has to be examined carefully before developing a topical dosage form.

In search of a vehicle to deliver the medicament into the skin layers, or through the skin and into systemic circulation, varied kinds of formulation systems and strategies have been involved, one such system is organogel.

Organogels are gels based on non-aqueous liquids, which have been mentioned in various pharmacopoeias as useful topical deliveries for lipophilic drugs. Organogels not only exert a local effect but also are capable of achieving systemic effect via transdermal absorption, when their lipophilic nature and occlusive effect are potentiated by the presence of a penetration enhances.

ORGANOGELS

The topical administration of drugs in order to achieve optimal cutaneous and percutaneous drug delivery has recently gained importance because of various advantages such as ease of administration, non invasive, better tolerated and compliance, local enhanced transdermal delivery, avoidance of local gastrointestinal toxicity and avoidance of first pass metabolism .

The search of a vehicle to deliver the medicament into the skin layer(cutaneous delivery) or through the skin and into systemic circulation (percutaneous absorption) and to target the skin , varied kind of formulation systems and strategies have been evolved .

Amongst the many, the lipid – based formulations have been in use since decades. Pharmaceutically, lipid emulsions may allow the sustained release of drugs by sink mechanism.

The importance of lipids has especially increased after realizing the utility of phospholipids. The natural bio-friendly molecules in collaboration with water can form diverse type of polymolecular/super molecular structure with retardant release in sustained release formulation.

The topical delivery has been attempted and made successful using a number of lipid based systems viz vesicular systems, lipid microsphere, lipid nanoparticles, lipid emulsion, polymeric gels.

In a recent development, spans in conjunction with some other additives have been shown to provide a very promising topical drug delivery vehicle i.e., organogel. Organogels are thermodynamically stable, clear, viscoelastic, biocompatible and isotropic gels composed of phospholipids, appropriate organic solvent and a polar solvent. The formation of three dimensional networks in the organogel is the result of transition at micellar level in a low viscous network liquid consisting of span cause micelles in non-polar organic liquid.

These spherical reverse micellar states of lipid aggregates, twins on to form elongated tubular micelles with the addition of after, and subsequently entangle to form a temporal three dimensional network in the solution bulk.

However, the transparency and optical isotropy of the organogel remain is maintained. For this reason, these systems are often called as polymer like micelles and are also termed as living or equilibrium polymer, worm like or thread like micelles.

ADVANTAGES OF ORGANOGELS

1. TEMPLATE VEHICLE: Organogels provide opportunities for incorporation of wide range of substances with diverse physicochemical characters viz: chemical nature, solubility, molecular weight, and size etc.
2. PROCESS BENEFITS: Spontaneity of organogel formation by virtue of self-assembled super molecular arrangement of surfactant molecule makes the process very simple and easy to handle.
3. STRUCTURAL/PHYSICAL STABILITY: Being thermodynamically stable, the structural integrity of organogels is maintained for longer time periods.
4. CHEMICAL STABILITY: Organogels are moisture insenstive and being organic also resists microbial contamination.
5. TOPICAL DELIVERY POTENTIAL: Being well balanced in hydrophilic and lipophilic character, they can efficiently partition with the skin and therefore enhance the skin penetration and transport of the molecules.
6. SAFETY: Use of biocompatible, biodegradable and non-immunogenic materials makes them safe for long-term applications.

LIMITATIONS OF ORGANOGELS:

- Should be stored in a proper condition.
- The organogel has greasy property
- Less stable to temperature.

ORGANOGEL-OVERVIEW

It was observed that addition of span caused an abrupt rise in the viscosity ($10\text{-}10^4$) , producing a transition of the initial non-viscous solution into gel of jelly like taste. The amount of water required to produce the gel was found to be critical but now, organogels have been studied extensively in many laboratories worldwide with regard to

their varied aspects such as formulation component, formation and gelling mechanism, physico-chemical properties etc and have been proposed as a matrix for topical drug delivery.

MECHANISM OF GEL PERMEATION INTO SKIN:

There are two possible mechanisms for gel permeation into skin has been proposed.

1. Gel permeation into the skin occurs by diffusion through lipid intercellular matrix in stratum corneum.

2. Gel provides a slight disorganization of the skin allowing the permeation of the gel and the active drug through the stratum corneum.

A table is mentioned below which enlists the applications of Organogels for topical drug delivery.

Topical Drug Delivery Applications of organogel-based systems

Organogel formulation	Major findings
Lecithin (200mM) IPP gels of broxaterol and scopolamine.	Transdermal delivery of compounds
Phosphatidylcholine (PC) gel in isopropyl palmitate (IPP) or cyclooctene.	Investigated for transdermal transport of various drugs along with amino acids and peptides
IPP-lecithin gel of diclofenac and indomethacin.	Enhanced efficacy of NSAIDs administered through topical route
Phytosphingosine or sphingosine lecithin organogel comprising soy PC, IPP, ethanol, and water.	Treatment of scars
Nicardipine lecithin-IPM organogel.	Enhanced skin permeation across guinea pig and human skin
LO gel of cardiac glycoside digoxin.	Topical administration of the compound in LO gel was found to be effective for the treatment of muscle spasm
Cyclobenzaprin in lecithin organogel (lecithin 10%-30%, IPM 10%-30%,	Topical formulation for bruxism

water 30%-60%).	
Soybean lecithin/IPP gels containing 10% to 20% short chain esters such as ethyl acetate or propyl acetate.	Transdermal delivery of aromatic tetra-amidines for anticancer activity
Propranolol hydrochloride in 200 mM lecithin/iso-octane organogel	Percutaneous delivery of compounds with poor permeability

SAFETY AND SKIN COMPATIBILITY STUDIES

Organogel systems i.e., gels are composed of pharmaceutically approved (non-immunogenic and biocompatible) excipients. However, the level of surfactant and organic solvents in organogels is fairly high. Therefore, it is important to consider the safety and irritancy of the formulation on prolonged use. The irritation potential of organogels has been assessed by Dreher et al, by carrying out human skin irritation study. Results indicated a very low cumulative skin irritation potential of organogels that supports the suitability of organogels as a topical vehicle for long-term applications.

RATIONALE OF STUDY:

Most of the chemical entities that are being discovered today are lipophilic in nature and have poor aqueous solubility, there by posing problems in their formulation into delivery systems.

More than 60% of the potential drug products suffer from poor water solubility. Currently a number of newer technologies are available to address the poor solubility, dissolution rate and bio availability of insoluble drugs. These include prodrugs, polymeric forms, use of solvates and hydrates, micronisation, solid dispersions etc.

Topical delivery of drugs is one such approach which has been attempted and made successful to overcome the above mentioned draw backs. Topically administrated drugs have advantage over systemic drugs in that they deliver the medication directly to the targeted site, less likely to provoke side effects, bypasses the hepatic metabolism etc.

Amongst the various types of topical dosage forms, gels are gaining importance as relatively effective topical dosage forms. A gel can be described as the cross linked material that retains a large amount of solvent inside its

medium and if the solvent retained is organic one, such material is known as organogel. Traditionally, organogel type systems are applied topically when the active agent is oil soluble or, if we need sustained release of the drug in the deep skin layers.

Organogels show diverse physicochemical properties like thermoreversibility, ability to incorporate all types of drug molecules, controlled release, increased resistance to microbial contamination etc.

Non- steroidal Anti inflammatory drugs have been widely used for postoperative and emergency treatment of pain. However it accompanies adverse effects like respiratory depression, GI irritation, drowsiness and poor patient satisfaction. One alternative is the transdermal application of these drugs which allow the patient to experience relief without unwanted side effects. Transdermal application of gels containing Non- steroidal Anti inflammatory drugs have been successful in treating post-operative pain.

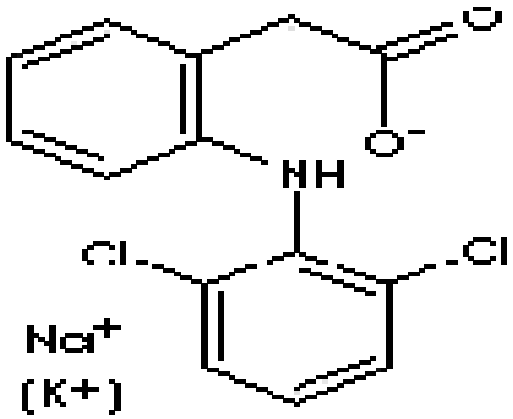
ORGANOGELS USING *DICLOFENAC SODIUM*:

DICLOFENAC SODIUM

Generic name: Diclofenac sodium

Class: Analgesic

Structure:



Chemical name: Sod-[(2, 6-dichlorophenyl)-amino] phenyl acetate.

Molecular Formula: $C_{14}H_{10}Cl_2NNaO_2$. Molecular weight: 318.13

Description: White to slightly yellowish crystalline powder, slightly hygroscopic.

Physico-chemical properties:

Solubility: Fairly soluble in methanol; soluble in ethanol (95%); sparingly soluble in water and glacial acetic acid; practically soluble in ether, and in toulene.

Standard: Diclofenac sodium contains not less than 98.5% and not more than 101.0% of $C_{14}H_{10}Cl_2NNaO_2$, calculated with reference to the dried substance.

Pharmacological profile:

Mechanism of action: Diclofenac sodium is an inhibitor of COX. It also appears to reduce intracellular concentration of 3 arachidonate in leucocytes. Its potency is greater than Indomethacin and Naproxen.

Pharmacokinetics: After oral, administration, it is rapidly completely absorbed. It shows substantial form effect and is high protein bound. It is metabolized and excreted in urine and bile.

VEHICLE : ISOPROPYL MYRISTATE

SURFACTANTS : SPAN-80 , TWEEN-80

CONSTRUCTION OF CALIBRATION CURVE OF DICLOFENAC SODIUM

Spectrophotometric method of estimation of diclofenac sodium:

The standard calibration curve of diclofenac sodium was prepared in 100ml phosphate buffer pH 7.4.

STANDARD SOLUTION: Accurately weighed 100mg of diclofenac sodium was dissolved in 30ml of methanol and the solution was transferred into a 100ml volumetric flask and the volume was made upto 100ml using phosphate buffer pH 7.4.

STOCK SOLUTION: From the standard solution, stock solution was prepared to give a concentration of 1mg/ml. From the stock solution, dilutions were made to give a 2, 4, 6, 8, 10 mcg/ml concentrations of diclofenac sodium respectively. The absorbances of prepared solutions of diclofenac sodium were measured at 276nm in UV spectrophotometer against an appropriate blank.

The standard calibration curve yields a straight line, which follows Beer's law in concentration range of 0-10mcg/ml.

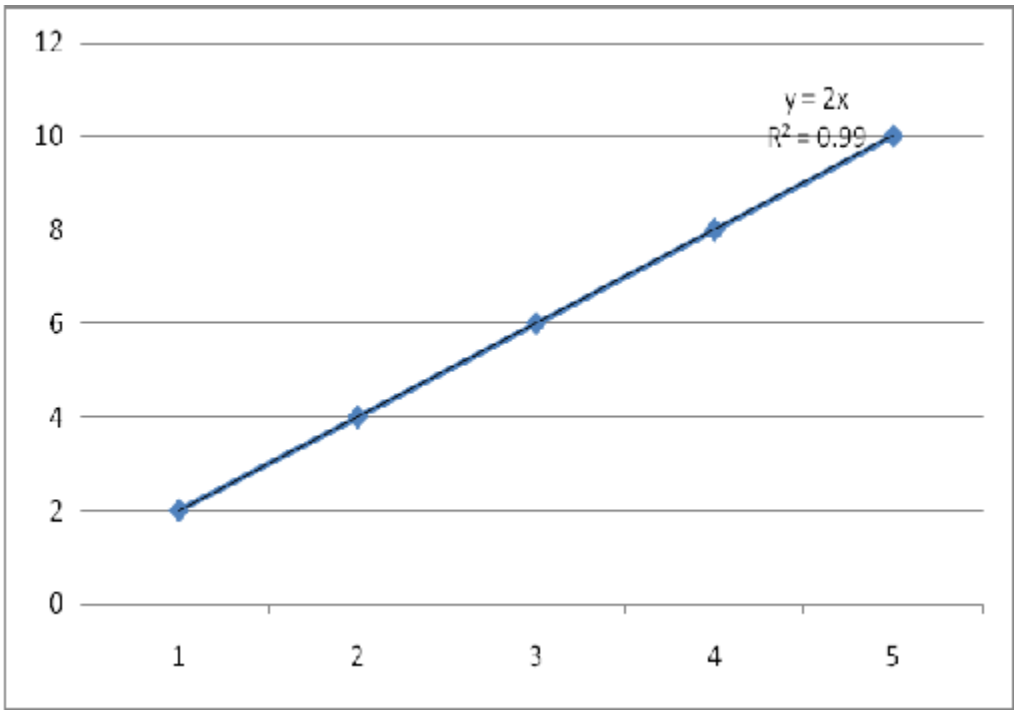
Preparation of Phosphate Buffer:

Take 50ml of 0.2M KH_2PO_4 in 200ml volumetric flask. Add 44.5ml of NaOH then add 200ml water to make up the volume.

Preparation of 0.2M KH_2PO_4: Dissolve 27.218gm of KH_2PO_4 in water and dilute to 1000ml with distilled water.

Standard calibration curve for Diclofenac sodium in Phosphate Buffer pH 7.4 (λ276nm)

S.No	Concentration (mcg/ml)	Absorbance
1.	2	0.0895
2.	4	0.172
3.	6	0.270
4.	8	0.363
5.	10	0.440



Concentration (mcg/ml)

PREPARATION OF DICLOFENAC SODIUM LOADED ORGANOGEL

Preparation of Organogels loaded with Diclofenac Sodium

Organogels based systems were prepared using Span– 80 and tween– 80 in different composition were dissolved in isopropyl myristate (IPM). After incorporation of the drug, gelation was achieved on addition of the aqueous phase where the concentrations were made by optimization process.

EVALUATION OF DICLOFENAC SODIUM ORGANOGELS:

pH

pH is the negative logarithm concentration of the H^+ ion concentration. pH value is important because the pH of the formulation determines the skin irritability indirectly. If the formulation has a high acidic pH, it implies that the skin will have a burning sensation. Digital pen pH meter was used to measure the pH of the gel at constant temperature. Prior to this pH meter was calibrated using the buffer solution of pH 7.4. Then the electrode was

washed with the demineralised water. The electrode was inserted in to the sample 10 min prior to taking the readings. The method for the preparation of the Phosphate buffer is as mentioned below:

Take 50ml of 0.2M KH_2PO_4 in 200ml volumetric flask. Add 44.5ml of NaOH then add 200ml water to make up the volume. (Preparation of 0.2M KH_2PO_4: Dissolve 27.218gm of KH_2PO_4 in water and dilute to 1000ml with distilled water).

Fig: 2: Digital pen pH meter.

Stability Studies

The stability of the formulations kept in the containers was assessed at the room temperature, refrigerator and hot air oven at 60^0 C. Samples were kept at constant temperature 25^0 C were tested for their physical stability, organoleptic properties and macroscopical appearance of the organogels. And based on this the most stable formulation at the normal storage condition was found out.

Determination of viscosity

The viscosity of the formulated organogels is determined using the Brookefield viscometer. The sample holder taken for the viscosity measurement is filled with the sample and then inserted into a flow jacket mounted on the viscometer. The sample adaptor (spindle), rotated at an optimum speed is used to measure the viscosity of the

preparation; the sample is allowed to settle for five min prior to taking the readings. And the viscosity is determined at an rpm value of 5. The value of the viscosity is displayed in the form of cps.

Fig: 3: Brookefield viscometer.

Determination of the Diclofenac Sodium content release rate

Preparation of phosphate buffer:

Take 1.36g of KH2PO4 (0.2M) and dissolve in 50ml water. Add 0.374g of NaOH dissolved in 44.5ml of distilled water and make up the volume to 200ml in standard volumetric flask.

Preparation of 0.2M KH2PO4:

Dissolve 27.21g of KH2PO4 in water and dilute to 1000ml with distilled water.

Preparation of egg membrane: The egg is taken in a beaker and required quantity of dilute hydrochloric acid or H2SO4 acetic acid is added and rotated with stirrer and after 10minutes it is washed and the egg is taken out and the yolk is removed with the help of blade and the outer white membrane is obtained.

Experimental procedure: The phosphate buffer of 100ml is taken in a beaker and then to the mouth of broken end of test tube the egg membrane is tied with the help of rubber band and then the beaker is placed on magnetic stirrer set at 100rpm, temp37±5ºc then allowed to stir till the experiment is continued i.e for maximum of 6 hours.

Then the prepared formulation i.e organogel about 1gm is placed on the egg membrane from the broken end of test tube and the samples are withdrawn at every 15min time interval i.e around 4ml of solution is taken and the same amount of phosphate buffer is replaced back. The sample is examined in U.V spectrophotometer at 285nm and the absorbance is noted.

Fig: 4: UV – Visible spectrophotometer.

Ref:

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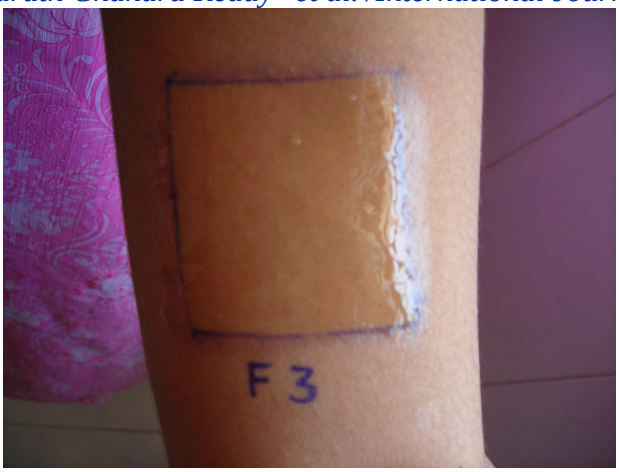
Skin Irritation Test

The skin irritation test is performed by drawing a square of 4cm on the hand with a water insoluble ink pen or a marker. Then the area on the hand is cleaned with a spirit cotton swab. Then the organogel is applied uniformly on the square drawn on the hand and was allowed to stand for 3hours. After the specified time the patch was observed and there was no sign of erythema or swelling seen. So, the formulations are found to be best and safe.



Homogeneity

Homogeneity of various formulations is tested by visual observations.

Determination of Gel Strength:

Gel strength of the samples is determined using the method described by Wainewright (1997) . The formulated gels prepared are stored for 16-25h at room temperature followed by determination of gel strength by using a Texture Analyzer. The load cell is 5 kg, crosshead speed 1 mm/s, equipped with a 0.5 in. in diameter, flat-bottomed plunger. The beaker is placed centrally under the plunger and the penetration test is carried out to determine the maximum force (in g) when the probe proceeded to penetrate into the gel to a depth of 5 mm, 10mm and 15mm.

Fig-5 : Texture Analyzer.

CONCLUSION AND SUMMARY:

Organogels are readily obtained by adding minimal amount of the water to a solution of surfactant in organic solvents. Surprisingly high viscosities can be achieved in organic solvent on addition of water. Such systems have currently generated great interest as topical and transdermal drug delivery carriers.

In the present study, organogels were studied as topical carriers for diclofenac sodium, an analgesic with molecular formula $C_{14}H_{10}Cl_2$ $NNaO_2$ and practically insoluble in water. It may be concluded that organogels have good potential as carrier for topical delivery of NSAIDS agent such as diclofenac sodium.

REFERENCES:

1. YIE. W. Chien, Novel Drug Delivery systems, 2nd Edition, Page 1.
2. Physical Pharmacy, Alfred Martin, 2nd Edition, page 496.
3. Tutorial Pharmacy, cooper and Gunn's, Page 65.
4. Popli N, Sharma SN. Transdermal drug delivery system. The Eastern Pharmacist, May 1990; 41-47.
5. Klinman MD. A biological brief on percutaneous absorption. Drug Development and industrial pharmacy,9(4):521-560.
6. Mehta R. "Topical and Transdermal Drug Delivery: What a pharmacist need to know." http://www..inetce.org.
7. Walters KA. Transdermal drug delivery in: Topics in pharmacy, Routes of drug administration.Flourence AT, salole EG (Ed), Wright 78-135:1990.
8. http://www.xenexlab.com/technical%20information.html.
9. The Theory and Practice of Industrial Pharmacy. 3rd Edition by Leon Lachman, Herbert AL and Joseph LK, published by Varghese Publishing House , bombay, P-221:1987.
10. Encyclopedia of Pharmaceutical technology, 2nd Edition edited by Graham Nairn J, published by Marcel Dekker Inc., New york, vol 15; 4-61; 1987.

11. Kulkarni PK andPradeep Kaatgi. Emulsion-gels as Topical drug delivery vehicle – A Review. Indian J.pharm. educ 2002 july-sept;36(6): 119-123.
12. R Chien YW. Logics of Transdermal Controlled drug administration. Drug Development and Industrial pharmacy1983; 497-520.
13. R Cairns RJ. Anatomy Development and Immunologic of the skin, In:Dermatology, Current concept and Practice , smith HP, Cairn RJ, 3rd Edition, Published by Butte wostber and co.Ltd., 1-10: 1981.
14. Aulton ME. Pharmaceutics: The science of dosage form design, 2nd Edition, Published by Churchill Livingstone, London. 503:2002.
15. Chowdary KPR, Vijayasrinivas S Biopharmaceutical Classification system. The Indian Pharmacist 2004, 111, 30.
16. Tejan Shah Lipid Emulsions as drug delivery systems. An overview. The Pharma review,2005 jan-feb ;41-48.
17. Sojan jose, Kulkarni PK, Self-emulsifying drug delivery systems; Review Indian j .Pharma Educ 2002 oct-dec; 184-190.
18. Jayne Lawrence M,Gareth D, Rees Microemulsion-based medias novel drug delivery systems.Advanced Drug delivery Reviews,2000;45;89-121.
19. Tamilavanan S.oil in water lipid emulsion implications for parentral and ocular delivering systems. Progress in Lipid Research 2004; 43; 489-533.
20. Remington “The Science and Practice of Pharmacy”, 9 th Edition, vol.2; Mack Publishing Company , Easton, Pennsylvania, P-1577; 1995.
21. Kumar R, Katare OP. Lecithin organogels as a potential phospholipids – structural system for topical drug delivery – A review. AAPS Pharma Sci. Tech. 2005 April; 1 – 47.
22. Murdan S, Gregoriadis G, Florecence AT. Inverse toroidal vesicle: Precursor of Tubules in sorbitan mono stearate organogels. International Journal of Pharmaceutics, 1999; 183:47 – 49.

23. Lecithin Organogels as model carrier of pharmaceutical; Edited by Zoumpainoti M, Karavas E, Skopelilis C published by Progress in Colloid and Polymer Science. Springer – Verlag Heidelberg, vol. 123; 2004.
24. Scartazzini R and Loisi PC. Organogels from lecithin. The Journal of Physical chemistry 1998, vol 92(3): 829 – 833.
25. William N, Walde P, Luisi L, Gazzaninga A, Stroppolo F. Lecithin organogels as marix for transdermal transport of drugs. Journal of Pharmaceutical Sciences, 1992 Sept., vol. 81, No. 9 :871- 874.
26. Hoffmann G, Marks SL, taboada J. Hosgood GL, Wolfsheiner KJ. Transdermal methimazole treatment in cats with hyperthyroidism. Journal of Feline medicine and surgery, 2003; 5:27- 82.
27. Pharmaceutical Dosage Form and Drug Delivery System. 5th Edition edited by Howard C Asel Published by Lea and Febiger,London , 307; 1990.
28. Medical Microbiology, Mackie R and McCartney. 3rd Edition Published by ELBS Publication, Vol. 1; P – 541- 544: 1984.
29. Microbiology edited by Michael J, Pelgar JL, Scham EC, Kring NR, 5th edition published by Tata McGraw Hill Publishing Co. LTD ., New Delhi P- 345- 360.
30. Pharmacology Edited by R Rang HP, Dale MM,Ritter JN, 4th Edition, P- 723: 1999.
31. Meying Ning, Zhong Wei GU, Nuaizhong Pan, Heining YU and Kai Xiao. Preparation and *in vitro* evaluation of liposomes,niosomes delivery system system andantifungal drug clotrimazole. Indian Journal of Experimental Biology, 2005 feb; vol. 43: 150- 157.
32. Williamann HL, Luisi PL. Lecithin organogels as matrix for the trandermal transport of drugs. Biochemical and Biophysical Research Communication 1991 june: Vol . 177(3):897 – 900.
33. Drenher F, Walde P, Walter P, Wehli E, Interaction of a lecithin microemulsion gel with stratum corneum and its effect on trandermal transport. J. Control Release 1997; 95 :131 – 140.
34. Crandall, Wilson T. Method for topical treatmenr os scars with protein kinase C inhibitor.US Patent 6 306 2001.

35. Ford Peter R. Topical analgesic composition containing cream type carriers . US Patent Appl Publ.2002028789, 2002.
36. Aboofazeli RZ, Hossein N, Thomas EN. Transdermal delivery of nicardipine: AN approach to in vitro permeation enhancement. Drug Delivery 2002; 9(4): 239 – 247.
37. Charles C, Mallhew D. Cardiac Glycoside for treating muscle pain and spasm. US Pat Appl Publ.20030229029 (2003).
38. Drher F, Walde P, Luisi PL, Elsner P. Human skin irriation studies of a lecithin microemulsion gel and liposomes . Skin Pharmacol 1996; 9 124 -129.
39. Keith Anderson. Pharm PK Diffusimax – Transdermal delivery, 1999 june. www.david .at.boomer.org.
40. Valenta C, Wanka M, Heildlas J. Evaluation of novel soya lecithin fformulation for dermal use containing ketoprofen as a model drug. Journal Of Controlled Release, 200 (63): 165-173.
41. Rajani V, Verma PR. In vitro study of ibuprofen from ointment base. Indian Journal of Pharmaceutical Sciences, 1995; 57(1):1 – 6.
42. Ilango R. Formulation and evalution of nimulsulide gel. The Eastern Pharmacist 1998 Nov; 123 – 125.
43. Shelke VB, Thopte K, Wawdw GM, Pisal SS, Kadam SS. Nasal delivery of propranalo hyldrochloride for sorbitan monoseatrate organogels : Preformulation Study . Indian J. Pharm. Sci, 2005; 67(2): 200 – 205.
44. N. R. Munjal**,**Indian Drugs 41(9) sep . 2004 page no – 550.
45. Bagyalakshmi, AS William, AW Mithun, TK Ravi, R Manavalan, PK Manna, Indian Journal of Pharmaceutical sciences (IJPS) July – August 2006.
46. N. R. Munjal, Indian drugs – 41 (11) nov. 2004, page no – 550.
47. SK Jain, MK Chaurasia, R Dengre, Indian Journal of Pharmaceutical sciences (IJPS) Jan-Feb 2005.
48. VG Jamakandi, JS Mulla, BL Vinay, HN Shivakumar Indian Journal of Pharmaceutical Excipients2005, 67 (4) page no – 473.
49. Indian Pharmacopoeia, Volume – I, 1996.

50. Martindale, The Extra Pharmacopoeia, 31st Edition, Page no- 1409.

51. Martindale, The Extra Pharmacopoeia, 31st Edition, Page no- 1346

52. Martindale, The Extra Pharmacopoeia, 31st Edition, Page no- 1345.

53. Indian Journal of Pharmaceutical Excipients, July-Dec. 2003, page no – 72 – 82.

54. Nasseri AA, Aboofazeli R, Zia H, Thomas EN. Lecithin – Stabilized microemulsion – based organogels for topical application of ketolac tromethimine II. In vitro release study. Iranian Journal Of Pharmaceutical

55. Research, 2003 May; 117- 124.

56. Veena S Belgamwar , Asian Journal of Pharmaceutics, Volume- - I, Issue - I, April - June 2007.

57. Ravi Kumar ***et al*** /Int.J. PharmTech Res.2009,1(3)

58. Veena S Belgamwar , Asian Journal of Pharmaceutics, Volume- - I, Issue - I, April - June 2007.

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