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Review Article

A REVIEW ON LIPOSOMAL GEL FOR ACNE VULGARIS

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Abstract:
Many different basic sciences have established liposomes as a promising new drug delivery method. Liposomes are tiny spheres made of an aqueous core and one or more lipid-based outer shells that are organized in a bilayer pattern. The ability to encapsulate hydrophilic and lipophilic medications and shield them from deterioration makes liposomes acceptable better carriers. It can penetrate deeper into the skin and, as a result, provide higher absorption. It also has an affinity for the keratin of the horny layer of skin. When applied to the skin, liposomes may function as a local depot, a matrix for solubilizing poorly soluble medicines, and an enhancer of penetration while also reducing their negative effects. Topical liposome formulations have the potential to be less harmful and more effective than standard formulations. The extended and controlled release of the topical dose forms used in liposome gel formulations may increase efficacy and patient compliance while producing therapeutically superior effects compared to those of standard formulations.

Keywords: *liposomes, gel formation*

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1. INTRODUCTION

1.1 Liposomal Gel

Most favourable therapeutic outcomes necessitate appropriate drug selection. In human body, the skin is a best available space for drug delivery.[1,2] In human body skin covers an area of about 2m and this multi-layered.

In total skin surface consist of 1/1000 of hair follicles in every tetragon centimetre of the skin area. The most gladly reachable. [3,4] The aera of skin where the drug is introduced. Skin are most important barrier for the access of any materials. Transdermal drug delivery crosses the drug at a control systemic circulation. It has intention narrow aera.[5,6]

1.1.1 Classification of liposomes

For the classification of liposomes many techniques are use. It is use with size and structure. Categorization is the other name of different classification of liposomal composition.[7,8]

1.1.1.1 Classification of liposome according to size and shape

(a) Multilamellar vesicles (MLVs)

In this liposome one or more than one lamella is present and it has a size between 100 to 1000 nm.

(b) Small Unilamellar vesicles (SUVs)

The size of this liposome is 0.1µm. it has single lamella. The maximum size is attained by the composition of the membrane. When the liposome is in minimum size it shows the variation in size.

(c) Large Unilamellar vesicles (LUVs)

The size of this liposome is 0.1µm. it has 1000nm size. It is nearly the size of a living cells. it has single lamella

(d) Oligolamellar vesicles

It consists of some lamellae and are known as oligolamellar liposomes. It has 2-5 bilayers and it has a range of 50 to 250nm.

(e) Giant vesicles

In this vesicle the average diameter is 100 µm. It is a unilamellar. In this method the liposome magnitude is greater than two-three liposomal.[9,10,11]

1.1.1.2 Classification of liposomes according to composition

Liposomal are the natural components and has extensively varied and have materials artificial.

Tweaking proportion the ingredients which is modified the manufacturer of liposome.

(a) Conventional liposomes

Liposome are made and collected from natural sources and cholesterol. The RES (reticulo-endothelial system) is used for the targeting the liposomes. this may shorten the liposome in circulation. These are known as lysosomes.

(b) pH-sensitive liposomes

Liposome are composed of cholesterol hemisuccinate, phosphatidyl ethanolamine, oleic acid (OA) or dioleoylphosphatidyl ethanolamine. If pH is low the fusion of liposomal in the cell. Macromolecules and weak bases are perfect for the delivery of liposome.[12,13]

(c) Cationic liposomes

Cationic ions are made up of membrane of these liposomal.

(d) Long-circulating liposomes (LCL)

Neutral lipids are use for the formulation with high TC. Cholesterol (5 and 10%) is use in the formulation. Liposomes are long circulation with half-life 40hours.

1.1.2 Immuno-liposomes

These are also known as LCL (long circulating liposome) and CL (Conventional liposomes). These are also known as antibody with recognition sequences. These formulation of liposomal are bind with cell and release during drug release. This may go to the targeted delivery system. [14,15]

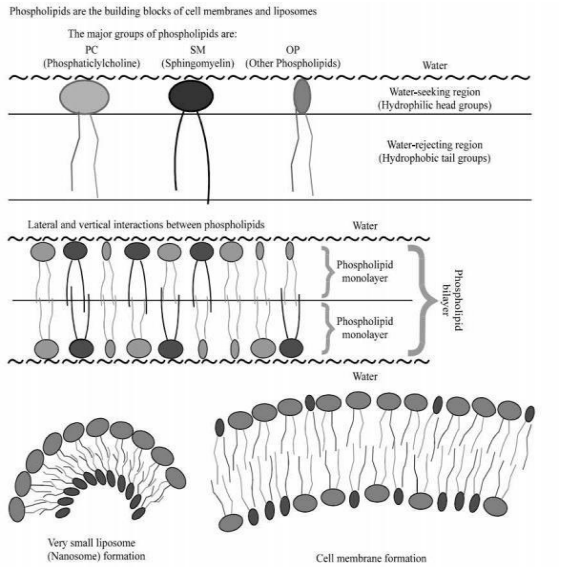

Figure 1. Composition of Liposomes

1.2 Components of Transdermal drug delivery system

1. Polymer matrix
2. Permeation enhancers.
3. Pressure sensitive adhesive (PSA).
4. laminated Backing.
5. Release liner.
6. Other excipients like plasticizers and solvents[16,17]

1.3 Advantages

Transdermal drug delivery has some advantage like:

1. Avoiding decomposition due to hepatic "first-pass" metabolism effect.
2. it decreases side effects by decreasing the plasma conc. levels of drugs.
3. The drug plasma level is reduced.
4. Exploitation of drug entity having small half-life and lower therapeutic index
5. patient compliance are enhancing by decreasing the dosing frequency. [18,19]

1.4 Limitations

1. Heavy drugs entities (>500 Da) frequently complex to penetrate the uppermost layer of skin.
2. Drugs with extreme partitioning constant are not conducive and so it fails to reach blood circulation.
3. Drug should have a less M.P.[20,21]

1.5 Transdermal Applications:

There are some applications of transdermal drug delivery system like:

1.5.1 Membrane-controlled transdermal system:

The drug metallic plastic laminate the Membrane-controlled transdermal system in shallow compartment molded. The drug control was made up of solid polymer matrix and viscous liquid with rate controlling membrane and silicon polymer or polyacrylate.

1.5.2 Adhesive Diffusion-Controlled System:

The membrane moderate system has the adhesive diffusion control system. The adhesive polymer is directly dispersed. The metallic plates are impermeable to solvents. At last adhesive layer.[22,23]

1.6 Optimizing Transdermal Drug Delivery

There are many advantages of transdermal route of conventional routes. It avoid the first pas metabolism effects, activity of extended period and predictable, side effects can be minimizing, the drug utilise goes shorter half-life, improve in physiological and pharmacological. This helps in avoiding the drug level fluctuation also reduce the variabilities. It helps to improve the patient compliances. [24,25]

For the transfer of drugs dermally and transdermal a vesicular system of drug delivery is introduced. For overcome this problem liposomes are use. The bilayer lipid vesicles, phospholipids and cholesterols.[26,27] Bangham and colleagues discover the liposomes by drug delivery system. The solvents are separated from each other. These solvents are closed, spherical. The exterior envelops of a liposome are allowed to passes the drug by lipophilic skin. This treatment is use for the both local and internal skin disorders. Cosmetic formulation has show the systemic effects.[28,29]

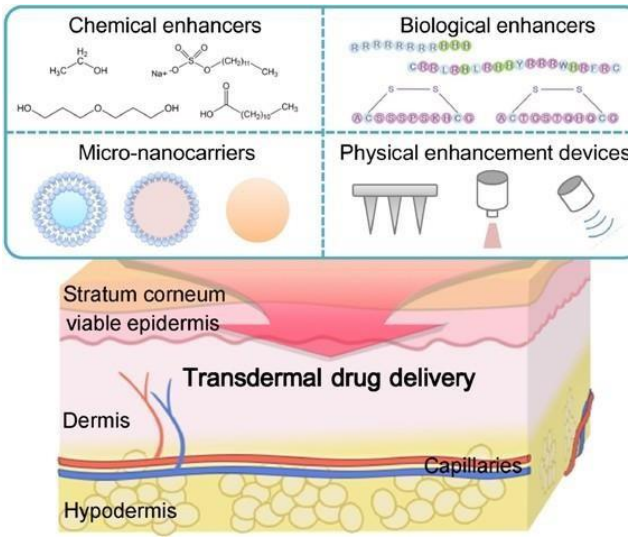

Figure 2. Transdermal Drug Delivery

1.7 Stability of Liposomes

During the manufacturing of liposomes, it is very necessary take care. Estimator of the oxidative stability is lipid peroxidation. It is found process of degradation of poly unsaturated fatty acids. Mostly enhanced diets composed of polyunsaturated fatty acids. It is prone to peroxides if it exposed to high temperature and high oxygen levels. It show the oxidation terminal toxic compounds.[30,31] Capability of entrapment and the release rate is also vary in accordance to physical characteristic of the drug predominantly that is its octanol - Water divider coefficient. Entrapment for those drugs is much higher. The leakage rate of liposome is usually higher in case of non-polar drugs. Liposomes enclosed in proteins were separated quickly from the movement of liver and spleen, with modest contribution by previous tissues. Reticuloendothelial system, mainly the Kupffer cells of the liver, plays the main role in liposomal removal from the circulation, though there is also other electron microscopic confirmation method by which hepatic parenchyma cells confirms the liposome clearance. In addition, it has been recommended that the nature of charge on liposome influences their tissue distribution, which is possible by movement of liposomes within cellular membranes.[32,33] The fraction globulin inside plasma proteins can bind highly to liposomes thus pressurizing both- (1) uptake of cellular rate (2) hoax drugs escaping. Liposomes, at least that bear an optimistic charge, have been seen to be in motion in the pathway of human equilibrium, and this could possibly lead to lyses of liposomes. Liposomes are also subject to decomposition by plasma phospholipids action. Liposomal are physically stable with colloidal fixedness. DLVO theory is use for the for the steadiness of colloidal solution. The two depended predicated is fixed for non-dependent types of forces. The Vander walls forces and repulsive forces are present in between these forces. These changes in colloidal solution have molecular level and has the molecular level. The main aggregation, synthesis, co-acervation and floating are the particle level. Liposome aggregation and fusion is the main reason for the instability of these. Vander wall interaction is present in between aggregation and sedimentation. These have smooth and flat surface of membranes. For the enhancement of the process attributes of residual solvents are most important.[34,35] For uncharged membranes arrangement of liposome aggregates. Medically formulation made of pH sensitive liposomes should be stable in the blood stream. In blood mechanisms acts as destabilisations for liposomes, including high density lipoprotein (HDL) and the balance system. The pH-sensitivity of liposomes is decreased after

incubation in plasma. Divalent cations, such as Ca2+ and Mg2+, are significant. The cation shows synthesis of phosphatidyl serine vesicles and DOPE/OA liposomes. Ca2+ and Mg2+ are cation and anion it become more stable. [36,37]

1.8 Application of Liposomes

(1) Medicinal applications of liposomes

In pharmacology, liposome has some application. It helps to classified the medicine, therapeutic and diagnosis. Many of the drugs are exceptionally slender therapeutic windows. It has the potent dose and lethal dose is very low. Toxicity can be decreases and increases by carrier of drugs and it changes the chronological arrangement. It has pharmacokinetic and bio-distribution. For liposomal indemnity and limitations of drugs are used. Liposomal communication the cells and their in-vivo study after admiration. The cell fusion rarer. bilayer constituent is most complex immune system. The coating is massive with bio macromolecules. It has small particles. Microbes and bacteria and colloids are present in this cell. Immune system improves the biocompatible and non-recognizable surfaces. [38,39]

(2) Improved solubility of lipophilic and amphiphilic drugs

Some anticancer drugs is been encapsulated by liposome with various concentration and it was soluble in aqueous. The drug precipitation and formation of gel by liposome is encapsulated.[40,41]

(3) Liposomes in parasitic diseases and infections

phagocytic cells which are present in the body may digest the liposomes. It was injected intravenous. The ideal vehicle for drug molecules targeting is macrophages. Trojan horse like mechanism is the best example of this. There are several parasitic diseases. It has several mononuclear phagocytic systems.

(4) Anticancer therapy by liposomes

The anticancer mediators are toxic and the liposomal shows less free drugs. The cell dividing is stop by anthracyclines. In which DNA is stop dividing. Tumours contains these types of cells. These are also found in GIT mucosa, hair and blood cells. These are very toxic. Adriamycin are most use. Above all, acute toxicities and dose of drug is limited by its cumulative cardiotoxicity.[42,43]

(5) Liposome in immunology

Liposomes are the most important carriers of this antigens. This antigen may contain excipients. The pathogens are mimic by this antigen. It develops the immune system. Mechanism which promotes the antigen cells and encapsulated the lymphocytes. Immuno-potentiators are improve the liposomes. Immunological events are investigation by liposomal vesicles. Foreign cell are damage and membrane sensitized haptenic antigens. It has cytotoxic effector cells. [44,45]

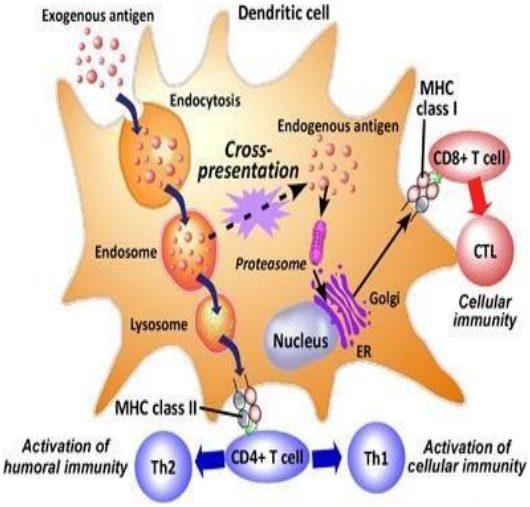

Figure 3. Liposome in immunology

(6) Application of liposomes in Cosmetic industry

It also be used in delivery of various cosmetic products. In addition, liposome acts as a carrier themselves offering compensation. Liposomes can as a reservoir which replenishes lipids mainly, linolenic acid.

The recent drugs and delivery of the compounds are harsh. It is used for the administration and cosmetic products. Liposomal paste has cosmetic products is use as a creams, gels and ointments. It is use as extracts, moisturizers and antibiotics. It has recombinant proteins for wound and healing. Anti-aging creams are available for this category. 10% of market liposomal are share over $10 billion dollars. Liposomes are non-interactive, non-irritating, water-based matrix with active ingredients.[46,47]

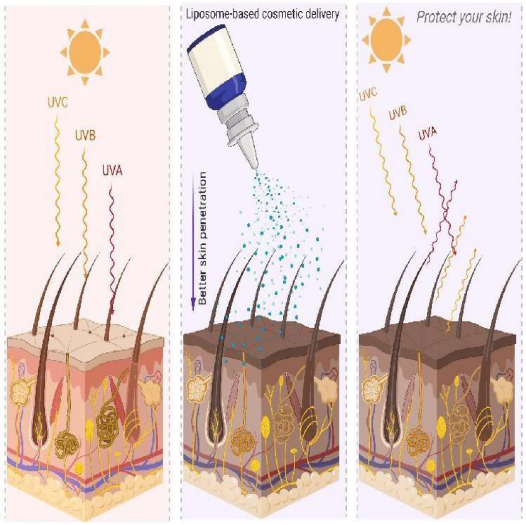

Figure 4. liposomes in Cosmetic industry

1.9 Acne vulgaris

This is also known as acne. It was characterized by human skin. It shows red skin and whiteheads, pinheads and papules, pimple and scarring. Skin is affected by acne with dense sebaceous follicles. It affected face, chest and back. It was inflammatory and non-inflammatory. Androgen stimulation are affected by pilosebaceous lesions. 80-90% of teenagers are affected by acne. This caused by androgen level increase. It was occurring during releasing of testosterone in puberty. It was vanished by time and age. When it become large it causes cyst and inflammatory are also called nodulocystic. It was grown on hair follicles, groin and armpit area. Acne usually occurs during adolescence. Come dones is shown by acne. Rosacea acne is the synonym. Chloracne is the polyhalogenated compounds.[48,49,50]

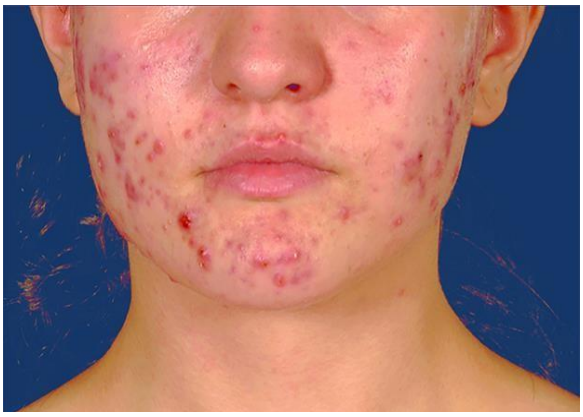

Figure 5. Face acne

1.9.1 Signs and Symptoms of Acne

papules, nodules and seborrhoea are symptoms of acne. It shows psychological and social problems with skin colour.

1.9.2 Etiology

When the follicle, hyperkeratinisation and keratin is blocked acne is developed. Production of androgen are enlarged and the production of sebum is increased. Comedo is formed when enlargement of microcomedo and closed comedo. Comedomes is formed when sebaceous gland is clogging with sebum and oil or skin dead cells.

The bacteria which cause acne is *bacterium Propionibacterium acnes.* These bacteria cause inflammation and infected the papules in dermis. It gives redness, scarring and hyper pigmentation.[51,52]

1.9.3 Environmental Factors

High humidity, sweating and skin hydration are the main factors which causes acne. Certain dirt and cooking vaporization like petroleum derivatives are affected this.

1.9.3.1 Hormonal

In the age of puberty, menstrual cycle may cause acne. The androgens hormone level is increased and the follicle glands may enlarge and the production of sebum is increases. Some steroids like anabolic steroids may also give this affect. In older these problems may also arise.[53,54]

1.9.3.2 Genetic

The polygenic disease is not followed by Mendelian inheritance pattern. It may include the Tumor necrosis factor-alpha, Interleukin-1 alpha, CYP1A1.[55,56]

1.10 Diagnosis

a) Pillsbury scale: It classifies the severity of acne ranging from 1 (least severe) to 4 (most severe).

b) Cook's acne grading scale: It sees the images to grade severity of acne ranging from 0 (least severe) to 8 (most severe).

c) Leeds acne grading technique: It counts and classifies inflammatory and noninflammatory lesions ranging from 0 to 10.[57,58]

1.11 Management

Various medicines are used for treatment of acne. Benzoyl peroxide is first line treatment for mild and moderate acne due to its effectiveness and mild side effects like irritant dermatitis, dryness of the skin, redness and peeling. It helps to prevent formation of comedones caused by P. acnes bacterium and has anti-inflammatory properties.

1.12 Antibiotics

Antibiotics are used against antimicrobial activity. Antibiotics including Clindamycin, erythromycin and tetracyclines. [59,60]

1.12.1 Antiseborrheic Drugs

Concentration of sulfur may affect the skin. It act as a antiseborrheic and keratolytic effect.

1.12.2 Topical Sulfur and Sodium Sulphacetamide

Sulfur is present in every cosmetic product like lotions, creams, etc. sulfur is useful in the treatment of dermatitis. It has anti-inflammatory properties which is use for the treatment of acne.

1.12.3 Salicylic acid

These drugs may be use for the bactericidal properties. This drug can obstruct the pores of skin and shedding promotes in epithelial cells of skin. This may cause hyperpigmentation.[61,62]

1.12.4 Anti-androgen treatment

Oral contraceptives is use for the treatment of acne. Combination of drugs of progestins may give the beneficial.

1.12.5 Topical retinoids

Anti-inflammation may posses' topical retinoids. Follicle cell is preventing the hyperkeratization blocking. Some drugs which are use adapalene and tazarotene. Vitamin A and isotretinoin have some side effect like skin irritation and flushing.[63,64]

1.12.6 Oral retinoids

Moderate and severe acne is affected by Isotretinoin. 80% of people are reported. Around 50 to 20% patient is second.[65,66,67]

2. CONCLUSION

Because of their advantages, liposomes appear to be a promising candidate for use as drug carriers for topical medications. They can function as sustained release depots, releasing encapsulated medicines with half-

lives varying from 0.6 to 11 days. They are diverse in terms of size and surface features. In addition, a new type of liposomes, the so-called "collagen modified liposomes," can modulate the interaction between liposomes and between liposomes and cells thanks to the features of the collagen on their surfaces. This may really increase the ability to regulate the release of the medicine. Liposomal formulations that are administered topically, especially those made from lipid mixes with a stratum corneum-like composition, would be an efficient delivery system for the treatment of skin conditions. These liposomal formulations can meter enough medication into deeper tissue to treat skin symptomology because they give sustained, increased levels in deeper strata of the skin. This metering should also lessen the likelihood of unfavorable systemic drug side effects or increased systemic drug absorption.

3. REFERENCES

1. Andreas, W., Karola, V.U., 2011. Impact of Alcoholic Solvents on the Recovery of Phospholipids in HPLC Analysis. *Journal of Drug Delivery*. 1-9.
2. Azanza, J.R., Sadaba, B., Reis, J., 2015. Liposomal formulations of amphotericin B: differences according to the scientific evidence. *Revista Espanola De Quimioterapia.* 28(6), 275-281.
3. Abraham, S.A., Waterhouse, D.N., Mayer, L.D., Cullis, P.R., Madden, T.D., Bally, M.B., 2005.The liposomal formulation of doxorubicin.*Methods in Enzymology*.391, 71-97.
4. Azad Hussain, L., Shahida, H.,Tanzeel ,A. ,Mohd A., 2012. Effect of a Polyherbal Unani formulation in acne vulgaris: A preliminary study. *Journal of Ayurveda and integrative medicine*.3 (4), 180-3.
5. Akbarzadeh, A.,Rezaei-Sadabady, R., Davaran, S., Joo ,S.W., Zarghami ,N. Y., Samiei, M., Kouhi ,M., Nejati-Koshki, K., 2013.Liposome: classification, preparation, and applications..*Nanoscale Research Letters*.8(1),102.
6. Abbasi,M.A.,Kausar,A.,Rehman,AU .,Saleem,H.,Jahangir,S.M.,Siddiqui,S .Z.,Ahmad, V.U.,2010.Preparation of New Formulations of Antiacne Creams and their efficacy..*African Journal of Pharmacy and Pharmacology*.4(6),298-303.
7. Bangham, A.D., Standish, M.M., Watkins, J.C., 1965.Diffusion of univalent ions across the lamellae of swollen phospholipids. *Journal* of *Molecular Biology*.13(1), 238-52.
8. Benner, N., Sammons, D., 2013. Overview of the Treatment of Acne Vulgaris, *Osteopathic Family Physician*. 5(5), 185–90.
9. Benech, R.O., Kheadr, E.E., Laridi, R., Lacroix, C., Fliss, I., 2002. Inhibition of Listeria innocua in cheddar cheese by

addition of Nisin Z in liposomes or by in situ production in mixed culture. *Applied and Environmental Microbiology*. 68, 3683–3690.

10. Betageri,G.V., 1993. "Liposome Drug Delivery System". *Technomic Publishing Co., Inc*., Pennsylvania.
11. Bhardwaj, A, Kori, M.L., 2015. Novel Spectrophotometric method development and validation for the estimation of Tazarotene and hydroquinone in liposomal gel formulation. *Current Research in Biological and Pharmaceutical Sciences*.4 (6), 6-11.
12. Bhardwaj,A., Kori, M.L.Mishra V.D., 2015. Polymer: Classification, Methods, Properties and their Characterization Review Article. *World Journal of Pharmaceutical Research*.4 (3), 1-21.
13. Bhardwaj,A. Kori, M.L., 2018. Devlopment and evaluation of Topical Liposomal Gel Loaded with Tazarotene in Combination with Hydroquinone. *Asian Journal of Pharmaceutical Education and Research* .7 (2), 70-85.
14. Bhardwaj,A. Kori, M.L., 2018. Evaluation of Tazarotene Loaded Topical Liposomal Gel. *Asian Journal of Pharmaceutical Education and Research*.7 (2), 105-114.
15. Bhalani, U., Shah, K., 2015. Preparation and Evaluation of Topical Gel of Nigella sativa (kalonji). *International Journal of Research and Development in Pharmacy and Life Sciences.* 4(.4), 1669-1672.
16. Bhavsar, B., Choksi, B., Sanmukhani, J., Dogra, A., Haq, R., Mehta, S., Mukherjee, S., Subramanian, V., Sheikh, S., Mittal, R., 2015. Clindamycin 1% Nano-emulsion Gel Formulation for the Treatment of Acne Vulgaris: Results of a Randomized, Active Controlled, Multicentre Phase IV Clinical Trial. *Journal of Clinical and Diagnostic Research.* 8(8), 05-09.
17. Batzri,S., Korn,E.D., 1973.Single Bilayer Liposomes prepared without Sonication.*Biochimica et Biophysica Acta*.298(4), 1015–1019.
18. Budhiraja, A., Dhingra, G., 2015. Development and Characterization of a Novel Anti acne Niosomal Gel of Rosmarinic Acid. *Drug Delivery*. 22(6), 723-730.
19. Colom H. D., Obach R. M., 1991. *Journal of Pharmaceutical Sciences*. 80(10), 932-934.
20. Chang, H.I., Cheng, M.Y., Yeh, M.K., 2012. Clinically-Proven Liposome-Based Drug Delivery: Formulation, Characterization and Therapeutic Efficacy. *Open Access Scientific Reports*. 1(3), 2-8.

21. Charde, Y.M., Sharma, P.H., Choudhary, N.G., Avari, J.G., 2014. Development and Evaluation of Herbal Formulation for the Treatment of Acne. *International Journal of Pharma Sciences and Research*. 5(6), 2250-2260.
22. Cipolla, D., Blanchard, J., Gonda, I., 2016. Development of Liposomal Ciprofloxacin to Treat Lung Infections. *Pharmaceutics*. 8 (6), 2-31.
23. Cipolla, D., Huiying, W., Eastman, S., Redelmeier, T., Gonda, I., Hak-Kim, C., 2014. Development and Characterization of an In-Vitro Release Assay for Liposomal Ciprofloxacin for Inhalation. *Journal of pharmaceutical sciences*. 103, 314-327.
24. Devi, R., Prasad, C.M., Renganathan, A., Kasthuri, S., Sundhararajan, R. Deepa, N., 2015. Formulation Characterization and Evaluation of Fluconazole Liposomes. *Der Pharmacia Sinica*. 6(5), 61-66.
25. Dhole, A.R., Shendage, S., Pethkar, S., 2014. Drug used in Psoriasis. *International Journal of Universal Pharmacy and Bio Sciences*. 3(2), 210-212.
26. Daud, F.S., Wankhede, S., Joshi, M., Pande, G., 2013. Development of Herbal Anti acne Gel and its Evaluation Against Acne Causing Bacteria Propionibacterium Acne and Staphylococcus Epidermidi. *International Journal of Research in Ayurveda and Pharmacy*.4(5), 781-786.
27. Dawson, A.L., Dellavalle, R.P., 2013. Acne Vulgaris.*BMJ*.346, 2634.
28. Danilo, D.L. 1997. "Liposomes in Gene Delivery". *CRC press*.
29. Deamer, D., Bangham, A.D., 1976. Large volume Liposomes by an ether Vaporization Method. *Biochemistry Biophysics Acta*. 443(3), 629–634.
30. Dua, J.S.,Rana, A.C.,Bhandari,A.K.,2012.Liposome: Methods of Preparation and Applications. *International Journal of Pharmaceutical Studies* and *Research*. 14-20.
31. De, A.,Gil, A. K., 2013. Proniosomal Gel of Tretinoin for the Treatment of Acne Vulgaris .*Journal of Applied Pharmaceutical Science*.3(07),081-086,
32. Egbaria, K., Weiner, N., 1990. Liposomes as a Topical Drug Delivery System. *Advanced Drug Delivery Reviews*. 5,287-300.
33. Ezhumalai, K., Ilavarasan, P., Murali Mugundhan, R., Sathiyaraj, U., Rajalakshmi, A.N., 2011.Transdermal Patches in Novel Drug Delivery System. .*International Journal of Pharmacy&Technology*. 3(2), 2402-2419.
34. Fatima, G.X., Joan, V.R., Rahul, R.S., Shanthi, S., Latha, S., Shanmuganathan, S., 2015. Formulation and Evaluation of

Polyherbal Anti-acne Gel. *Advanced Journal Pharma Life Science and Research*. 31,5-8.

35. Flaten, G.E.,, Chang ,T.T., Phillips, W.T., Brandl, M., Bao, A.,Goins, B., 2012. Liposomal Formulations of Poorly Soluble Camptothecin-Drug Retention and Biodistribution 3-30.
36. Gabizon, A., Goren, D., Cohen, R., Barenholz, Y., 1998. Development of Liposomal Anthracyclines: from basics to Clinical Applications. *Journal of Control Release*. 53, 275–279.
37. Goodman, G., 2006. Managing Acne Vulgaris Effectively: *Australian Family Physician*. 35(9), 705-9.
38. Gregoriadis, G., 1984. Liposome Technology. *CRC Press, Boca Raton*, Volumes I, II and III, 268, 231,292.
39. Gupta, A.K., Nicol, K., 2004.The Use of Sulfur in Dermatology. *Journal of drugs in dermatology*. 3(4), 427-431.
40. Ganesh,G.N.K.,Meghna,G.,Karri,N. R.V.V.S.,Tiwari,S.V.,Gunda,R.,Che nnareddy,S.R .,2014.Formulation and Evaluation of Tolnaftate Loaded Topical Liposomal Gel for Effective Skin Drug Delivery to Treat Fungal Diseases. *Journal of Chemical and Pharmaceutical Research*.6(10),856-866.
41. Harper, J.C., 2009. Acne Vulgaris, eMedicine. *South African Pharmaceutical Journal*. 12-21.
42. Hamilton, R.L., Guo, L.S.S., 1984. Liposomes Preparation Methods. *Journal of Clinical Biochememistry Nutrition*. 7,175.
43. Himanshu, A., Sitasharan, P., Singhai, A.K., 2011. Liposome-as Drug Carriers..*International Journal of Pharmacy & Life Sciences*. 2(7), 945–951.
44. Horwitz, S., Lowe, N., Tanghetti, E., Draelos, Z., Menter, A., 2006. Tazarotene Versus Tazarotene Plus Hydroquinone in theTtreatment of Photo Damaged Facial Skin: a Multicenter, Double-Blind, Randomized Study. *Journal of Cosmetic Laser Therapy*. 8(3), 121-127.
45. Higuchi, T., 1963.Mechanism of Sustained-Action Medication, Theoretical Analysis of Rate of Release of Solid Drugs Dispersed in Solid Matrices. *Journal of Pharmaceutical Sciences*. 52,1145-9.
46. Hsieh,M-Fa.,Chen,C-H., 2012.Review:Delivery of Pharmaceutical Agents to Treat Acne Vulgaris: Current Status and Perspectives. *Journal of Medical and Biological Engineering*.32(4),215-224.

47. Indian pharmacopoeia, 2007. Government of India, Ministry of Health and Family Welfare, the Indian pharmacopoeia commission, Ghaziabad (India); 4th edition volume 1.
48. Irby, C.E., Yentzer, B.A., Feldman, S.R., 2008. A Review of Adapalene in the Treatment of Acne Vulgaris. *Journal of Adolescent Health*. 43, 421–424.
49. Ismail,S.,Khattab,A., 2016.Formulation and Evaluation of Oxiconazole Nitrate Mucoadhesive Nanoemulsion Based Gel for Treatment of Fungal Vaginal Infection. *International Journal of Pharmacy and Pharmaceutical Sciences.* 8(3), 33-40.
50. Jain, N. K., 2001. Advances in Controlled and Novel Drug Delivery. 1st Edn, CBS Publication, New Delhi. 428- 451.
51. Korsmeyer, R.W., Gurny, R., Doelker, E., Buri,P.I., Peppas, N.A., 1983. Mechanisms of Solute Release from Porous Hydrophilic Polymers. *International Journal of Pharmaceutics*. 15(1), 25-35.
52. Khoshneviszadeh R., Bazzaz, B.S.F. .Housaindokht, M.R, Ebrahim-Habibi A., Rajabi, O., 2015. UV Spectrophotometric Determination and Validation of Hydroquinone in Liposome. *Iranian Journal of Pharmaceutical Research.*14 (2): 473-478.
53. Leyden, J.J., Philadelphia, M.D., Pennsylvania, D., 2003. A Review of the use of Combination Therapies for the Treatment of Acne Vulgaris. *Journal of The American academy of dermatology.* 49(3), 200-210.
54. Lieberman, H.A., Lachman, L., Schwartz, J.B., 1989. Pharmaceutical Dosage Forms, 2nd edition, Marcel Dekker Inc, New York. 1,195-229.
55. LopezGarcia,P.,Santoro,M.I.,Kedor-Hackman,E.R.M.,Singh,A.K.,2005.Development and Validation of a HPLC and UV Derivative Spectrophotometric Methods for Determination of Hydroquinone in Gel and Cream Preparations. *Journal of Pharmaceutical and Biomedical Analysis*.39 (3-4), 764-768.
56. Maheswaran, A., Brindha, P., Mullaicharam, A.R., Masilamani, K., 2013. Design Development and Evaluation of Curcumin Liposomes. *World journal of pharmacy and pharmaceutical sciences*.3 (1), 480-492.
57. Makhmalzadeh, B.S., Zahra, A. Azarpanah, A., 2011. Preparation and Evaluation of Mafenide Acetate Liposomal Formulation as Escher Delivery System. *International*

Journal of Drug Development & Research.3 (4), 129-140.

58. Mallesh, K. Diwan, P.V., 2011. Estimation of Prednisolone in Proliposomal Formulation Using rp-hplc Method. *International Journal of Research in Pharmaceutical and Biomedical Sciences*. 2(4), 1663-1669.
59. Mallesh, K., Srinivas, C., Nagasree, K., Prakash, V., Diwan, S., 2012. Formulation and Evaluation of Prednisolone Proliposomal Gel for Effective Topical Pharmacotherapy. *International Journal of Pharmaceutical Sciences and Drug Research*. 4 (1), 35-43.
60. Messerer, C.L., Ramsay, E.C., Waterhouse, D., Ng R., Simms, E.M., Harasym, N., Tardi, P., Mayer, L.D., Bally, M.B., 2004. Liposomal Irinotecan: Formulation Development and Therapeutic Assessment in Murine Xenograft Models of Colorectal Cancer.*Clinical Cancer Research.*10 (19), 6638-49.
61. Jain, S., Bhandra, D., Jain, S., Jain, N. K., 1997. Controlled and Novel Drug Delivery. 1st Edn, CBS Publishers and Distributors, New Delhi. 426-451.
62. Jain ,S., Dubey, P.K., Mishra, V., Mahor, S., Vyas, S.P., 2004.Liposomes Modified with Cyclic RGD Peptide for Tumor Targeting. *Journal of Drug Targeting.* 12(5), 257-264.
63. Jain, S., Umamaheshwari, R. B., Bhadra, D., Jain, N.K., 2004. Ethosomes: A Novel Vesicular Carrier for Enhanced Transdermal Delivery of an Anti-HIV Agent. *Indian Journal of Pharmaceutical Sciences.* 66(1), 72- 81.
64. Jogarami, R., Jain, P., Sharma, S., 2012.Validated UV Spectrophotometric Method Development for Simultaneous Estimation of Tazarotene and Hydroquinone in Gel Preparation. *Journal of Pharmacy Research* .5(4), 2273-2275.
65. Johnston, M.J., Semple, S.C., Klimuk, S.K., Ansell, S., Maurer, N., Cullis, P.R., 2007. Characterization of the Drug Retention and Pharmacokinetic Propertiesof Liposomal Nanoparticles Containing Dihydrosphingomyelin.*Biochimistry Biophysics Acta*.1768 (5):1121-1127.
66. Joshi, A.A.,Nagarsenker, M.S., 1997. Preparation, Characterization, and Evaluation of Liposomal Dispersions of Lidocaine. Drug Development and Industrial Pharmacy. 23, 1159-1165.
67. Katsambas, A.K., Essinioti, C.D., 2008. New and Emerging Treatments in Dermatology: Acne. *Dermatologic Therapy*. 21, 86–95.