IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

TRANSFEROSOMES- NOVEL DRUG DELIVERY SYSYTEM – A REVIEW

Dr.Sunitha Reddy M. and Anusha M*

Department of Pharmaceutics, Center for Pharmaceutical Sciences, Institute of Science and Technology, JNTUH, Kukatpally, Hyderabad, 500085, Telangana,India.

Abstract: Transferosomes is a proprietary drug delivery technology, an artificial vesicle suitable for controlled and potentially targeted drug delivery. Transferosomes have recently been introduced, which are capable of delivery of low as well as high molecular weight drugs. This offers several potential advantages like avoidance of first pass metabolism, predictable and extended duration of activity, minimizing undesirable side effects, utility of short half life drugs, improving physiological and pharmacological response and have been applied to increases the efficiency of the material transfer across the intact skin. Composition of transferosomes contains edge activators and phospholipids. Transferosomes penetrate the stratum corneum by intracellular route or the Tran cellular route by the generation of "osmotic gradient". The characterization of Transferosomes is similar to that of other vesicles like liposomes, noisome and micelles.

KEY WORDS: Transferosomes, Targeted drug delivery, Controlled drug delivery, Osmotic gradient, Tran-cellular route.

INTRODUCTION

Transferosomes have been defined as specially designed vesicular particles consisting of at least one inner aqueous compartment enclosed by lipid vesicles; liposomes in morphology, but, functionally, transferosomes are suitably deformable to go through pores much smaller than their own size. The word Transferosomes was introduced by Gregor Cevc in the year 1991.transferosome is a combination of two words transfero and soma. Transfero means to carry across and soma means body. Transferosomes is an artificial vesicle designed to exhibit the characteristics of cell vesicle or a cell engaged in exocytosis and thus suitable for controlled and potentially, targeted drug delivery. The reason for using vesicles in transdermal drug delivery is based on the fact that they act as drug carriers to deliver entrapped drug molecule across the skin, as well as penetration enhancers because of their composition. Transferosomes can deform and pass through narrow constriction without measurable loss. Transferosomes can pass through tiny pores nearly as efficiently as water, which is 1500 times smaller.

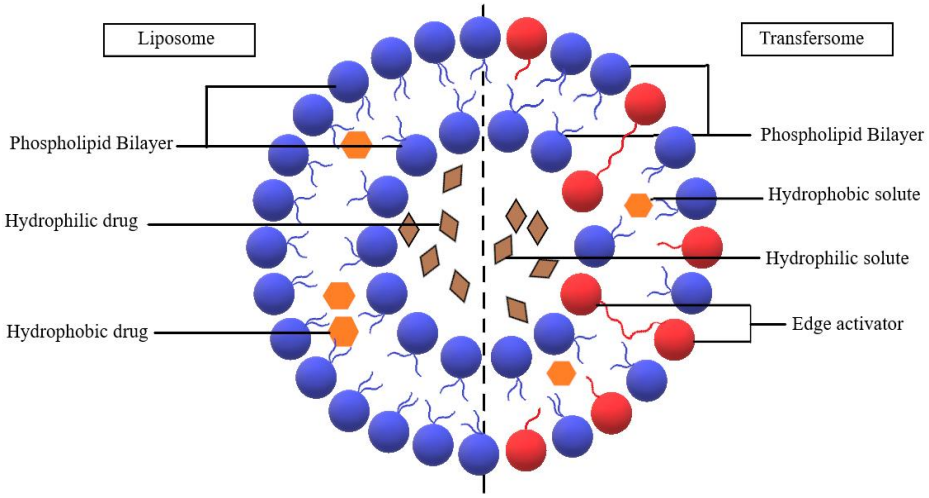
Advantages

- They are biocompatible and biodegradable as they are made from natural phospholipids similar to liposomes.
- They protect the encapsulated drug from metabolic degradation.
- Transferosomes shows greater permeation of the drugs through the skin.
- These serves as carrier for both small and large molecular weight drugs.
- In Transferosomes, percentage of the drug entrapment is more. In case of lipophilic drug near to 90%.
- Protects the entrapped drug from atmospheric degradation.
- They have high entrapment efficiency this high deformability gives better penetration of intact vesicles.
- They can act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anesthetic, corticosteroids, sex hormone, anticancer, insulin, gap junction protein, and albumin.
- Transferosomes possess an infrastructure consisting of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with wide range of solubility.
- They act as depot, releasing their contents slowly and gradually.
- They can be used for both systemic as well as topical delivery of drug.

Disadvantages

- Transferosomes are chemically unstable because of their predisposition to oxidative degradation.
- Purity of natural phospholipids is another criteria militating against adoption of transferosomes as drug delivery vehicles.
- These formulations are very expensive.
- Hydrophilic nature of drugs permeates the skin slowly to be of therapeutic benefit.
- Transdermal drug delivery system is not suitable for drugs with higher doses.
- Delivery of drug through transdermal route may cause skin irritation and hypersensitivity reaction.
- Drug molecule which is using for transferosomal delivery must be potent.

Structure and composition of Transferosomes



Composition:

- Transferosomes are mainly composed of 2 main aggregates like phospholipids and edge activators.

Phospholipids:

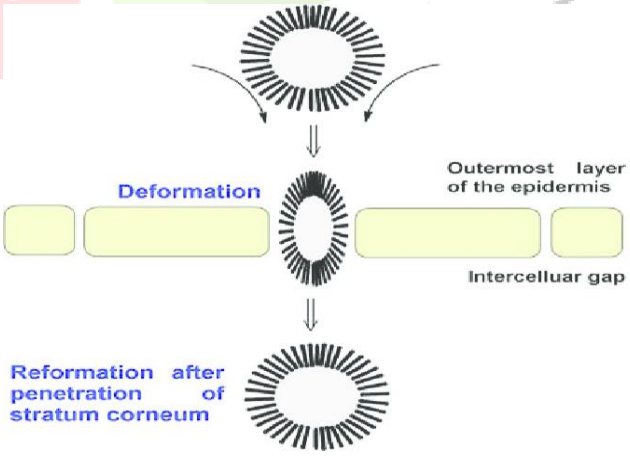
- Phospholipids form the membrane and provide stability to vesicles. Therefore, both membrane forming agents i.e. phospholipids and the destabilizing agent.
- Among phospholipids, soya phospholipids like soya phosphatidylcholine and hydrogenated soya phosphatidylcholine are most commonly used.

Edge activators:

- An edge activator consists usually of single chain surfactant of non ionic nature that causes destabilization of the lipid bilayer thereby increasing its fluidity and elasticity.
- Various edge activators like span 40, span 60, span 80, span 85, tween 20, tween 60, tween 80, sodium oleate, sodium cholate, sodium deoxycholate, dicetylphosphate (DCP), KG (dipotasium glycrhizinate) etc. have been reported for preparation of transferosomes.
- The nature and ratio of different edge activators affect the physicochemical properties of vesicles including their size, entrapment efficiency and zeta potential.

Mechanism of Action of Transferosomes:

- Interaction between the lipid residue and the proximal water makes the lipid to attract water molecules inducing hydration and the lipid vesicles move to the site of higher water concentration. This difference in water content across the skin stratum and epidermis develops transdermal osmotic gradient leading to penetration of transferosomes across the skin.
- Mechanism of drug penetration the mechanism of drug penetration can be described in three purposed mechanisms.
- Transferosomes by enforcing its own route induce hydration that widens the hydrophilic pores of the skin causing the gradual release of the drug that bind to the target organ.
- Transferosomes act as permeation enhancers that disrupt the intercellular lipid from the stratum that ultimately widens the pores and facilitates the molecular interaction and penetration of system across the skin.

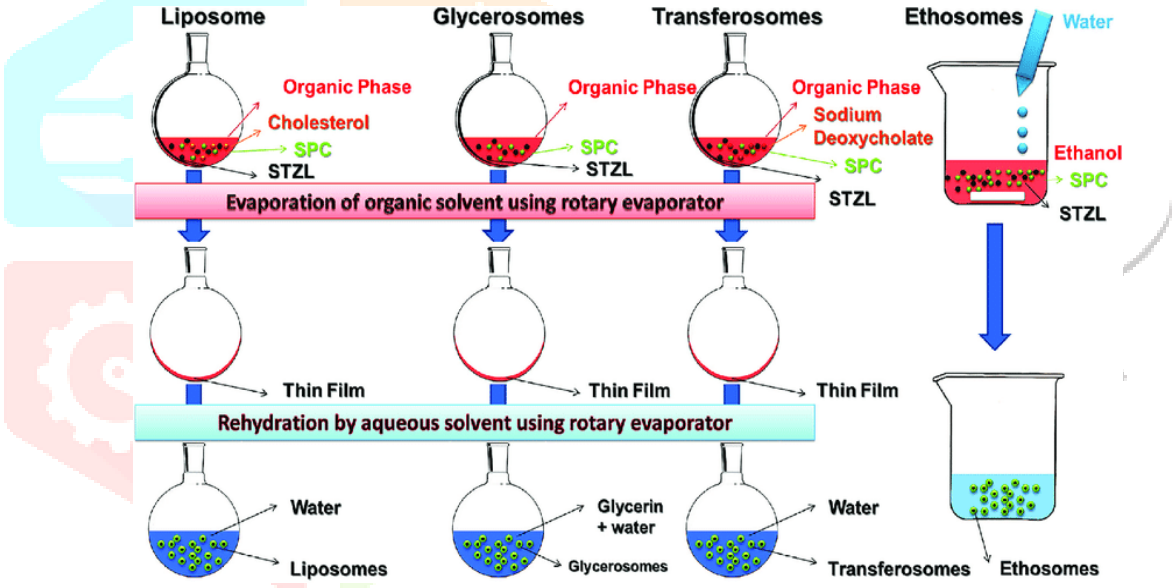


Method of Preparation of Transferosomes

1. **Rotary Film Evaporation Method**
2. **Reverse Phase Evaporation Method**
3. **Vortex/Sonication Method**
4. **Ethanol Injection Method**
5. **Freeze Thaw Method**

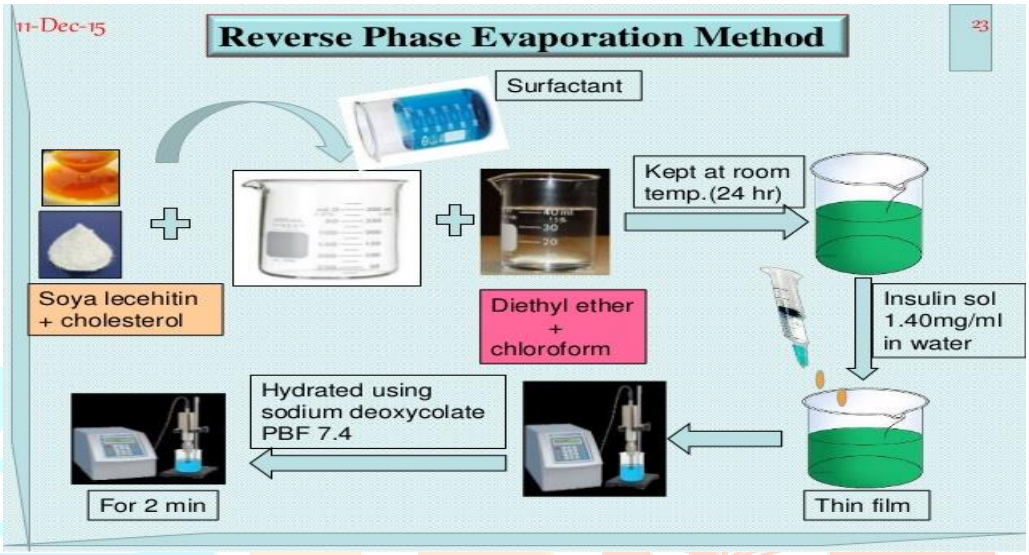
1. Rotary Film Evaporation Method/ Modified Hand Shaking Method

This method is also known s modified hand shaking method. Lecithin along with the edge activator (surfactant) and drug are dissolved in a mixture of chloroform and ethanol (1:1 ratio). The mixture is subjected to evaporation to remove the organic solvent using temperature above the transition temperature of lipid by hand shaking. The thin lipid film is left overnight to ensure complete removal of the organic solvent. Above prepared thin film is hydrated by using pH6.5 buffer by rotation at 60RPM for 1hr at corresponding temperature. The resulting vesicles were swollen for 2hrs at room temperature. To prepare small vesicles, resulting vesicles were sonicated at room temperature.



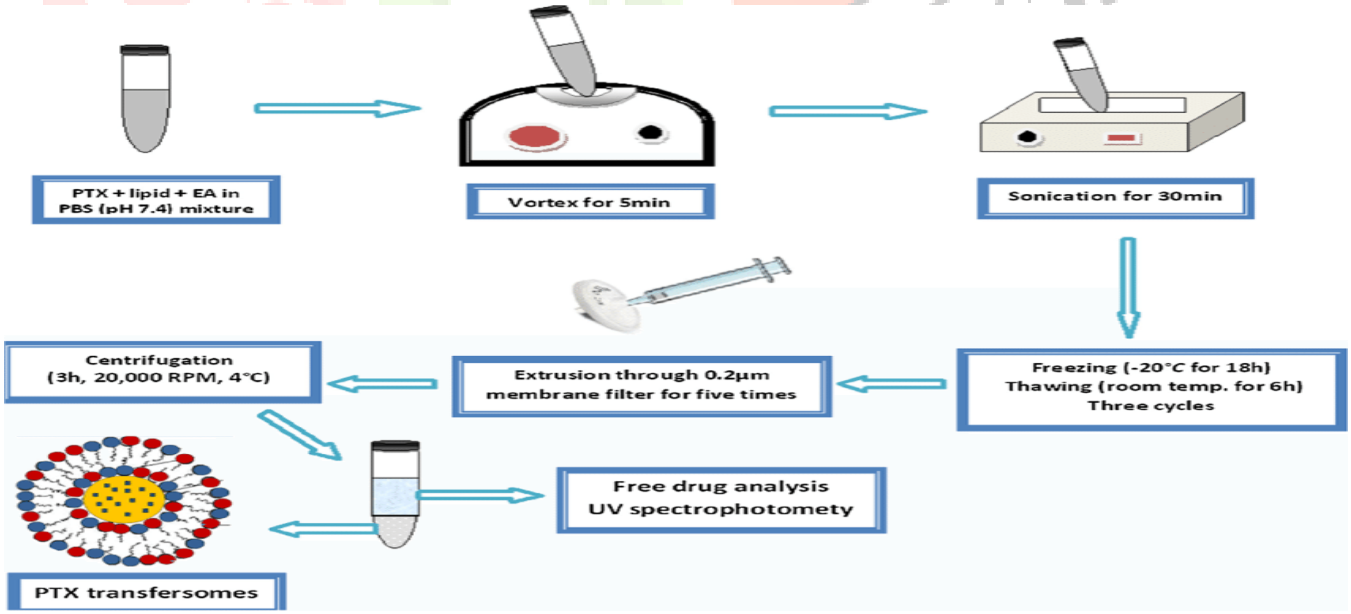
2. Reverse Phase Evaporation Method:

In this method, lipids dissolved in organic solvents are taken in a round bottom flask. Aqueous media containing edge activators is added under nitrogen purging. The drug can be added to the lipid or aqueous medium based on its solubility characters. The formed system is then sonicate until it become a homogeneous dispersion and should not separate for at least 30 minutes after sonication. The organic solvent is then removed under reduced pressure. At this point, the system will convert to a viscous gel followed by the formation of vesicles. The non-encapsulated material and residual solvents can be removed using dialysis or centrifugation.



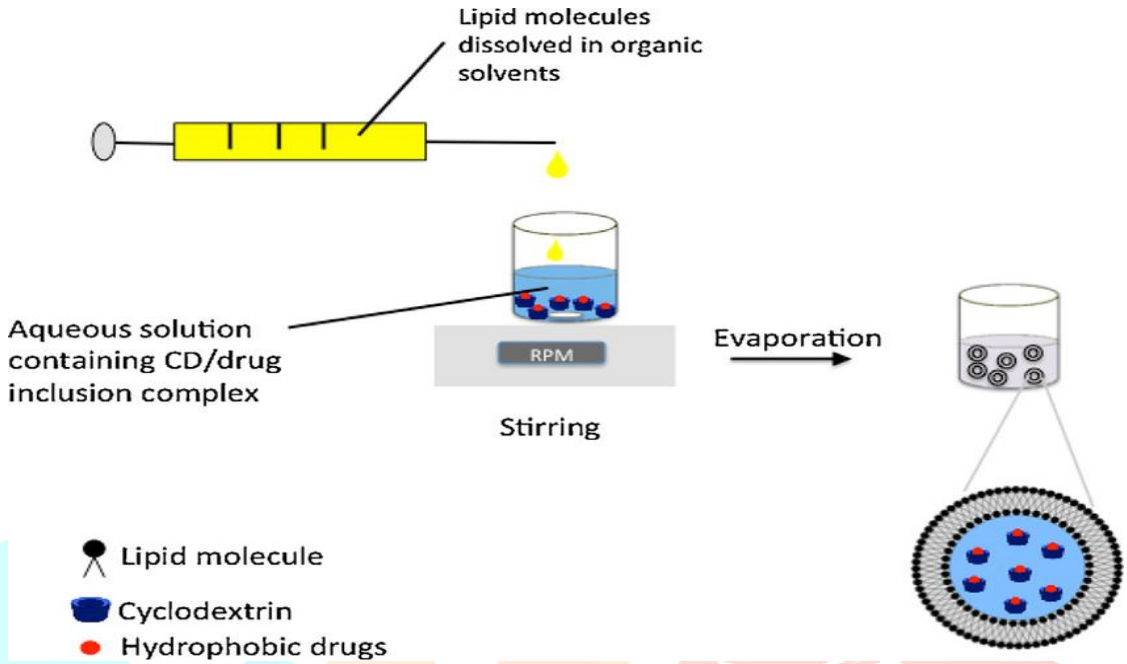
3. Vortex/Sonication Method:

In this method, phospholipids and edge activators are mixed by vigorous shaking and agitation in order to suspend them in phosphate buffer. The formed milky suspension is then sonicated using vortex or bath sonicator followed by extrusion through polycarbonate membranes



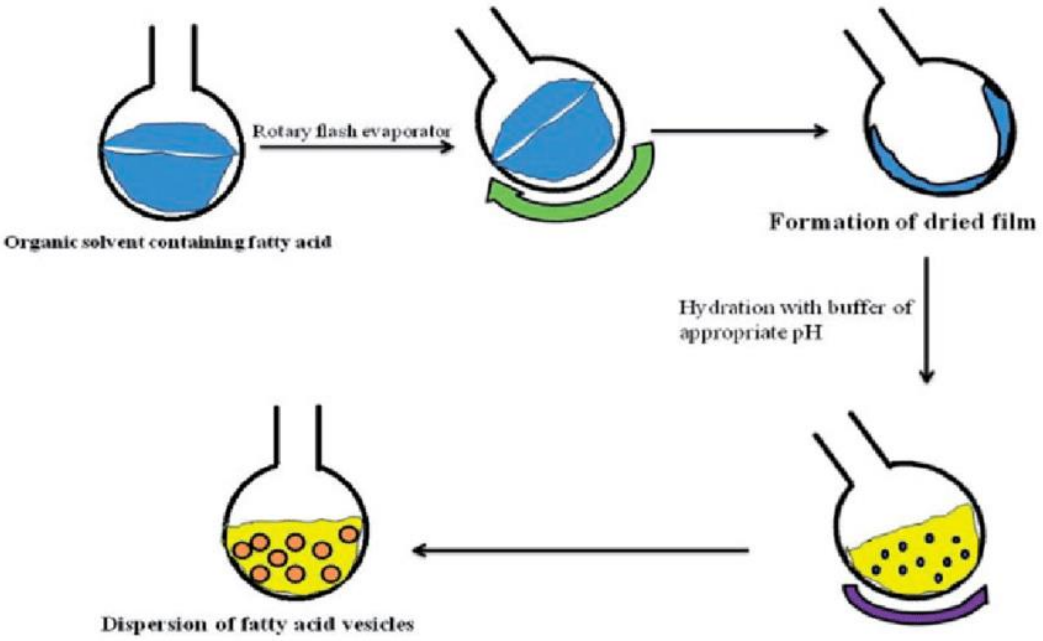
4. Ethanol Injection Method :

In this method, Drug along with aqueous solution is heated with continuous stirring at constant temperature... Ethanolic solution containing phospholipids and edge activators are injected into an aqueous solution drop wise. When the solution comes in contact with aqueous media the lipid molecules get precipitated and form bilayered structures. This method is more advantageous than other methods.



5. Freeze Thaw Method:

This method involves the exposure of prepared multi lamellar vesicles suspension to alternate cycles of very low temperature for freezing followed by exposure to very high temperature. The prepared suspension is transferred to a tube and dipped in a nitrogen bath (-30° C) for 30seconds. After freezing, it is exposed to high temperature in a water bath. This process is repeated for 8-9 times.



Characterization of Transferosomes:

The characterization of transferosomes resembles that of other vesicles like liposomes, niosomes and micelles.

a) **Vesicle Size, Size Distribution and Vesicle Diameter**
b) **Vesicle Shape and Type**
c) **Number of Vesicle per cubic mm**
d) **Entrapment Efficiency**
e) **Drug Content**
f) **Turbidity Measurement**
g) **Surface Charge and Charge Density**
h) **Penetration Ability**
i) **Occlusion Effect**
j) ***In-vitro* Drug Release**
k) ***In-vitro* Skin Permeation Studies**

Applications of Transferosomes:

a) Controlled release of drug
b) Peripheral drug targeting
c) Transport of large molecular weight compounds
d) Delivery of proteins and peptides
e) Delivery of insulin
f) Delivery of interferon
g) Delivery of anesthetics
h) Transdermal immunization
i) Delivery of NSAIDS
j) Delivery of Herbal Drugs
k) Delivery of Anticancer Drugs

Conclusion:

Ultra deformable vesicles like transferosomes are capable of providing an ideal solution to all transdermal drug delivery and transport related problems. Such highly deformable particles can thus be used to bring drugs across the biological permeability barriers, such as skin. They are especially useful for delivery of troublesome molecules like peptides and proteins. The elastic vesicles deform themselves to penetrate the skin through pores. It is more efficient & safer in composition then others. In this type of delivery, Drug release can also be controlled according to the requirement.

The exceptional quality of transferosomes to deform themselves depending on the environmental stress due to the presence of surfactants, often referred to as edge activators makes them very flexible for delivery of a wide range of molecules also having a good scope for targeted delivery. Transferosomes, thus, hold a bright and promising future in transdermal delivery of drugs.

References

1.Modi CD, Bharadia PD. Transfersomes: A newdominants for transdermal drug delivery. Am J PharmTech Res 2012; 2:71-91

2. Barry BW. Novel mechanisms and devices to enable successful transdermal drug delivery. Eur J Pharm Sci 2001; 14:101-14.

3.Hamidi M, Azadi A, Rafiei P. Hydrogel nanoparticles in drugdelivery.AdvDrug Deliv Rev 2008;60:1638-49.

4.Karande P, Mitragotri S. Enhancement of transdermal drug delivery via synergistic action of chemicals. Biochim Biophys Acta 2009;1788:2362-73.

5.Crommelin DJ, Eling WM, Steerenberg PA, Nässander UK, Storm G, De Jong WH, et al. Liposomes and immunoliposomes for controlled release or site specific delivery of anti-parasitic drugs and cytostatics. J Control Release 1991;16:147-54.

6.Yavlovich A, Singh A, Blumenthal R, Puri A. A novel class of photo-triggerable liposomes containing DPPC: DC8, 9PC as vehicles for delivery of doxorubcin to cells. Biochim Biophys Acta 2011;1808:117-26.

7. Patel N. N., Roop chandani V. K., Gupta A., "Proniosomes For Improved Transdermal Drug Delivery" The pharma research A Journal of Pharmacy Research, 2013; 8(2): 62-82.

8.Gupta A., Aggarawal G., Singla S., Rora R., A, "Transfersomes: A Novel Vesicular Carrier for Enhanced Transdermal Delivery of Sertraline: Development, Characterization and performance Evaluation," Sci Pharm, 2012; 80: 1061-1080.

9.Delivery System" International Journal of Applied Biology and Pharmaceutical Technology, Jan-Mar-2011; Wavle J.R BakliwalS.R, Rane B.R, Pawer S.P, "Transfersomes: A surrogated Carrier For Transdermal Drug 2(1). 13. Kavitha K, Bharath N, Mani T T., "Physical Permeation Enhancers for Transdermal Drug Delivery "Research of Journal of pharmaceutical, Biological and Chemical sciences, October- December 2011; 2(4): 66.

10. Benson HA. Transfersomes for transdermal drug delivery. Expert Opin Drug Deliv 2006;3:727-37.

11.Dubey V, Mishra D, Asthana A, Jain NK. Transdermal delivery of a pineal hormone: Melatonin viaelastic liposomes. Biomaterials 2006;27:3491-6.

Modi CD, Bharadia PD.

12.: A newdominants for transdermal drug delivery. Am J PharmTech Res 2012;2:71-91.

13.Nagasamy VenkateshD, KalyaniK, TulasiK,Swetha PriyankaV, Abid AliSK, KiranHC,Transfersomes: transdermal drug deliveryInternational Journal of Research in Pharmaceutical and Nano Sciences.2014; 3(4):266 – 276

14. Planas ME, Gonzalez P, Rodriguez L, et al. Noninvasive percutaneous induction of topical analgesia by a new type of drug carrier, and prolongation of local pain insensitivity by anesthetic liposomes. Anesth Analg. 1992;75:615–621. [Crossref], [Web of Science ®], [Google Scholar]

15. Mahor S, Rawat A, Dubey PK, et al. Cationic transfersomes based topical genetic vaccine against hepatitis B. Int J Pharm. 2007;340:13–19. [Crossref], [Web of Science ®], [Google Scholar]

16. Choi MJ, Maibach HI. Elastic vesicles as topical/transdermal drug delivery system. Int J Cosm Sci. 2005;27:211–221. [Crossref], [Google Scholar]

17. Guo J, Ping Q, Sun G, et al. Lecithin vesicular carriers for transdermal delivery of cyclosporin A. Int J Pharm. 2000;194:201–207. [Crossref], [Web of Science ®], [Google Scholar]

18. Jain S, Mishra D, Kuksal A, et al. Vesicular approach for drug delivery into or across the skin: current status and future prospects. Pharm Online. 2006;1:1–32. [Google Scholar]

19. Morrow DIJ, McCarron PA, Woolfson AD, et al. Innovative strategies for enhancing topical and transdermal drug delivery. Open Drug Deliv J. 2007;1:36–59. [Crossref], [Google Scholar]

20. Zaafarany GME, Awad GAS, Holayel SM, et al. Role of edge activators and surface charge in developing ultradeformable vesicles with enhanced skin delivery. Int J Pharm. 2010;397:164–172. [Crossref], [Google Scholar]

21. Cevc G. Transdermal drug delivery of insulin with ultradeformable carriers. Clin Pharmacokinet. 2003;42:461–474. [Crossref], [Web of Science ®], [Google Scholar]

22. Kumar R, Philip A. Modified transdermal technologies: breaking the barriers of drug permeation via the skin. Tropic J Pharm Res. 2007;6:633–644. [Crossref], [Web of Science ®], [Google Scholar]

23. Maurya SD. Enhanced transdermal delivery of Indinavir sulphate via transfersomes. Int J Comp Pharm. 2010;1:1–7. [Google Scholar]

24. Bangham AD, Standish MM, Watkins JC. Diffusion of univalent ions across the lamellae of swollen phospholipids. J Mol Biol. 1965;13:238–252. [Crossref], [Web of Science ®], [Google Scholar]

25. Singh H, Utreja P, Tiwary A, et al. Elastic liposomal formulation for sustained delivery of colchicine: in vitro characterization and in vivo evaluation of anti-gout activity. Aaps J. 2009;11:54–64. [Crossref], [Web of Science ®], [Google Scholar]

26. Kumar A, Adde S, Kamble R, et al. Development and characterization of liposomal drug delivery system for nimesulide. Int J Pharm Pharm Sci. 2010;2:87–89. [Google Scholar]

27. Charcosset C, Juban A, Valour J, et al. Preperation of liposomes at large scale using ethanol injection method: effect of scale up and injection devices. Chem Eng Res Des. 2015;94:508–515. [Crossref], [Web of Science ®], [Google Scholar]

28. Maestrelli F, Rodriguez M, Rabasco A, et al. Effect of preparation techniques on the properties of liposomes encapsulating ketoprofen- cyclodextrine complexes aimed for transdermal delivery. Int J Pharm. 2006;312:53–60. [Crossref], [Web of Science ®], [Google Scholar]

29.Zhang Y, Ng W, Feng X, et al. Lipid vesicular nanocarrier: quick encapsulation efficiency determination and transcutaneous application. Int J Pharm. 2017 10;516:225–230. [Crossref], [Web of Science ®], [Google Scholar]

30. Schlich M, Lai F, Murgia S, et al. Needle-free jet injection of intact phospholipid vesicles across the skin: a feasibility study. Biomed Microdevices. 2016;18:67. [Crossref], [Web of Science ®], [Google Scholar]

31. Ghanbarzadeh S, Arami S. Enhanced transdermal delivery of diclofenac sodium via conventional liposomes, ethosomes, and transfersomes. Biomed Res Int. 2013;2013:1–7. [Crossref], [Web of Science ®], [Google Scholar]

32. Ghannoum M, Isham N, Henry W, et al. Evaluation of the morphological effects of TDT 067 (terbinafine in Transfersome) and conventional terbinafine on dermatophyte hyphae in vitro and in vivo. Antimicrob Agents Chemother. 2012;56:2530–2534. [Crossref], [Web of Science ®], [Google Scholar]

33. Zhang YT, Xu YM, Zhang SJ, et al. In vivo microdialysis for the evaluation of transfersomes as a novel transdermal delivery vehicle for cinnamic acid. Drug. 2014;40:301–307. [Taylor & Francis Online], [Google Scholar]

34. Sigurgeirsson B, Ghannoum M. Therapeutic potential of TDT 067 (terbinafine in Transfersome): a carrier-based dosage form of terbinafine for onychomycosis. Expert Opin Investig Drugs. 2012;21:1549–1562. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

35. Rajan R, Vasudevan DT. Effect of permeation enhancers on the penetration mechanism of transfersomal gel of ketoconazole. J Adv Pharm Technol Res. 2012;3:112–116. [Crossref], [Google Scholar]
36. Vanic Z, Hafner A, Bego M, et al. Characterization of various deformable liposomes with metronidazole. Drug Dev Ind Pharm. 2013;39:481–488. [Taylor & Francis Online], [Web of Science ®], [Google Scholar]

37. Schmitt JV, Miot HA. Actinic keratosis: a clinical and epidemiological revision. An Bras sDermatol. 2012;87:425–434. [Crossref], [Web of Science ®], [Google Scholar]

38. Memon AA, Tomenson JA, Bothwell J, et al. Prevalence of solar damage and actinic keratosis in a Merseyside population. Br J Dermatol. 2000;142:1154–1159. [Crossref], [Web of Science ®], [Google Scholar]

39. Gupta AK, Paquet M, Villanueva E, et al. Interventions for actinic keratoses. Cochrane Database Syst Rev. 2012;12:CD004415. [Web of Science ®], [Google Scholar]