

Transfersomes: A Promising Nanoencapsulation Technique for Transdermal Drug Delivery System

¹Thorat Sanket B., ²Gadge Vinayak D., ³Thorat Aniket B., ⁴Gadge Shubham. C.,

⁵Datkhile Sachin V., ⁶Walmik Nikhil V., ⁷Indre Umesh M.

Students, Samarth Institute of Pharmacy, Belhe, Maharashtra, India^{1,2,6,7}

Students, Ashwin College of Pharmacy, Manchi hill, Maharashtra, India³

⁴Department of Pharmacology, Samarth Institute of Pharmacy, Belhe, Maharashtra., India

⁴Dr. Vitthalrao Vikhe Patil's Foundation College of Pharmacy, Ahemadnagar, Maharashtra, India

⁵Department of Pharmaceutics, Samarth Institute of Pharmacy, Belhe, Maharashtra., India

Abstract: *Transdermal delivery systems have gained a lot of interest in recent years due to their benefits compared to conventional oral and parenteral delivery system. It is the controlled and self-regulatory delivery systems that can improve patient compliance and provide a controlled release of therapeutic agents. The biggest challenge for transdermal delivery systems is the task of preventing the outer layer of the skin. Molecules weighing more than 500 Da and ionized compounds usually do not pass through the skin. Therefore, only a limited number of drugs can be administered by this route. The combination of drugs in transfersomes is one of the most effective ways to overcome this problem. Transfersomes combine the characteristics of liposomes with niosomes because Contain both liposomes (phospholipids and cholesterol) and niosomes as substances (nonionic surfactants; activists on edge). They have a two-dimensional structure that facilitates the encapsulation of lipophilic and hydrophilic, as well as amphiphilic, drugs with relatively high efficacy compared to conventional liposomes. Transfersomes are elastic in nature, can be deformed and squeeze like a solid fabric into holes that are much smaller than their size. This review aims to explain the concept of transfersomes, methodology, various methods of preparation and manufacture of materials and properties affecting transfersomes, as well as their latest applications in the administration of commercial drugs.*

Keywords: Transfersomes; Nano-encapsulation; Transdermal drug delivery system, Phospholipid.

REFERENCES

- [1]. Chaurasiya, P.; Ganju, E.; Upmanyu, N.; Ray, S.K.; Jain, P. Transfersomes: A novel technique for transdermal drug delivery. *J. Drug Deliv. Ther.* 2019, 9, 279–285.
- [2]. Modi, C.; Bharadia, P. Transfersomes: New dominants for transdermal drug delivery. *Am. J. PharmTech. Res.* 2012, 2, 71–91.
- [3]. Jain, A.K.; Kumar, F. Transfersomes: Ultradeformable vesicles for transdermal drug delivery. *Asian J. Biomater. Res.* 2017, 3, 1–13.
- [4]. Elsayed, M.A.; Abdallah, O.Y.; Naggar, V.F.; Khalafallah, N.M. Lipid vesicles for skin delivery of drugs: Reviewing three decades of research. *Int. J. Pharm.* 2007, 332, 1–16.
- [5]. Touitou, E.; Junginger, H.E.; Weiner, N.D.; Nagai, T.; Mezei, M. Liposomes as carriers for topical and transdermal delivery. *J. Pharm. Sci.* 1994, 83, 1189–1203.
- [6]. Yadav, D.; Sandeep, K.; Pandey, D.; Dutta, R.K. Liposomes for drug delivery. *J. Biotechnol. Biomater.* 2017, 7, 1–8.
- [7]. Cevc, G. Transfersomes, liposomes and other lipid suspensions on the skin: Permeation enhancement, vesicle penetration, and transdermal drug delivery. *Crit. Rev. Ther. Drug Carr. Syst.* 1996, 13, 257–388.
- [8]. Rajan, R.; Jose, S.; Mukund, V.P.B.; Vasudevan, D.T. Transfersomes—A vesicular transdermal delivery system for enhanced drug permeation. *J. Adv. Pharm. Technol. Res.* 2011, 2, 138–143.
- [9]. Lymberopoulos, A.; Demopoulou, C.; Kyriazi, M.; Katsarou, M.; Demertzis, N.; Hatziandoniou, S.; Maswadeh,

- H.; Papaioanou, G.; Demetzos, C.; Maibach, H.; et al. Liposome percutaneous penetration in vivo. *Toxicol. Res. Appl.* 2017, 1, 1–6.
- [10]. Li, J. Microneedle Patches as Drug and Vaccine Delivery Platform. *Curr. Med. Chem.* 2017, 24, 2413–2422.
- [11]. Wang, M.; Marepally, S.; Vemula, P.; Xu, C. Inorganic Nanoparticles for Transdermal Drug Delivery and Topical Application. In *Nanoscience in Dermatology*; Elsevier: Amsterdam, The Netherlands, 2016; pp. 57–72.
- [12]. Xu, B.; Jiang, G.; Yu, W.; Liu, D.; Zhang, Y.; Zhou, J.; Sun, S.; Liu, Y. H₂O₂-Responsive mesoporous silica nanoparticles integrated With microneedle patches for the glucose-monitored transdermal delivery of insulin. *J. Mater. Chem. B* 2017, 5, 8200–8208.
- [13]. Pegoraro, C.; MacNeil, S.; Battaglia, G. Transdermal drug delivery: From micro to nano. *Nanoscale* 2012, 4, 1881–1894.
- [14]. Fesq, H.; Lehmann, J.; Kontny, A.; Erdmann, I.; Theiling, K.; Rother, M.; Ring, J.; Cevc, G.; Abeck, D. Improved Risk-benefit ratio for topical triamcinolone acetonide in Transfersome in comparison with equipotent cream and ointment: A randomized controlled trial. *Brit. J. Dermatol.* 2003, 149, 611–619.
- [15]. Cevc, G. Transfersomes: Innovative transdermal drug carriers. In *Modified-Release Drug Delivery Technology*, 1st ed.; Rathbone, M.J., Hadgraft, J., Roberts, M.S., Eds.; Marcel Dekker, Inc.: New York, NY, USA, 2002; Volume 126, pp. 533–546. ISBN 0-8247-0869-5.
- [16]. Rai, S.; Pandey, V.; Rai, G. Transfersomes as versatile and flexible nano-vesicular carriers in skin cancer therapy: The state of the art. *Nano Rev. Exp.* 2017, 8, 1325708.
- [17]. Fernández-García R, Lalatsa A, Statts L, Bolás-Fernández F, Ballesteros MP, Serrano DR. Transfersomes as Nanocarriers for drugs across the skin: Quality by design from lab to industrial Scale. *Int J Pharm.* 2020;573:118817
- [18]. Walve, J.R.; Bakliwal, S.R.; Rane, B.R.; Pawar, S.P. Transfersomes: A surrogated carrier for transdermal drug delivery system. *Int. J. Appl. Biol. Pharm. Technol.* 2011, 2, 204–213.
- [19]. Sivannarayana, P.; Rani, A.P.; Saikishore, V.; VenuBabu, C.; SriRekha, V. Transfersomes: Ultra deformable vesicular carrier systems in transdermal drug delivery system. *Res. J. Pharm. Dos. Forms Technol.* 2012, 4, 243–255.
- [20]. Sachan, R.; Parashar, T.; Soniya, S.V.; Singh, G.; Tyagi, S.; Patel, C.; Gupta, A. Drug carrier transfersomes: A novel tool for transdermal drug delivery system. *Int. J. Res. Dev. Pharm. Life Sci.* 2013, 2, 309–316.
- [21]. Li, J.; Wang, X.; Zhang, T.; Wang, C.; Huang, Z.; Luo, X.; Deng, Y. A review on phospholipids and their main Applications in drug delivery systems. *Asian J. Pharm. Sci.* 2015, 10, 81–98.
- [22]. Bhasin, B.; Londhe, V.Y. An overview of transfersomal drug delivery. *Int. J. Pharm. Sci. Res.* 2018, 9, 2175–2184.
- [23]. Lei, W.; Yu, C.; Lin, H.; Zhou, X. Development of tacrolimus-loaded transfersomes for deeper skin penetration Enhancement and therapeutic effect improvement in vivo. *Asian J. Pharm. Sci.* 2013, 8, 336–345.
- [24]. Pandey, A. Role of surfactants as penetration enhancer in transdermal drug delivery system. *J. Mol. Pharm. Org. Process. Res.* 2014, 2, 1–10.
- [25]. Duangjit, S.; Opanasopit, P.; Rojanarata, T.; Ngawhirunpat, T. Characterization and in vitro skin permeation Of meloxicam-loaded Liposomes versus Transfersomes. *J. Drug Deliv.* 2010, 2011, 1–9.
- [26]. Aggarwal, N.; Goindi, S. Preparation and evaluation of antifungal efficacy of griseofulvin loaded deformable Membrane vesicles in optimized guinea pig model of *Microsporum canis*—Dermatophytosis. *Int. J. Pharm.* 2012, 437, 277–287.
- [27]. Chen, J.; Lu, W.-L.; Gu, W.; Lu, S.-S.; Chen, Z.-P.; Cai, B.-C. Skin permeation behavior of elastic liposomes: Role of formulation ingredients. *Expert Opin. Drug Deliv.* 2013, 10, 845–856.
- [28]. Dhopavkar S, Kadu P. Transfersomes-a Boon for transdermal delivery. *Indo American Journal Of Pharmaceutical Sciences.* 2017;4(9):2908-19.
- [29]. Moawad, F.A.; Ali, A.A.; Salem, H.F. Nanotransfersomes-loaded thermosensitive in situ gel as a rectal Delivery system of tizanidine HCl: Preparation, in vitro and in vivo performance. *Drug Deliv.* 2017, 24, 252–260.

- [30]. Bnyan, R.; Khan, I.; Ehtezazi, T.; Saleem, I.; Gordon, S.; Neill, F.O.; Roberts, M. Surfactant effects on lipid-based Vesicles properties. *J. Pharm. Sci.* 2018, 107, 1237–1246.
- [31]. Suresh. D. Kumavat*. Transfersomes: A Promising Approach for Transdermal Drug Delivery System. *Asian journal of Pharmaceutical sciences and research* 2013;3.
- [32]. Van Hoogevest, P.; Wendel, A. The use of natural and synthetic phospholipids as pharmaceutical excipients. *Eur. J. Lipid Sci. Technol.* 2014, 116, 1088–1107.
- [33]. Mathur, M. Approaches for improving the pharmacological and pharmacokinetics properties of herbal drugs. *Int. Res. J. Pharm. Appl. Sci.* 2013, 3, 40–50.
- [34]. Cevc, G. Transdermal drug delivery of insulin with ultradeformable carriers. *Clin. Pharmacokinet.* 2003, 42, 461–474.
- [35]. Jadupati, M.; Kumar, N.A. Transfersome: An opportunistic carrier for transdermal drug delivery system. *Int. Res. J. Pharm.* 2012, 3, 35–38.
- [36]. Cevc, G.; Blume, G.; Schätzlein, A.; Gebauer, D.; Paul, A. The skin: A pathway for systemic treatment with Patches and lipid-based agent carriers. *Adv. Drug Deliv. Rev.* 1996, 18, 349–378.
- [37]. Mandal, U.K.; Mahmood, S.; Taher, M. Experimental design and optimization of raloxifene hydrochloride Loaded nanotransfersomes for transdermal application. *Int. J. Nanomed.* 2014, 9, 4331–4346.
- [38]. Cevc, G.; Schatzlein, A.G.; Richardsen, H. Ultradeformable lipid vesicles can penetrate the skin and other Semi-permeable barriers unfragmented. Evidence from double label CLSM experiments and direct size Measurements. *Biochim. Et Biophys. Acta (BBA)-Biomembr.* 2002, 1564, 21–30.
- [39]. Chauhan, P.; Tyagi, B.K. Herbal novel drug delivery systems and transfersomes. *J. Drug Deliv. Ther.* 2018, 8, 162–168.
- [40]. Kumar, G.P.; Rajeshwarrao, P. Nonionic surfactant vesicular systems for effective drug delivery—An overview. *Acta Pharm. Sin. B* 2011, 1, 208–219.
- [41]. Cipolla, D.; Wu, H.; Gonda, I.; Eastman, S.; Redelmeier, T.; Chan, H.-K. Modifying the release properties of liposomes toward personalized medicine. *J. Pharm. Sci.* 2014, 103, 1851–1862.
- [42]. Dudhipala, N.; Mohammed, R.P.; Youssef, A.A.A.; Banala, N. Effect of lipid and edge activator concentration on development of Aceclofenac loaded transfersomes gel for transdermal application: In vitro and ex vivo skin permeation. *Drug Dev. Ind. Pharm.* 2020, 46, 1–28.
- [43]. Iskandarsyah; Rahmi, A.D.; Pangesti, D.M. Comparison of the characteristics of transfersomes and Protransfersomes containing azelaic acid. *J. Young-Pharm.* 2018, 10, S11–S15.
- [44]. Kotla, N.G.; Chandrasekar, B.; Rooney, P.; Sivaraman, G.; Larrañaga, A.; Krishna, K.V.; Pandit, A.; Rochev, Y. Biomimetic lipid-based nanosystems for enhanced dermal delivery of drugs and bioactive Agents. *ACS Biomater. Sci. Eng.* 2017, 3, 1262–1272.
- [45]. Shakthi Apsara Thejani Opatha, Varin Titapiwatanakun and Romchat Chutoprapat *. Transfersomes: A Promising Nanoencapsulation Technique for Transdermal Drug Delivery.
- [46]. El Zaafarany, G.M.; Awad, G.A.S.; Holayel, S.M.; Mortada, N. Role of edge activators and surface charge In developing ultradeformable vesicles with enhanced skin delivery. *Int. J. Pharm.* 2010, 397, 164–172.
- [47]. Malakar J, Sen SO, Nayak AK, Sen KK. Formulation, optimization and evaluation of Transfersosomal gel for transdermal insulin Delivery. *Saudi Pharm J.* 2012;20:355–63.
- [48]. Ghai, I.; Chaudhary, H.; Ghai, S.; Kohli, K.; Kr, V. A review of transdermal drug delivery using nano-vesicular Carriers: Transfersomes. *Recent Pat. Nanomed.* 2012, 2, 164–171.
- [49]. Chaurasiya P., Ganju E., Upmanyu N., Ray S.K., Jain P. Transfersomes: A novel technique for transdermal drug delivery. *J. Drug Deliv. Ther.* 2019;9:279–285. Doi: 10.22270/jddt.v9i1.2198.
- [50]. Celtic Pharma Acquires Stake In Idea AG “21.7% Shareholding Purchased in Europe”’s Leading targeted therapeutics Company IDEA prepares to Expand its late stage Clinical Development programmes,” Hamilton, Bermuda And Munich, Germany: September 28, 2005.
- [51]. Qvist M.H. Hoeck U. kreilgaard B. Madsen F. Hovgaard L. Froljaer S. Application of Confocal scanning microscopy in Characertisation of chemical enhancers in Drug in adhesive transdermal patches. *AAPS Pharm Sci* 2002;4:11-18.

- [52]. Walve JR, Bakliwal SR, Rane BR, Pawar SP. Transfersomes: a surrogated carrier for Transdermal drug delivery system. *Int J Applied Biology Pharma Technol* 2011;2:204- 213.
- [53]. Wu, P.-S.; Li, Y.-S.; Kuo, Y.-C.; Tsai, S.-J.J.; Lin, C.-C. Preparation and evaluation of novel transfersomes Combined with the natural antioxidant resveratrol. *Molecules* 2019, 24, 600.
- [54]. Jiang, T.; Wang, T.; Li, T.; Ma, Y.; Shen, S.; He, B.; Mo, R. Enhanced transdermal drug delivery by Transfersome-embedded oligopeptide hydrogel for topical chemotherapy of melanoma. *ACS Nano* 2018, 12, 9693–9701.
- [55]. Cevc, G.; Blume, G. Biological activity and characteristics of triamcinolone-acetonide formulated with the self-regulating drug carriers, Transfersomes®. *Biochim. Et Biophys. Acta (BBA) Biomembr.* 2003, 1614, 156–164.
- [56]. Shabana, S.; Sailaja, A.K. Formulation and evaluation of diclofenac sodium transfersomes using different surfactants by thin film hydration method. *Der Pharm. Lett.* 2015, 7, 43–53.
- [57]. Shaji J and Lal M: Preparation, optimization and Evaluation of transferosomal formulation for enhanced Transdermal delivery of a COX-2 inhibitor. *Int J Pharm Pharm Sci* 2014; 6: 467-77.
- [58]. Benson HA: Transfersomes for transdermal drug delivery. *Expert opinion on Drug Delivery* 2006; 3(6): 727-37.
- [59]. El Zaaferany, G.M.; Awad, G.A.S.; Holayel, S.M.; Mortada, N. Role of edge activators and surface charge In developing ultradeformable vesicles with enhanced skin delivery. *Int. J. Pharm.* 2010, 397, 164–172.