Letters in Applied NanoBioScience
Open-Access Journal (ISSN: 2284-6808)

Review
Volume 13, Issue 1, 2024, 24
https://doi.org/10.33263/LIANBS131.024

Past Successful Attempts So Far on Nano Vesicular Transdermal Delivery Patches: A Beginning Step Toward a Giant Leap in Drug Delivery

Kadae Eediga Sailaja [1,*], Bhupalam Pradeepkumar [2]

[1] Research Scholar, Department of Pharmaceutical Sciences, JNTUA, Ananthapuramu-515001, Andhra Pradesh, India, charansailajaotpri@gmail.com (K.E.S.);
[2] Department of Pharmacology, Raghavendra Institute of Pharmaceutical Education and Research (RIPER)-Autonomous, K. R. Palli Cross, Ananthapuramu-515721, Andhra Pradesh, India; bhupalampradeep@gmail.com (B.P.);
* Correspondence: charansailajaotpri@gmail.com (K.E.S.);

Scopus Author ID 57194788789

Received: 17.11.2022; Accepted: 8.01.2023; Published: 13.08.2023

Abstract: There is no doubt that nanoformulations are incredibly beneficial instruments for drug delivery applications. In this present "golden age" of pharmaceutical nanocarriers, watching the original conceptions and ideas mature. Before starting the process of choosing, the previous successful initiatives must be considered when optimizing and assuring the safety and effectiveness of these systems. Nano vesicular systems have gained popularity since they are frequently viewed as non-toxic, biocompatible, and simple-to-produce formulations. An overview of the numerous nano vesicular transdermal systems and accomplished attempts is provided at the outset of this review. Previous attempts by the authors to develop various nano vesicular systems for transdermal drug delivery were successful.

Keywords: delivery; drug; literature; nanovesicles; polymer; transdermal.

© 2023 by the authors. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

It has been demonstrated that localized, topical therapy is more successful with the SLN method than transdermal systemic delivery [1]. These carriers also have low drug loading, spill medication during storage, and have high water content in SLN dispersions. Though there was a long lag time, the developed approach demonstrated higher bioavailability [2].

Transfersomes are lipid-based vesicle carriers that can heritably traverse the skin to improve transdermal distribution [3,4]. They are self-optimizing, extremely adaptable, and boundary activators [5]. According to several investigations, when used on an open biological barrier under non-occlusive circumstances, it is effective at penetrating intact skin and delivering medications at therapeutic quantities [6]. The highly flexible lipid bilayer vesicle system in the liquid state, which enables them to easily pass even extremely small strictures under the influence of hydration gradients, is crucial in improving skin penetration via transfersomes. The vesicle can deform without losing structural integrity thanks to the edge activator's presence [7].

Edge activators have a variety of stress-dependent modifications that reduce barriers to their transit via constrained channels and enable non-invasive drug delivery. These adaptations result from their capacity to aggregate at high-stress locations and curved structures.

Nanoparticles (NPs) are colloidal particles of 10-1000 nm size [8,9]. They are produced using artificial or natural polymers and are excellent for enhancing drug distribution and lowering toxicity [10]. They have become a flexible substitute for liposomes as drug carriers. NPs' ability to pass through different anatomical barriers, the prolonged release of their contents, and their stability at the nanoscale scale are all necessary for their successful application in drug delivery [11]. However, the widespread use of NPs in clinical medicine has been constrained by the lack of secure, regulatory-approved polymers and their high cost [12].

Lipids have been suggested as potential substitutes for polymeric NPs to get over these drawbacks, especially for lipophilic drugs [13]. Solid lipid nanoparticles (SLNs), that is, these lipid NPs, are gaining popularity among formulators all over the world. Over the past ten years, colloidal carriers known as SLNs have been created as an alternative to currently used conventional carriers (liposomes/emulsions/NPs) [14]. They belong to a brand-new class of lipid emulsions with a sub-micron size in which the oil (liquid lipid) has been swapped out for a solid lipid. SLNs are desirable because they have the potential to improve the performance of pharmaceuticals, nutraceuticals, and other materials [15]. They offer distinctive possessions viz., small size, high surface area, high drug loading, and phase interaction at interfaces.

Since they don't have any known drawbacks like biocompatibility, they are readily acceptable by the body system. The solubility of the medicament in the lipid melt, the lipid matrix's structure, and the lipid matrix's polymeric state all impact the drug-loading capacity of traditional SLNs. A flawless crystal with few flaws forms when the molecules making up the lipid matrix (such as tristearin or tripalmitin) are comparable [16]. A highly ordered crystal lattice cannot hold significant amounts of the drug since integrated medicines are present in crystal defects as well as between lipid layers and fatty acid chains. As a result, higher drug loading is more sensitive when using more complex lipids.

2. Major Types of Nanovesicles

2.1. Nanostructured lipid carriers (NLC).

To get over any potential issues with SLNs, NLCs were developed[17]. It was intended to increase drug exposure while preventing drug release. Three approaches could be used to visualize this. The first model combines various fatty acids to form spatially distinct lipids (such as glycerides)[18].

Greater distances between the glyceride fatty acid chains and noticeable gaps within the crystal structure arise due to the incorporation of spatially distinct lipids. This, in turn, provides increased space for the inclusion of guest molecules. The maximum quantity of medication loading (oils) may be attained by combining minor volumes of liquid lipids with solid lipids. The name of this model is the incomplete NLC type.

Since the progressive crystallization or change of the solid lipid is what leads to drug excretion, the creation of the 3rd type of NLC, the amorphous-type NLC, can stop this from occurring. Here, the particles are solid, but adding specific lipids such as octacosanol hydroxyl, hydroxyl stearate, and isopropyl myristate prevents them from crystallizing upon cooling[19].

Drugs that exhibit greater solubility in oils can be solubilized in the oil and still be dwindling from deprivation by surrounding solid lipids. These NLCs are known as multiple-type NLCs and, like w/o/w emulsions, are a dispersion of oil in solid and lipid in water [20].

2.2. Lipid drug conjugates (LDC)

Due to dispersion effects during manufacturing, SLNs have a limited capacity to load hydrophilic medicines, which is a significant issue. The solid lipid matrix can only be properly integrated with powerful, low-dose hydrophilic medicines. So-called LDC NPs with up to 33% drug-loading capacities have been created to get around this restriction[21]. A mass of insoluble drug-lipid conjugate is first made by covalent attachment or salification (using, for example, a fatty acid). This LDC is then treated by high-pressure homogenization into a nanoparticle formulation with Tweens. These matrices may be used to target hydrophilic drugs in the brain to handle severe protozoal infections.

2.3. Mode of SLN making.

SLNs can be made by high shear, hot, cold, high-speed homogenization, solvent, micro, or double emulsification, supercritical fluid, or spray drying methods[22,23].

3. SLN Characterization

The SLNs were characterized by their particle size (measured by dynamic light scattering, static light scattering, Fraunhofer diffraction/acoustic methods) and zeta potential measurements (such as nuclear magnetic resonance, electron microscopy, and atomic force microscopy)[24,25]. These SLNs can be given by oral, parenteral, or transdermal routes.

The current review explores the past attempts made using transfersomes to safely increase the bioavailability of various drugs while avoiding extensive hepatic first-pass metabolism, ensuring adequate drug retention in the skin for an extended period, and administering the drug systemically to maintain therapeutic blood levels.

The past successful attempts so far made on nano vesicular transdermal systems are illustrated in Table 1.

Table 1. Past work done on nano vesicular transdermal systems.

Drug	Polymer	Method	References
Carvedilol	Tween 80	Thin film hydration (TFH)	[26]
Diclofenac sodium and ketoprofen	Cetyltrimethylammonium bromide	TFH	[27]
Glipizide	SL, chitosan, and CHL	TFH	[28]
Raloxifene-Graphene	CHL	TFH	[29]
Rizatriptan benzoate	Carbopol 934P	EI and sonication	[30]
Methotrexate	sodium carboxy methyl cellulose, and HPMC	Solvent casting technique	[31]
Celecoxib (CLB)	Hydrogenated soy phosphatidylcholine (HSPC)	TFH	[32]
Pramipexole	1-Decanoyl-2-Hydroxy-sn-3-Phosphocholine (DPC)	TFH	[33]
Econazole nitrate	SPC and CHL	REM	[34]
Tacrolimus	SL and CHL	TFH and Curvature tuned method	[35]
Pramipexole	1-Arachidonoyl-2-Hydroxy-sn-Glycero-3-Phosphocholine (APC)	TFH	[36]
Itraconazole	Carbopol 980	TFH	[37]
Chlorophenyl benzyl ether	PC	TFH	[38].
Ketoprofen	PEG 4000	TFH	[39]
Abiraterone acetate	CHL	TFH	[40]
Aceclofenac	Phosphatidylcholine (PTC)	hand shaking technique	[41]
Raloxifene	PTC	TFH	[42]
Levofloxacin	SL and CHL	TFH	[43]
Sitagliptin	SL and CHL	EI	[44]
Rivastigmine	Propylene glycol (PG) and CHL	TFH	[45]

Drug	Polymer	Method	References
Letrozole	Lactose	SDM	[46]
Linezolid	SL	TFH	[47]
Baclofen	SL and stearic acid	EI	[48]
Lopinavir	Phospholipid 85G	SDM	[49]
Tretinoin and 5-fluorouracil	CHL and SL	Ethanol injection (EI)	[50]
5 Fluorouracil and Tretinoin	CHL and SL	EI	[50]
Verapamil hydrochloride	SPC, Span 80, and Sephadex G-50	Modified extrusion method	[51]
Dapsone and Cloxacillin Sodium	SL and Carbopol 934	Cold method	[52]
Tamoxifen citrate	Ethyl cellulose (EC), and hydroxypropyl methylcellulose (HPMC)	solvent displacement method	[53]
Griseofulvin	SPC	TFH	[54]
Glimepiride	SL, PG, and dimethyl sulfoxide	Phase evaporation Method and melting method	[55]
Celecoxib	SL and CHL	TFH	[56]
Avanafil	SL and CHL	TFH	[57]
Itraconazole	Carbopol 934P	TFH	[58]
Clotrimazole	Soya phosphatidylcholine (SPC), Span 80, and CHL	Rotary evaporation method (REM)	[59]
Sodium Diclofenac	Scotchpak and Cotran 9720	TFH	[60]
Ketorolac tromethamine	Tween80 and Sephadex-G-10	TFH	[61]
Fluconazole	phospholipid (PL 90H) and cholesterol (CHL), and stearic acid.	TFH	[62]
Ketoconazole	Soya lecithin (SL)	TFH	[63]
Cyproterone acetate	Hydroxyl ethyl cellulose (HEC)	TFH	[64]
Tropicamide	Phospholipon 90	TFH	[65]

4. Conclusions

Solid lipid nanoparticles are colloidal dispersions with altered characteristics compared to other types of nanoparticles, including liposomes, suspensions, microemulsions, and polymeric nanoparticles. SLNs can be used to gradually avoid the major issues associated with nanoparticles, leading to the development of a more flexible drug delivery system that is chemically stable and physiologically appropriate. Their only issue appears to be their propensity to gel, but nanostructured lipid carriers offer a potential solution. Additionally, due to the heat and stress created during the hot homogenization method's manufacture, the active component, or the medicine, may be degraded. So it is important to pick the right production technique. Other issues that must be addressed include particle size, the coexistence of distinct colloidal forms, diverse morphologies, and drug ejection from the lipid matrix. The numerous tried-and-true techniques for mass-producing and characterizing the SLN matrix were discussed. Thermolabile drugs with a poorer pharmacokinetic profile or incompatible physicochemically can all be delivered to the target site using SLNs. SLNs can also be used to transport proteins and peptides more effectively and with less toxicity. Therefore, the addition of the therapeutic strategy using SLNs has the potential to change the course of both therapies and diagnostics.

Funding

This review received no external funding.

Acknowledgments

Declared none.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Mishra, V.; Bansal, K. K.; Verma, A.; Yadav, N.; Thakur, S.; Sudhakar, K.; Rosenholm, J. M., Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems. *Pharmaceutics* **2018,** *10* , 191. https://doi.org/10.3390/pharmaceutics10040191.
2. Paliwal, R.; Paliwal, S. R.; Kenwat, R.; Kurmi, B. D.; Sahu, M. K., Solid lipid nanoparticles: A review on recent perspectives and patents. *Expert opinion on therapeutic patents* **2020,** *30*, 179-194. https://doi.org/10.1080/13543776.2020.1720649.
3. Ahad, H. A.; Kumar, C. S.; Ravindra, B.; Sasidhar, C.; Ramakrishna, G.; Venkatnath, L.; Gangadhar, P.; Navya, K. Characterization and permeation studies of Diltiazem hydrochloride-ficus reticuleta fruit mucilage Transdermal patches. *International Journal of Pharmaceutical Sciences Review and Research* **2010,** *1*, 32-7.
4. Elsherbeeny, W.; El-Gogary, R.; Nasr, M.; Sammour, O. Current progress of oral site-specific dosage forms: Emphasis on gastroretentive drug delivery systems. *Archives of Pharmaceutical Sciences Ain Shams University* **2022,** *6* (2), 221-238.
5. Opatha, S. A. T.; Titapiwatanakun, V.; Chutoprapat, R., Transfersomes: A promising nanoencapsulation technique for transdermal drug delivery. *Pharmaceutics* **2020,** *12* , 855. https://doi.org/10.3390/pharmaceutics12090855.
6. Fernández-García, R.; Lalatsa, A.; Statts, L.; Bolás-Fernández, F.; Ballesteros, M. P.; Serrano, D. R., Transferosomes as nanocarriers for drugs across the skin: Quality by design from lab to industrial scale. *International journal of pharmaceutics* **2020,** *573*, 118817. https://doi.org/10.1016/j.ijpharm.2019.118817.
7. Swetha, T.; Ahad, H. A.; Reddy, K. K.; Sekhar, A.; Sivaji, S.; Kumar, B. Formulation and in-vitro permeation studies of Ketoprofen-Ficus reticulata fruit mucilage transdermal patches. *Der Pharmacia Lettre* **2010,** *2*, 190-199, https://www.cabdirect.org/globalhealth/abstract/20113034162.
8. Abdul, A. H.; Bala, A. G.; Chintaginjala, H.; Manchikanti, S. P.; Kamsali, A. K.; Dasari, R. R. D. Equator Assessment of Nanoparticles Using the Design-Expert Software. *International Journal of Pharmaceutical Sciences and Nanotechnology* **2020,** *13*, 4766-4772, https://www.ijpsnonline.com/index.php/ijpsn/article/view/251.
9. Ahad, H. A.; Chintaginjala, H.; Rahamathulla, S.; Rupasree, A.; Kumar, A. S.; Pallavi, B. P. Pathfinder Nanosponges for Drug Targeting by Factorial Design: A Glance Review. **2021**, https://www.indianjournals.com/ijor.aspx?target=ijor:rjpdft&volume=13&issue=4&article=012.
10. Hindustan, A. A.; Kumar, C. S.; Anuradha, C.; Reddy, K. K.; CHANDRA, S. A. A Novel Mucilage from Ficus glomerata Fruits for Transdermal Patches: Taking Indomethacin as a Model Drug. **2011**, http://www.ijps.ir/article_2147.html.
11. Fouziya, B.; Ahad, H. A.; Charan, D. S.; Vidya, J. S.; Reddy, U. C.; Reddy, P. N. Fabrication and Evaluation of Cefpodoxime Proxetil Niosomes. *Asian Journal of Pharmacy and Technology* **2022,** *12* (2), 109-112, https://doi.org/10.52711/2231-5713.2022.00018.
12. Sheikholeslami, M. Numerical analysis of solar energy storage within a double pipe utilizing nanoparticles for expedition of melting. *Solar Energy Materials and Solar Cells* **2022,** *245*, 111856, https://doi.org/10.1016/j.solmat.2022.111856.
13. Shravani, Y.; Ahad, H. A.; Haranath, C.; gari Poojitha, B.; Rahamathulla, S.; Rupasree, A. Past Decade Work Done On Cubosomes Using Factorial Design: A Fast Track Information for Researchers..(2021). *Int. J. Life Sci. Pharma Res 11*, P124-135, http://dx.doi.org/10.22376/ijpbs/lpr.2021.11.1.P124-135.
14. Tenchov, R.; Bird, R.; Curtze, A. E.; Zhou, Q., Lipid nanoparticles─ from liposomes to mRNA vaccine delivery, a landscape of research diversity and advancement. *ACS nano* **2021,** *15* , 16982-17015. https://doi.org/10.1021/acsnano.1c04996.
15. McClements, D. J.; Zou, L.; Zhang, R.; Salvia-Trujillo, L.; Kumosani, T.; Xiao, H. Enhancing nutraceutical performance using excipient foods: Designing food structures and compositions to increase bioavailability. *Comprehensive Reviews in Food Science and Food Safety* **2015,** *14*, 824-847, https://doi.org/10.1111/1541-4337.12170.
16. Sadiq, A. A.; Rassol, A. A. Formulation and evaluation of silibinin loaded solid lipid nanoparticles for peroral use targeting lower part of gastrointestinal tract. *Int J Pharm Pharm Sci* **2014,** *6* , 55-67.
17. Naseri, N.; Valizadeh, H.; Zakeri-Milani, P. Solid lipid nanoparticles and nanostructured lipid carriers: structure, preparation and application. *Advanced pharmaceutical bulletin* **2015,** *5*, 305. https://doi.org/10.15171/apb.2015.043
18. Nieto González, N.; Obinu, A.; Rassu, G.; Giunchedi, P.; Gavini, E. Polymeric and Lipid Nanoparticles: Which Applications in Pediatrics? *Pharmaceutics* **2021,** *13* , 670, https://doi.org/10.3390/pharmaceutics13050670.

19. Pottoo, F. H.; Sharma, S.; Javed, M. N.; Barkat, M. A.; Harshita; Alam, M. S.; Naim, M. J.; Alam, O.; Ansari, M. A.; Barreto, G. E. Lipid-based nanoformulations in the treatment of neurological disorders. *Drug Metabolism Reviews* **2020,** *52*, 185-204. https://doi.org/10.1080/03602532.2020.1726942.
20. Attama, A. A.; Momoh, M. A.; Builders, P. F. Lipid nanoparticulate drug delivery systems: a revolution in dosage form design and development. *Recent advances in novel drug carrier systems* **2012,** *5*, 107-140, https://www.intechopen.com/chapters/40253.
21. Banerjee, S.; Kundu, A. Lipid-drug conjugates: a potential nanocarrier system for oral drug delivery applications. *DARU Journal of Pharmaceutical Sciences* **2018,** *26*, 65-75. https://doi.org/10.1007/s40199-018-0209-1.
22. Yadav, N.; Khatak, S.; Sara, U. S. Solid lipid nanoparticles-a review. *Int. J. Appl. Pharm* **2013,** *5* , 8-18.
23. Deshmukh, A. S. Solid lipid nanoparticles. *Research Journal of Pharmaceutical Dosage Forms and Technology* **2014,** *6*, 282, https://www.researchgate.net/publication/329144276_Solid_Lipid_Nanoparticles.
24. Duan, Y.; Dhar, A.; Patel, C.; Khimani, M.; Neogi, S.; Sharma, P.; Kumar, N. S.; Vekariya, R. L., A brief review on solid lipid nanoparticles: Part and parcel of contemporary drug delivery systems. *RSC advances* **2020,** *10*, 26777-26791. https://doi.org/10.1039/d0ra03491f.
25. Rajpoot, K., Solid lipid nanoparticles: a promising nanomaterial in drug delivery. *Current pharmaceutical design* **2019,** *25* (37), 3943-3959. https://doi.org/10.2174/1381612825666190903155321.
26. Maan, S.; Khar, R. K.; Mazumder, R.; Yadav, N.; Khan, U. A. Fabrication and Evaluation of Controlled Release Transdermal Drug Delivery System of Carvedilol using Design Expert® Software for the Management of Hypertension. *Journal of Young Pharmacists* **2022,** *14* , 295, http://dx.doi.org/10.5530/jyp.2022.14.58.
27. Kuznetsova, D. A.; Vasilieva, E. A.; Kuznetsov, D. M.; Lenina, O. A.; Filippov, S. K.; Petrov, K. A.; Zakharova, L. Y.; Sinyashin, O. G., Enhancement of the Transdermal Delivery of Nonsteroidal Anti-Inflammatory Drugs Using Liposomes Containing Cationic Surfactants. *ACS omega* **2022,** *7*, 25741-25750, https://doi.org/10.1021/acsomega.2c03039.
28. Patel, C.; Mangukia, D. K.; Asija, R.; Asija, S.; Kataria, S., Formulation and evaluation of matrix diffusion controlled transdermal drug delivery system of Glipizide. *Journal of Drug Delivery and Therapeutics* **2012,** *2*, http://jddtonline.info/index.php/jddt/article/view/66.
29. Altyar, A. E.; Fahmy, O. Preparation of Liposomal Raloxifene-Graphene Nanosheet and Evaluation of Its In Vitro Anticancer Effects. *Dose-Response* **2022,** *20*, 15593258211063983. https://doi.org/10.1177/15593258211063983.
30. Kempwade, A.; Taranalli, A.; Hiremath, R.; Joshi, S. Formulation and Evaluation of Flexible Liposome Embedded In Situ Thermoreversible Intranasal Gel of Rizatriptan Benzoate. *Indian Journal of Pharmaceutical Sciences* **2022,** *84*, 863-873.
31. Latif, M. S.; Al-Harbi, F. F.; Nawaz, A.; Rashid, S. A.; Farid, A.; Mohaini, M. A.; Alsalman, A. J.; Hawaj, M. A. A.; Alhashem, Y. N. Formulation and Evaluation of Hydrophilic Polymer Based Methotrexate Patches: In Vitro and In Vivo Characterization. *Polymers* **2022,** *14*, 1310. https://doi.org/10.3390/polym14071310.
32. Begum, M. Y.; M. Osmani, R. A.; Alqahtani, A.; Ghazwani, M.; Hani, U.; Ather, H.; Atiya, A.; Rahamathulla, M.; Siddiqua, A., Development of stealth liposomal formulation of celecoxib: In vitro and in vivo evaluation. *Plos one* **2022,** *17*, e0264518. https://doi.org/10.1371/journal.pone.0264518
33. Trivedi, R.; Umekar, M.; Kotagale, N.; Bonde, S.; Taksande, J. Design, evaluation and in vivo pharmacokinetic study of a cationic flexible liposomes for enhanced transdermal delivery of pramipexole. *Journal of drug delivery science and technology* **2021,** *61*, 102313, https://doi.org/10.1016/j.jddst.2020.102313.
34. Maharaj, S. K.; Sharma, R.; Rathi, J. C. Formulation, development and evaluation of liposomal gel for treatment of fungal infection. **2021**, https://wjpr.s3.ap-south-1.amazonaws.com/article_issue/1619803958.pdf.
35. Jindal, S.; Awasthi, R.; Singare, D.; Kulkarni, G. T. Preparation and in vitro evaluation of Tacrolimus loaded liposomal vesicles by two methods: A comparative study. *Journal of Research in Pharmacy* **2021,** *25*, 34-41, http://dx.doi.org/10.35333/jrp.2021.292.
36. Mayangsari, F.; Surini, S.; Iswandana, R. Development of transfersomal emulgel to enhance the permeation of berberine chloride for transdermal delivery. *Journal of Applied Pharmaceutical Science* **2022,** *12* , 048-055, http://dx.doi.org/10.7324/JAPS.2021.120205.
37. Kumar, N.; Goindi, S. Development, characterization and preclinical evaluation of nanosized liposomes of itraconazole for topical application: 32 full factorial design to estimate the relationship between formulation components. *Journal of Drug Delivery Science and Technology* **2021,** *66*, 102785, https://doi.org/10.1016/j.jddst.2021.102785.
38. Singpanna, K.; Dechsri, K.; Patrojanasophon, P.; Limpachayaporn, P.; Opanasopit, P.; Nuntharatanapong, N. Transdermal delivery, cytotoxicity and anti-melanogenic activity of p-chlorophenyl benzyl ether loaded-liposomes. *Journal of Drug Delivery Science and Technology* **2021,** *65*, 102746, https://doi.org/10.1016/j.jddst.2021.102746.

39. Thomas, J. A.; Abraham, S.; Raju, S. P.; Das, C.; Abraham, A.; Varghese, S. A.; Abraham, E. Formulation and Evaluation of Anti-Arthritis Drug Loaded Stealth Liposomes. *Research Journal of Pharmacy and Technology* **2021,** *14*, 1313-1318, https://doi.org/10.5958/0974-360X.2021.00233.X.
40. Das, S.; Samanta, A.; Mondal, S.; Roy, D.; Nayak, A. K., Design and release kinetics of liposomes containing abiraterone acetate for treatment of prostate cancer. *Sensors International* **2021,** *2*, 100077, https://doi.org/10.1016/j.sintl.2020.100077.
41. Sasikala, A.; Tarakeswari, V. Anti-Inflammatory Flexible Liposomal Gel for Treatment of Rheumatoid Arthritis. *J Pharm Adv Res* **2021,** *4*, 1334-1345, https://www.jparonline.com/research/JPAR-2103-RSA-000203-Ms.%20Sasikala.pdf.
42. Mahmood, S.; Chatterjee, B.; Mandal, U. K. Pharmacokinetic evaluation of the synergistic effect of raloxifene loaded transfersomes for transdermal delivery. *Journal of Drug Delivery Science and Technology* **2021,** *63*, 102545, https://doi.org/10.1016/j.jddst.2021.102545,
43. Joseph, A. E.; Abraham, S.; Raju, S. P.; Pillai, H. H.; Jose, F.; Abraham, E. Formulation and Evaluation of levofloxacin stealth liposome using different polymers. *Research Journal of Pharmacy and Technology* **2021,** *14*, 1493-1498, https://doi.org/10.5958/0974-360X.2021.00265.1.
44. Sharma, D.; Raj, S.; Singhal, M.; Kumar, B. Preparation and Evaluation of Gliptin Liposomes for Targetting Ocular Region in Neurodegeneration. *Nanoscience & Nanotechnology-Asia* **2021,** *11*, 197-203, https://doi.org/10.2174/2210681210999200414104232.
45. Salimi, A.; Ghobadian, H.; Sharif Makhmalzadeh, B., Dermal pharmacokinetics of rivastigmine-loaded liposomes: an ex vivo–in vivo correlation study. *Journal of Liposome Research* **2021,** *31*, 246-254. https://doi.org/10.1080/08982104.2020.1787440.
46. Maniyar, M.; Chakraborty, A.; Kokare, C., Formulation and evaluation of letrozole-loaded spray dried liposomes with PEs for topical application. *Journal of Liposome Research* **2020,** *30*, 274-284. https://doi.org/10.1080/08982104.2019.1634723
47. Campioli, C. C.; Barth, D.; Garrigos, Z. E.; Saleh, O. A.; Sohail, R. M.; Sia, I. G., Linezolid and fentanyl: An underrecognized drug-to-drug interaction. *Journal of Clinical Pharmacy and Therapeutics* **2020,** *45*, 825-827. https://doi.org/10.1111/jcpt.13143.
48. Keservani, R. K.; Gautam, S. P. Formulación y evaluación de vesículas de liposomas de baclofeno usando lecitina. *Ars Pharmaceutica* **2020,** *61*, 175-180, https://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S2340-98942020000300004.
49. Maniyar, M. G.; Kokare, C. R. Formulation and evaluation of spray dried liposomes of lopinavir for topical application. *Journal of Pharmaceutical Investigation* **2019,** *49*, 259-270, https://link.springer.com/article/10.1007/s40005-018-0403-7.
50. Tiwari, R.; Tiwari, G.; Wal, A.; Gupta, C. Liposomal delivery of 5 Fluorouracil and Tretinoin: An Aspect of Topical treatment of skin warts. *Ars Pharmaceutica* **2019,** *60*, 139-146, https://scielo.isciii.es/pdf/ars/v60n3/2340-9894-ars-60-03-139.pdf.
51. Jain, N.; Argal, A.; Gautam, G. Elastic liposomes mediated transdermal delivery of verapamil hydrochloride. *Journal of Drug Delivery and Therapeutics* **2018,** *8*, 16-21, https://doi.org/10.22270/jddt.v8i6.2073
52. Tiwari, R.; Tiwari, G.; Wal, P.; Wal, A.; Maurya, P. Development, characterization and transdermal delivery of dapsone and an antibiotic entrapped in ethanolic liposomal gel for the treatment of lapromatous leprosy. *The Open Nanomedicine Journal* **2018,** *5*, https://benthamopen.com/ABSTRACT/TONMJ-5-1.
53. Adhyapak, A. A.; Desai, B. G. Formulation and evaluation of liposomal transdermal patch for targeted drug delivery of tamoxifen citrate for breast cancer. *Indian Journal of Health Sciences and Biomedical Research (KLEU)* **2016,** *9*, 40, https://www.ijournalhs.org/article.asp?issn=2542-6214;year=2016;volume=9;issue=1;spage=40;epage=48;aulast=Adhyapak.
54. Bavarsad, N.; Kouchak, M.; Mohamadipour, P.; Sadeghi-Nejad, B. Preparation and physicochemical characterization of topical chitosan-based film containing griseofulvin-loaded liposomes. *Journal of advanced pharmaceutical technology & research* **2016,** *7*, 91. https://doi.org/10.4103/2231-4040.184591.
55. Ahmed, O. A. A.; Kurakula, M.; Banjar, Z. M.; Afouna, M. I.; Zidan, A. S., Quality by design coupled with near infrared in formulation of transdermal glimepiride liposomal films. *Journal of Pharmaceutical Sciences* **2015,** *104*, 2062-2075. https://doi.org/10.1002/jps.24448. Epub 20 15 Apr 13.
56. Moghimipour, E.; Salami, A.; Monjezi, M., Formulation and evaluation of liposomes for transdermal delivery of celecoxib. *Jundishapur journal of natural pharmaceutical products* **2015,** *10* . e17653. https://doi.org/10.17795/jjnpp-17653.
57. Hosny, K. M.; Aldawsari, H. M. Avanafil liposomes as transdermal drug delivery for erectile dysfunction treatment: Preparation, characterization, and in vitro, ex vivo and in vivo studies. *Tropical Journal of Pharmaceutical Research* **2015,** *14*, 559-565, https://doi.org/10.4314/tjpr.v14i4.1.
58. Sunitha, S.; Thirupathi, A.; Vijaya, K. Preparation and evaluation of liposome entrapped hydrogel complex system of itraconazole for enhanced transdermal permeation. *J pharm Sci Inn. 2014; 3: 25* **2014,** *29*, http://dx.doi.org/10.7897/2277-4572.031100.
59. Kumar, R.; Rana, A.; Bala, R.; Seth, N. Formulation and evaluation of elastic liposomes of clotrimazole. *International Journal of Drug Development and Research* **2012,** *4* , 10-20, https://www.itmedicalteam.pl/articles/formulation-and-evaluation-of-elastic-liposomes-of-clotrimazole.pdf.

60. Taghizadeh, S. M.; Bajgholi, S. A new liposomal-drug-in-adhesive patch for transdermal delivery of sodium diclofenac. *Journal of Biomaterials and Nanobiotechnology* **2011,** *2*, 576, http://dx.doi.org/10.4236/jbnb.2011.225069.
61. Nava, G.; Piñón, E.; Mendoza, L.; Mendoza, N.; Quintanar, D.; Ganem, A. Formulation and in vitro, ex vivo and in vivo evaluation of elastic liposomes for transdermal delivery of ketorolac tromethamine. *Pharmaceutics* **2011,** *3*, 954-970. https://doi.org/10.3390/pharmaceutics3040954.
62. Mitkari, B.; Korde, S.; Mahadik, K.; Kokare, C. Formulation and evaluation of topical liposomal gel for fluconazole. *Indian J Pharm Educ Res* **2010,** *44*, 324-333, https://www.researchgate.net/publication/233850733_Formulation_and_Evaluation_of_Topical_Liposomal_Gel_for_Fluconazole.
63. Patel, R. P.; Patel, H.; Baria, A. H. Formulation and evaluation of liposomes of ketoconazole. *Int J Drug Deliv Technol* **2009,** *1*, 16-23, https://impactfactor.org/PDF/IJDDT/1/IJDDT,Vol1,Issue1,Article3.pdf.
64. Mohammadi, S. S.; Montaseri, H.; Jamshidnejad, M. Preparation and evaluation of cyproterone acetate liposome for topical drug delivery. **2009,** http://www.ijps.ir/article_2030_8ffe0633aae32bbfdefb499d6b96cfff.pdf.
65. Nagarsenker, M.; Londhe, V. Y.; Nadkarni, G., Preparation and evaluation of liposomal formulations of tropicamide for ocular delivery. *International journal of pharmaceutics* **1999,** *190*, 63-71. https://doi.org/10.1016/s0378-5173(99)00265-3.