INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Niosomes: An Innovative Tailored Cancer Medication Delivery Mechanism

Shivani S. C. Gupta* , Punam K. Satav, Kalyani K. Malthane, Vaibhav S. Adhao, Jaya P. Ambhore, Nikita A. Deshmukh

Dr. Rajendra Gode College Of Pharmacy, Malkapur

ARTICLE INFO

Received: 11 April 2024
Accepted: 15 April 2024
Published: 19 April 2024

Keywords:
Niosomes , Anti – cancer activity, Nanocarrier, Targeted drug delivery .

DOI:
10.5281/zenodo.10998384

ABSTRACT

These days, nanotechnology is being applied to several scientific domains, the most apparent being medicine. An innovative approach to therapeutic techniques with effective mechanisms of action has been made possible by the use of nanoparticles in the diagnosis and treatment of medical conditions. Additionally, because personalized medicine has advanced so much, efforts are being made to give tailored treatments and minimize treatment side effects to the greatest extent possible. Because different drug structures require distinct delivery systems to ensure that the drug's effectiveness is maintained, targeted drug delivery is crucial for treating a variety of disorders, particularly in patients who are receiving combination medication. Polymeric nanoparticles known as niosomes have promising properties for medication delivery. Apart from their great absorption and biocompatibility, these nanoparticles also have the potential to target medication release, lower dosage, and deliver hydrophilic and lipophilic medicines via Niosome vesicles. Since different components, preparation techniques, and optimization strategies all have an impact on the size and formation of niosomal structures, this review started by looking at the features of niosome vesicles before going over the in silico tools for designing, predicting, and optimizing. Ultimately, anticancer drugs delivered via niosomes were compared and discussed as a viable model for developing therapeutic strategies. This study attempted to investigate every facet necessary for drug delivery engineering with niosomes, and by presenting real-world examples of these nanocarriers being used in cancer, its clinical features were also conveyed.

***Corresponding Author:** Shivani S. C. Gupta
Address: *Dr. Rajendra Gode College Of Pharmacy, Malkapur*
Email : shivaniborakhede@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

INTRODUCTION

Niosomes provide a novel drug delivery technology that may accommodate both hydrophilic and hydrophobic pharmaceuticals, as they trap hydrophilic drugs inside the core cavity and hydrophobic drugs within the non-polar region situated inside the bilayer [1]. The non-ionic surfactant that creates the vesicle encasing the medicine is the moniker given to niosomes because of its ampiphillic nature. Niosomes are extremely small particles [2]. The first niosome formulations were developed and patented by L'Oreal in 1975. when surfactants and the charge-inducing substances from the thermodynamically stable vesicles are correctly combined. Because niosomes reduce the disadvantages of liposomes, their primary application is as a liposome replacement [3]. Because they lack the chemical instability of liposomes, niosomes are superior to liposomes. Liposomes' chemical instability is caused by their oxidative degradation susceptibility and the variable purity of phospholipids. Niosomal system development aims to achieve several key objectives, including low production costs, low toxicity, chemical stability, biodegradability, biocompatibility, and ease of handling and storage [4,5]. Niosomes can be applied topically, sublingually, orally, and parenterally. A wide range of drugs, including synthetic and natural treatments, hormones, antigens, and other bioactive materials, are delivered via niosomes [6,7,8]. This page summarizes the key features of niosomes, describes how they are made, and discusses how they are currently used to encapsulate and distribute bioactive compounds.

In order to distinguish between their various varieties, niosomes can be categorized into three classes based on the size of their vesicles: There are three varieties of

1. Unicellar vesicles are accessible:

A. Small (SUV, size = 0.025-0.05μm);

B. Large (LUV, size = >0.10μm); and

2. Multilamellar (MLV, size = >0.05μm).[9]

Advantage of niosomes

1. Vesicle features can be altered by adjusting the vesicle composition, size lamellarity, surface charge, tapping volume, and concentration.
2. The drug can be released gradually and under supervision.
3. Surfactants do not require special handling or storage conditions, such as inert environments or low temperatures.
4. They can be used as a depot formulation, which allows for controlled release of the medication.
5. They increase the oral bioavailability of the poorly soluble medications.
6. They maintain a stable structure even as an emulsion.
7. Surfactants are biocompatible, biodegradable, non-immunogenic, and non-toxic.
8. They are reasonably priced for large-scale production.
9. They have the ability to protect the drug from enzyme metabolism.
10. They improve the medication's stability.[10-11]

Disadvantage of niosomes

The aqueous niosome solutions have a short shelf life because of drug encapsulation hydrolysis, fusion, aggregation, and leakage.

1. The preparation of multilamellar vesicles via the extrusion and sonication procedures requires a significant amount of time and specialized processing equipment. [12]

Role in Targeting drug delivery

The primary goal of pharmaceutical therapy is to reach a steady state blood or tissue level that is both therapeutically effective and nontoxic over an extended period of time. Attaining the goal required developing a suitable dosing schedule. By delivering the medication at the site of action and

supplying it at a rate dictated by the body's demands over the course of therapy, innovative drug delivery systems aim to achieve these two objectives. Targeted drug delivery is perceived to imply the selective and effective localization of the pharmacologically active moiety at the pre-identified (preselected) targeted in therapeutic contexts by limiting the drug's access to normal cellular linings that are not the target and thereby minimizing its toxic effect and optimizing its therapeutic index. Targeted drug delivery is the process by which a drug conjugate or carrier complex selectively delivers a drug to pre-identified target cells in a certain manner. The optical pharmacological action might be pursued by releasing functional molecules from their carrier at the site of action, where they would continue to function. The targeting methods fall into one of three categories: chemical, covalent bonding, or physical. To produce a derivative that was only active at the designated area, chemical methods involved modifying the original component. A range of physical procedures were used to utilise the carriers, which included liposomes, niosomes, resealed erythrocytes, platelets, magnetic microspheres, nanoparticles, and monoclonal antibodies. The benefits of the niosomal drug delivery system over conventional drug administration systems have drawn a lot of attention lately. It is also referred to as the particle colloidal carrier system [13–17].

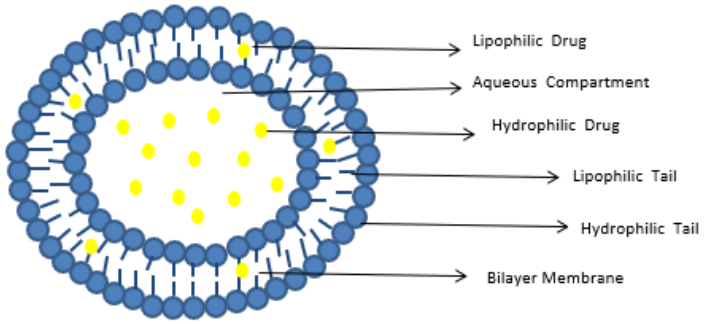

Figure 1 : Structure of Niosome

Components of Niosomes :

The two main substances that are used to prepare niosomes are nonionic surfactants and cholesterol. Cholesterol is used to give the niosomes their unyielding character and proper form. Surfactants have a significant role in the formation of niosomes. For the most part, the non-ionic surfactants that follow are used to organize niosomes in the spans (span 60,40,20,85,80), tweens (tween 20,40,60,80), and brijs (30,35,52,58,72,76).

Cholestrol :

Being an amphiphilic molecule, cholesterol aligns its aliphatic chain with the hydrocarbon chain of the surfactant and its OH group with the aqueous phase. In order to give non-ionic surfactants stiffness, cholesterol, a waxy steroid metabolite, is typically added. It is also known that cholesterol stops the gel to liquid phase transition, thereby preventing leaks.[18]

Non-ionic surfactants :

Niosomes are synthetic non-ionic surfactant vesicles that can be unilamellar or multilamellar. A non-ionic surfactant has a hydrophobic tail and a hydrophilic head group. The size of the niosome grows as the HLB value increases and the alkyl chain increases. HLB values 14–17 are therefore inappropriate for niosome formulation. 8 is the maximum entrapment efficiency for HLB values. These are non-ionic surfactants:

Ether-linked surfactants:

These surfactants have hydrophilic and hydrophobic moieties joined by ether. They are polyoxyethylene alkyl ethers, with the general

formula (CnEOm), where m = 3–7 represents the number of oxyethylene units and n = 12–18 represents the number of carbon atoms.

Di-alkyl chain surfactant:

The ability of this surfactant to transport sodium stibogluconate in experimental marine visceral leishmaniasis has been investigated. It was utilized as a key component of the niosomal formulation of stibogluconate.

C16H33CH-O[-CH2-CH-O]7-H
| |
CH2 CH2OH
|
C12H25-O (mol. Wt. 972)

Ester linked:

These surfactants are also known as ester linked surfactants because they feature an ester bond between hydrophilic and hydrophobic groups.

The application of this surfactant in the creation of niosomes carrying stibogluconate and in the transport of sodium stibogluconate to the experimental marine visceral leishmaniasis were also investigated.

C15H31CO[O-CH2-CH-CH2]2-OH
|
OH (mol. Wt. 393)

Sorbitan esters:

The ester-linked surfactants are called sorbitol esters. Commercial sorbitan esters are made by combining oleic acid with the partial esters of sorbital and its mono- and di-anhydrides.

CH2
|
H-C-OH
|
RCOO- C-H
|
H-C-OH
|
H-C-OOC-R
|
CH2OOC-R

Where, R is H or an alkyl chain.

These have been employed to ensnare a variety of medications, such as doxorubicin. Fatty acid and amino acid compounds: In certain niosome manufacturing processes, long chain fatty acids and amino acid moieties have been utilized to create "Ufasome" vesicles. [18, 19]

Charge inducers :

Positive and negative charge inducers are the two different categories of charged inducers. By introducing a charge to the surface of the produced vesicles, it improves their stability. It functions by offering larger zeta potential values and inhibiting the fusion of vesicles caused by repulsive forces of the same charge. Dicetyl phosphate, dihexadecyl phosphate, lipoamine acid, and sterylamine are the often used negative charge inducers whereas cetylpyridinium chloride and sterylamine are the regularly utilized positive charge inducers [18].

Anticancer activity of niosome :

Worldwide, cancer is the primary cause of mortality and a low quality of life. The effectiveness of various cancer treatments is questionable, despite the fact that numerous methods have been developed to lower mortality, lessen chronic pain, and enhance quality of life. Early cancer cell diagnosis and the administration of highly precise medications to limit toxicity are two of the most crucial elements to ensuring optimal cancer treatment. Since traditional cancer treatment and diagnostics are so harmful and inefficient, researchers are turning to alternative approaches, such as nanotechnology, to improve cancer detection and lessen the disease's severity. Immunotherapeutic drugs based on nanotechnology have been utilized for a long time to treat various cancers by preventing cancer cell invasion and maintaining the presence of healthy cells at the site [20]. Clinical usage of the medication is complicated by its poor solubility, which results in low bioavailability and quick degradation. Agarwal et al. overcame this by

employing a niosomic system that included cholesterol and the neon surfactant SPAN 60 to increase the drug's solubility in the aqueous phase. Smooth, homogenous, spherical, highly cytocompatible niosomes with an average size of 479 nm were produced with ease. Nanomorocin is readily distributed in an aqueous environment, in contrast to free morocin. In four distinct cancer cell lines, a very high entrapment efficacy (97%) controlled and sustained release of morocin was seen, leading to increased therapeutic efficacy. The findings imply that the morose niosome system is a potentially useful tactic to boost antitumor activity against a variety of cancer types and could be a key component of future targeted chemotherapeutic approaches [21]. Kong et al. reported on a different investigation in which operated niosomes were used as a transdermal medication delivery system for the treatment of tumors. These scientists have created a novel drug nanoparticle with the potential to target tumors that is based on hyaluronic acid and niosomes that enhances drug transport through the skin. Their findings showed that the endocytosis of nanocarriers in tumor cells was greatly enhanced by the addition of hyaluronic acid. Hyaluronic acid niosomes are thought to be safe, efficient skin penetration carriers as well as a useful and prospective treatment option for malignancies through dermal administration [22]. The physiological and biological properties of niosomes loaded with the nucleophilic Ru (III)-complex HoThyRu as an anticancer agent and the nucleolin-targeting AS1411 aptamer that enables the selective recognition of cancer cells were examined in another study by Bayindir et al. The morphology, average size, Zeta potential, electrophoretic mobility, and stability were examined using a variety of biophysical methods. The outcomes demonstrated a considerable increase in HeLa cells' antiproliferative activity. Ru (III)-containing niosomes' bioactivity was effectively increased by AS1411 in each of the examined cell lines [23, 24, 25].

Application of niosomal formulation in cancer therapy :

Molecular dynamic simulation:

A molecular dynamic simulation (MDS) tool is necessary for the design of an in silico drug delivery formulation because it predicts formulation features before synthesis and offers information about potential self-assembled structures. This reduces the need for in vitro and in vivo experiments [26 , 27]. MDSs are suitable for investigating atomic-level interactions between molecules; they are in charge of figuring out drug diffusivity, solubility, carrier-drug miscibility, drug build-up in organs, cell distribution, clearance, kidney filtration, and the drug release kinetics that impact niosomes [28]. Poor bioavailability resulting from inefficient cell membrane penetration is a major factor contributing to medication failure in clinical studies [29]. When used extensively, MDS is a reliable technique that has been used for the examination of interactions and orientations between drug molecules and bilayer forms [31].

It also estimates the drug-loaded nanocarrier permeation to a cell membrane [30]. The first critical stage in a drug's absorption from bilayer structures to the target is its solubility [32]. The production of niosomes requires the application of several processes in the solvent media. However, the solvent may have an impact on the production, purity, and reaction kinetics of processes like crystallization and extraction [33]. Therefore, solubility plays a crucial role in the pharmaceutical sector when choosing the right solvent. These days, molecular surface area evaluations, hydrophilicity/hydrophobicity calculations, electronic, and topological assessments are necessary for the computational prediction of solubility [34]. By adjusting the pH and salt content in a range of organs, drug nanocarrier

solubility changes can be fully understood using MDS. Multiple applied carrier molecules are responsible for boosting the drug's stability when it comes to moderately soluble or insoluble medicines [35, 36]. A computer approach is devised [37, 38] to determine the miscibility of medicines and carrier molecules. Drug loading and releasing assessment is one of the MDS components [39, 40]. The simulations demonstrated that the drug load variations lead to a considerable alteration in the naparroker structure. Regarding medication release, other critical factors include the drug's size, internal structure, and position within the nanocarriers [41, 42]. The location of medication components within nanocarriers and the manner in which they release can be greatly influenced by free energy calculations. Frequently, nanocarriers are engineered and modelled to release the medication assessment in reaction to pH variations [43, 44]. One of the essential physicochemical variables for describing the association and dissociation rates of a binding or non-binding ligand to its target using MDS techniques is kinetics [45]. The majority of proteins feature small-molecule binding pockets that are not easily identified, so while NMR and X-ray crystallographic structures frequently show ligand-binding pockets, experimental models can occasionally conceal other potentially druggable locations [46]. To be apparent, these allosteric [47] and cryptic [48] binding sites must undergo a conformational change.One important property of pharmaceuticals is their ability to crystallize in several forms or polymorphs. MDS can study the crystallization of complex drug crystals and the possibility of new polymorphs of the crystal structure. Each polymorph of the medicine may differ from others in physiochemical features, such as density, solubility, bioavailability, mechanical strength, dissolution rate, and alike, that can affect fabrication and the therapeutic performance [49–51]. Complete reports on every MDS niosome study conducted to date are available. Sanghwa et al. [52] provided the first report of a niosomal bilayer. The MD simulation of span 80 and cholesterol was studied on several physical properties, including number of hydrogen bonds, area per lipid, thickness, and diffusion coefficient, at a duration of 60 nanoseconds. After that, in 2016, Aksornnarong et al. [53] used the Span 60 with and without 50 mmol% cholesterol to create a niosome in 60 ns for each step, according to Gromaces 4.5.4 software. Niosome characteristics were computed from the dynamic simulation at temperature, including area per lipid, molecular orientation, membrane thickness, lateral and transversal diffusion, and the number and kinetics of hydrogen bonds with or without cholesterol. The dynamic simulation showed that the niosome favored gel-phase formation with a higher order structure when it was free of cholesterol, but it showed more fluidity and a less ordered structure when it was present. Yoochan et al. [54] used the Gromacs software tool (version 4.5.2) to model the interaction between the Span 60/cholesterol niosome with flavones. Low concentrations allowed flavone to pass through the bilayer, but high concentrations caused it to accumulate at the core of the niosome and thicken the membrane. Following that, in 2018, I [55] represented the dynamical characteristics and structure of a niosome generated by Span 60 and cholesterol molecules at different concentrations of cholesterol (ranging from 0 to 70 mol%) using molecular dynamics simulations. They investigated whether cholesterol affects the niosome's structure and properties, such as thickness, area per molecule, and compressibility. Lastly, in 2019, Barani et al. [56] used the Gromacs software (version 4.5.4) for MD simulation to show the dynamic properties of Span 60 / Teen 60 / cholesterol and Span 60 / Teen 60 / ergosterol. Additionally, they proposed loading DNA with protamine-compressed niosomes and

Fe3O4 nanoparticles containing ergosterol rather than cholesterol. Predicting formulations with benefits like high trapping efficiency and low cytotoxicity, decreased drug consumption frequency, and magnetic characteristics for targeted distribution are the goals of building drug delivery systems.

ADME properties:

Absorption, distribution, metabolism, and excretion (ADME) is necessary to achieve any therapeutic goal with a new drug delivery system from the early stages to the final clinical evaluations [57, 58]. On the other hand, pharmacokinetic knowledge of ADME is an essential component of the drug delivery system study. In order to verify the absorption, calculations are made for Caco-2 permeability, human intestinal absorption, F bioavailability (20% and 30%), Pgp inhibitor, and Pgp sub-strate. For distribution prediction, plasma protein binding, the blood–brain barrier, and volume distribution are evaluated. Membrane enzymes known as CYPs are primarily found in the intestinal and hepatocyte endoplasmic reticulum and mitochondria. CYPs, including CYPs 3A4, 2D6, 2C19, 2C9, and 1A2, are responsible for almost 80% of of clinically used drugs [59]. To assess exertion, clearance and T1/2 (half-life) are examined. Furthermore, human hepatotoxicity and hERG blockers are primarily used to assess toxicity [60, 61]. Biomolecules are absorbed differently depending on their hydrophobicity (log P), solubility (log S), polarity, ionization, molecular weight, and size. Chemical constructions also affect metabolism and excretion, thus it's important to determine the chemical groups that are most exposed to metabolism. For example, lipophilic compounds have a fast metabolism, but hydrophilic ones are quickly removed. To examine chemical characteristics, a variety of software tools are available, including SWISS ADME (http://www.swissadme.ch/) and ADMETLAB (http://admet.scbdd.com/calcpre/index/) [62–65].

Molecular docking:

Molecular coupling is another type of virtual screening that simulates biological systems and forecasts the interaction of two or more molecular structures (drug and protein or enzyme) with varying binding affinities and root mean square deviations [66]. Out of the sixty distinct molecular docking algorithms, MOE-Dock [67], AutoDock Vina [68] and GOLD [69] have the highest scores; also, GOLD [69] and LeDock [70] recognize the proper active sites, and both Glide (XP) [71] and GOLD identify postures with a 90.0% efficiency [72]. A representation of niosome molecular coupling is given. Combining in silico techniques such as artificial intelligence, molecular dynamics, molecular coupling, and binding free energy [73] can improve performance prediction.

To summarize, in silico design and simulations play a major role in drug delivery studies since they enable the creation of a fully detailed design that includes all of the molecular features of the medication and carrier for the patient. This breakthrough allows for considerably faster, less expensive, and more efficient design of nanocarriers with optimal characteristics [74, 75].

Anti - cancer drug loading into niosome :

Drugs	Preparation method	Cancer type	Cell line	Findings	References
Methotrexate (MTX)	Ether injection method	-	Liver cells in mice	Useful in maintaining the levels of MTX in the blood after	[76]

				intravenous injection	
Paclitaxel (PCT)	TFH	Liver and intestine car-cinoma	Liver and intestine cells in Wistar rat	Improving the oral bio-variability of PCT	[77]
Morusin	Thin-layer hydration method	Breast cancer	MDA-MB-453	High-drug entrapment efficiency (97%), controlled and sustained release	[78]
Vinblastine	TFH	Lung cancer	TC-1 cells	High stability, high entrapment efficacy, lower releasing rate	[79]
siRNA	Micro-fluidization method	Breast cancer	MDA-MB-231	Achieve a maximum of 65% of GFP silencing in human breast cancer cells	[80]
Nucleophilic Ru(III)-complex HoThyRu	Film-hydration method	Colorectal cancer, cervi-cal cancer	HeLa cells, HTB-38, HCC2998	Antiproliferative activity	[81 – 82]
Doxorubicin	REW	Liver cancer, lung cancer	S180 sarcoma in NMRI mice	Decrease side effect with the aid of targeting tumor cell lines	[83]
Topotecan	Micro-fluidization method	Glioma, cervical cancer	Glioblastoma (U87) cells	Improve anti-glioma treatment, long-term stability	[84]
Doxorubicin	TFH	Breast cancer	MDA-MB-231	More sustained release, enhanced biocompat-ibility	[85]
Curcumin	Sonication method	Lung cancer	HLF cells	Improve bioavailableity and decrease side effect, increase drug concentration, and decay time of curcumin	[86]
Withaferin A	REW	Prostate cancer	CD31 marker cells	High stability	[87]

GTE	TFH	Breast cancer	MCF-7, HepG2, HL-60	High trapping efficiency, high stability after 3 weeks	[88]
Melittin	Thin-layer hydration method	Breast cancer	4T1, SKBR3	Enhanced the apoptosis rate, inhibited cell migration	[89]

CONCLUSION :

A relatively new medication delivery technology, niosomes are made up of two layers of non-ionic surfactants. It is possible to load different medications into niosomes by adjusting the experiment parameters and the ratio of surfactant to cholesterol. Moreover, hydrophobic and hydrophilic medications can be incorporated into niosomes due to their amphipathic nature. Moreover, niosomes lessen medication toxicity, delay drug release, and improve drug stability. In contrast to alternative medication delivery methods, niosomes don't need special handling or storage conditions. Future advancements in theory and computational optimization have made it possible for in silico technologies to be highly influential in the drug delivery domain. In conclusion, it appears that more research will likely lead to a thriving market for niosomes in pharmaceutical biotechnology and cancer research, which is a viable avenue for cancer treatment in the future.

REFERENCE :

1. Shakya V. Niosomes: A Novel Trend in Drug Delivery. Ijrdp. 2014; 3: 1036- 1041.
2. Makeshwar K, Wasankar S. Niosomes: a novel drug delivery system. Asian J. Pharm. Res. 2013; 3: 16-20.
3. Punithavalli G, Vignesh M. Formulation of Niosomal Suspension with enhanced oral bioavailability of Diclofenac sodium. Journal of Global Trends in Pharmaceutical Sciences. 2012; 3: 656-671.
4. Katare R, Gupta P, Mahor S, Rawat A, Khatri K, Katare Y, Panda A, Vyas S. Development of polysaccharide-capped niosomes for oral immunization of tetanus toxoid. Journal Drug Del. Sci. Tech. 2006; 16: 167-172.
5. Shahiwala A, Misra A. Studies in topical application of niosomally entrapped nimesulide. Journal of Pharm. Pharmaceut. Sci. 2002; 5: 220-225.
6. Bagheri A, Chu B, Yaakob H. Niosomal Drug Delivery Systems: Formulation, Preparation and Applications. World Applied Sciences Journal. 2014; 32: 1671-1685.
7. Sudheer P, Kaushik K. Review on Niosomes-A Novel Approach For Drug Targeting, Journal of Pharmaceutical Research. 2015; 1-14.
8. Sunilkumar M. Niosomes As novel drug delivery system. International Research Journal of Pharmaceutical and Applied Science. 2015; 5: 1-7
9. Arora, S, Niosomes: The unique vesicular drug carriers, Journal of Drug Delivery & Therapeutics, 2012; 2, (1), 96-101.
10. Biju SS, Telegaonar S, Mishra PR, Khar RK. Vesicular system: an overview. Ind J Pharm Sci. 2006; 68: 141-153.
11. Vyas SP, Khar RK. Controlled drug delivery system: concept and advances. New Delhi: CBS Publishers and Distributors; 2002.
12. Verma S, Singh SK, Navneet S, Mathur P, Valecha V. Nanoparticle vesicular systems: a versatile tool for drug delivery. J Chem Pharm Res. 2010; 2(2): 496-509.
13. Baillie, AJ, Florence, AT, Hume, LR, Muirhead, GT, and Rogerson, A, The preparation and properties of niosomes non-

ionic surfactant vesicles, J Pharm Pharmacol, 1985; 37, 863–868.

14. Banker, GS, Rhodes, CT, Sustained and Controlled Release Drug Delivery Systems. In: Modern pharmaceutics, ed. 4, Vol. I, New York, Marcel Dekker, 2002: 503-519.
15. Hofland, HEJ, Vandergeest, R, Bodde, HE, Junginger, HE, and Bouwstra, JA, Estradiol permeation from nonionic surfactant vesicles through human stratum corneum, in-vitro, Pharm. Res., 1994; 11, 659–664.
16. Vyas, SP, Khar, RK, Novel carrier systems. In: Targeted and Controlled Drug Delivery, CBS Publishers & Distributors Pvt. Ltd., 2010: 249-279.
17. Baillie, AJ, Coombs, GH, Dolan, TF, and Laurie, J, Nonionic surfactant vesicles, Niosomes, as a delivery system for the anti-leishmanial drug, sodium stibogluconate, J Pharm Pharmacol, 1986; 38, 502–505.
18. Sankhyan A, Pawar P. Recent Trends in Niosome as Vesicular Drug Delivery System. Journal of Applied Pharmaceutical Science. 2012; 2: 20-32
19. Arul J. An Overview on Niosome as Carrier in Dermal Drug Delivery. J. Pharm. Sci. & Research. 2015; 7: 923-929.
20. Jin C, et al. Application of nanotechnology in cancer diagnosis and therapy-a mini-review. Int J Med Sci. 2020;17(18):2964.
21. Agarwal S, et al. Formulation, characterization and evaluation of morusin loaded niosomes for potentiation of anticancer therapy. RSC Adv. 2018;8(57):32621–36.
22. Muzzalupo R, Tavano L. Niosomal drug delivery for transdermal targeting: recent advances. Res Rep Transdermal Drug Deliv. 2015;4:23–33.
23. Mahale N, et al. Niosomes: novel sustained release nonionic stable vesicular systems—an overview. Adv Colloid Interface Sci. 2012;183:46–54.
24. Bayindir ZS, Yuksel N. Characterization of niosomes prepared with various nonionic surfactants for paclitaxel oral delivery. J Pharm Sci. 2010;99(4):2049–60.
25. Riccardi C, et al. AS1411-decorated niosomes as effective nano- carriers for Ru (III)-based drugs in anticancer strategies. J Mater Chem B. 2018;6(33):5368–84.
26. Katiyar RS, Jha PK. Molecular simulations in drug delivery: opportunities and challenges. Wiley Interdiscip Rev Comput Mol Sci. 2018;8(4):e1358.
27. Li Q, et al. Drug-loaded pH-responsive polymeric micelles: Simulations and experiments of micelle formation, drug loading and drug release. Colloids Surf B. 2017;158:709–16.
28. Xiang T-X, Anderson BD. Molecular dynamics simulation of amorphous hydroxypropylmethylcellulose and its mixtures with felodipine and water. J Pharm Sci. 2017;106(3):803–16.
29. Wen W, et al. Benzaldehyde, a new absorption promoter, acceler- ating absorption on low bioavailability drugs through membrane permeability. Front Pharmacol. 2021;12:1176.
30. Wadhwa R, et al. Molecular dynamics simulations and experi- mental studies reveal differential permeability of withaferin- A and withanone across the model cell membrane. Sci Rep. 2021;11(1):1–15.
31. Yousefpour A, et al. Interaction of PEGylated anti-hypertensive drugs, amlodipine, atenolol and lisinopril with lipid bilayer mem- brane: a molecular dynamics simulation study. Biochim Biophys Acta BBA-Biomembr. 2015;1848(8):1687–98.
32. Gao Y, Olsen KW. Molecular dynamics of drug crystal dissolu-tion: simulation of acetaminophen form I in water. Mol Pharm. 2013;10(3):905–17.

33. Gani R, et al. A modern approach to solvent selection: although chemists' and engineers' intuition is still important, powerful tools are becoming available to reduce the effort needed to select the right solvent. Chem Eng. 2006;113(3):30–44.
34. Seyf JY, Haghtalab A. A junction between molecular dynam- ics simulation and local composition models for computation of solid-liquid equilibrium-A pharmaceutical solubility application. Fluid Phase Equilib. 2017;437:83–95.
35. Xiang T-X, Anderson BD. Molecular dynamics simulation of amorphous hydroxypropyl-methylcellulose acetate succinate (HPMCAS): polymer model development, water distribution, and plasticization. Mol Pharm. 2014;11(7):2400–11.
36. Hassanvand A, et al. Biosynthesis of NanoSilver and its effect on key genes of flavonoids and physicochemical properties of Viola tricolor L. Iran J Sci Technol Trans A Sci. 2021;45(3):805–19.
37. Gupta J, et al. Prediction of solubility parameters and miscibility of pharmaceutical compounds by molecular dynamics simula-tions. J Phys Chem B. 2011;115(9):2014–23.
38. Abedi S, et al. Nitric oxide and selenium nanoparticles confer changes in growth, metabolism, antioxidant machinery, gene expression, and flowering in chicory (Cichorium intybus L.): potential benefits and risk assessment. Environ Sci Pollut Res. 2021;28(3):3136–48.
39. Shariatinia Z, Mazloom-Jalali A. Chitosan nanocomposite drug delivery systems designed for the ifosfamide anticancer drug using molecular dynamics simulations. J Mol Liq. 2019;273:346–67.
40. Moghadam AV, et al. New insights into the transcriptional, epi- genetic, and physiological responses to zinc oxide nanoparticles in datura stramonium; potential species for phytoremediation. J Plant Growth Regul. 2021;41:271.
41. Salo-Ahen OM, et al. Molecular dynamics simulations in drug discovery and pharmaceutical development. Processes. 2021;9(1):71.
42. Soleymanzadeh R, et al. Selenium nanoparticle protected straw- berry against salt stress through modifications in salicylic acid, Medical Oncology (2022) 39:2401 3 Page 21 of 22 240 ion homeostasis, antioxidant machinery, and photosynthesis per- formance. Acta Biol Cracoviensia s Bot. 2020;62:33–42.
43. Rog T, Bunker A. Mechanistic understanding from molecular dynamics simulation in pharmaceutical research 1: drug delivery. Front Mol Biosci. 2020;7:371.
44. Modi S, Anderson BD. Determination of drug release kinetics from nanoparticles: overcoming pitfalls of the dynamic dialysis method. Mol Pharm. 2013;10(8):3076–89.
45. De Vivo M, et al. Role of molecular dynamics and related methods in drug discovery. J Med Chem. 2016;59(9):4035–61.
46. Durrant JD, McCammon JA. Molecular dynamics simulations and drug discovery. BMC Biol. 2011;9(1):1–9.
47. Oleinikovas V, et al. Understanding cryptic pocket formation in protein targets by enhanced sampling simulations. J Am Chem Soc. 2016;138(43):14257–63.
48. Moghadam B, et al. Computational evidence of new putative allosteric sites in the acetylcholinesterase receptor. J Mol Gr Model. 2021;107:107981.
49. Mandal T, Marson RL, Larson RG. Coarse-grained modeling of crystal growth and polymorphism of a model pharmaceutical molecule. Soft Matter. 2016;12(39):8246–55.

50. Jha PK, Larson RG. Assessing the efficiency of polymeric excipients by atomistic molecular dynamics simulations. Mol Pharm. 2014;11(5):1676–86.
51. Rostamizadeh E, et al. Green synthesis of Fe. sub. 2O. sub. 3 nanoparticles using fruit extract of Cornus mas L. and its growth-promoting roles in Barley. J Nanostruct Chem. 2020;10(2):125–31.
52. Han S. Molecular dynamics simulation of sorbitan monooleate bilayers. Bull Korean Chem Soc. 2013;34(3):946–8.
53. Ritwiset A, Krongsuk S, Johns JR. Molecular structure and dynamical properties of niosome bilayers with and without cholesterol incorporation: a molecular dynamics simulation study. Appl Surf Sci. 2016;380:23–31.
54. Myung Y, Yeom S, Han S. A niosomal bilayer of sorbitan monostearate in complex with flavones: a molecular dynamics simulation study. J Liposome Res. 2016;26(4):336–44.
55. Somjid S, Krongsuk S, Johns JR. Cholesterol concentration effect on the bilayer properties and phase formation of niosome bilayers: a molecular dynamics simulation study. J Mol Liq. 2018;256:591–8.
56. Barani M, et al. In silico and in vitro study of magnetic niosomes for gene delivery: the effect of ergosterol and cholesterol. Mater Sci Eng C. 2019;94:234–46.
57. Bhosale RR, et al. Current perspectives on novel drug carrier systems and therapies for management of pancreatic cancer: an updated inclusive review. Crit Rev Ther Drug Carrier Syst. 2018;35(3):195.
58. Su C, et al. Absorption, distribution, metabolism and excretion of the biomaterials used in Nanocarrier drug delivery systems. Adv Drug Deliv Rev. 2019;143:97–114.
59. Beck TC, et al. Descriptors of cytochrome inhibitors and useful machine learning based methods for the design of safer drugs. Pharmaceuticals. 2021;14(5):472.
60. Dong J, et al. ADMETlab: a platform for systematic ADMET evaluation based on a comprehensively collected ADMET data-base. J Cheminform. 2018;10(1):1–11.
61. Xiong G, et al. ADMETlab 2.0: an integrated online platform for accurate and comprehensive predictions of ADMET properties. Nucleic Acids Res. 2021;49:W5.
62. Moss DM, Siccardi M. Optimizing nanomedicine pharmacoki- netics using physiologically based pharmacokinetics modelling. Br J Pharmacol. 2014;171(17):3963–79.
63. Farouk F, Shamma R. Chemical structure modifications and nano-technology applications for improving ADME-Tox prop-erties, a review. Arch Pharm. 2019;352(2):1800213.
64. Zolnik BS, Sadrieh N. Regulatory perspective on the importance of ADME assessment of nanoscale material containing drugs. Adv Drug Deliv Rev. 2009;61(6):422–7.
65. Li M, et al. Physiologically based pharmacokinetic (PBPK) modeling of pharmaceutical nanoparticles. AAPS J. 2017;19(1):26–42.
66. Badria FA, et al. Development of provesicular nanodelivery sys- tem of curcumin as a safe and effective antiviral agent: statistical optimization, in vitro characterization, and antiviral effectiveness. Molecules. 2020;25(23):5668.
67. Corbeil CR, Williams CI, Labute P. Variability in docking success rates due to dataset preparation. J Comput Aided Mol Des.2012;26(6):775–86. 168.
68. Österberg F, et al. Automated docking to multiple target structures: incorporation of protein mobility and structural water

heterogeneity in AutoDock. Proteins Struct Funct Bioinform. 2002;46(1):34–40.
69. Jones G, Willett P, Glen RC. Molecular recognition of receptor sites using a genetic algorithm with a description of desolvation. J Mol Biol. 1995;245(1):43–53.
70. Zhao H, Caflisch A. Discovery of ZAP70 inhibitors by high- throughput docking into a conformation of its kinase domain generated by molecular dynamics. Bioorg Med Chem Lett. 2013;23(20):5721–6.
71. Friesner RA, et al. Glide: a new approach for rapid, accurate docking and scoring. 1. Method and assessment of docking accuracy. J Med Chem. 2004;47(7):1739–49.
72. Pagadala NS, Syed K, Tuszynski J. Software for molecular dock- ing: a review. Biophys Rev. 2017;9(2):91–102.
73. Pinzi L, Rastelli G. Molecular docking: shifting paradigms in drug discovery. Int J Mol Sci. 2019;20(18):4331.
74. Siepmann J, Siepmann F. Modeling of diffusion controlled drug delivery. J Control Release. 2012;161(2):351–62.
75. Abd-algaleel SA, et al. Evolution of the computational phar- maceutics approaches in the modeling and prediction of drug payload in lipid and polymeric nanocarriers. Pharmaceuticals. 2021;14(7):645.
76. Azmin M, et al. The effect of non-ionic surfactant vesicle (niosome) entrapment on the absorption and distribution of methotrexate mice. J Pharm Pharmacol. 1985;37(4):237–42.
77. Sezgin-Bayindir Z, et al. Niosomes encapsulating paclitaxel for oral bioavailability enhancement: preparation, characterization, pharmacokinetics and biodistribution. J Microencapsul. 2013;30(8):796–804.
78. Agarwal S, et al. Formulation, characterization and evaluation of morusin loaded niosomes for potentiation of anticancer therapy. RSC Adv. 2018;8(57):32621–36.
79. Amiri B, et al. Delivery of vinblastine-containing niosomes results in potent in vitro/in vivo cytotoxicity on tumor cells. Drug Dev Ind Pharm. 2018;44(8):1371–6.
80. Obeid MA, et al. Formulation of nonionic surfactant vesicles (NISV) prepared by microfluidics for therapeutic delivery of siRNA into cancer cells. Mol Pharm. 2017;14(7):2450–8.
81. Riccardi C, et al. AS1411-decorated niosomes as effective nano- carriers for Ru (III)-based drugs in anticancer strategies. J Mater Chem B. 2018;6(33):5368–84.
82. Riccardi C, et al. Anticancer ruthenium (III) complexes and Ru (III)-containing nanoformulations: an update on the mechanism of action and biological activity. Pharmaceuticals. 2019;12(4):146.
83. Rohde LE, et al. Health outcomes in decompensated congestive heart failure: a comparison of tertiary hospitals in Brazil and United States. Int J Cardiol. 2005;102(1):71–7.
84. Ag Seleci D, et al. Rapid microfluidic preparation of niosomes for targeted drug delivery. Int J Mol Sci. 2019;20(19):4696.
85. Barani M, et al. A new formulation of hydrophobin-coated niosome as a drug carrier to cancer cells. Mater Sci Eng. 2020;113:110975.
86. Marianecci C, et al. Non-ionic surfactant vesicles in pulmonary glucocorticoid delivery: characterization and interaction with human lung fibroblasts. J Control Release. 2010;147(1):127–35.
87. Shah HS, et al. Preparation, characterization, and pharmacological investigation of withaferin-A loaded nanosponges for cancer therapy; in vitro, in vivo and molecular

docking studies. Molecules. 2021;26(22):6990.

88. Baranei M, et al. Anticancer effect of green tea extract (GTE)- Loaded pH-responsive niosome Coated with PEG against different cell lines. Mater Today Commun. 2021;26:101751.
89. Dabbagh Moghaddam F, et al. Delivery of melittin-loaded niosomes for breast cancer treatment: an in vitro and in vivo evaluation of anti-cancer effect. Cancer Nanotechnol. 2021;12(1):1–35.
90. Akbarzadeh I, et al. Optimized doxycycline-loaded niosomal formulation for treatment of infection-associated prostate cancer: an in-vitro investigation. J Drug Deliv Sci Technol. 2020;57:101715.

HOW TO CITE: Shivani S. C. Gupta, Punam K. Satav, Kalyani K. Malthane, Vaibhav S. Adhao, Jaya P. Ambhore, Nikita A. Deshmukh, Niosomes: An Innovative Tailored Cancer Medication Delivery Mechanism, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 4, 803-816. https://doi.org/10.5281/zenodo.10998384