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Non-ionic surfactant vesicles; A future of nano-carrier system

Diwas Manger, Dr. S Rajarajan, Dr. Beny Baby, Mr. Suryakant KR Das, Hitesh Mohanty

Karnataka College of Pharmacy, Bangalore

Abstract

Niosomes are generally indicated as non- ionic surfactant. Niosomes have the potential advantage inside the cure sector because of their exceptional conduct in encapsulation either hydrophobic as well as hydrophilic agents. Recently, vesicles are found that it can work on the bioactivity of drug. Furthermore, it can work as another methodology to cause the eternal group of therapeutical agents, for example, synthetic drug, albumen medications and nucleic acid substance with less harmfulness and wanted focusing on effectiveness. niosomes have substantially better established during the formulation system and capacity then liposomes. Hereby new release structure is similarly simple to develop furthermore, increment with minimum yield rate. The niosomes tend to stack distinct classes of drug. In this review articles it summarizes niosomes structure, types, components, methods of niosomes preparation and application of niosomes that are recently used as drug transport system.

Keyword; Niosomes, Drug transport system, Preparation method of niosomes, vesicles and application.

INTRODUCTION

Drug delivery is process by which active drug can be transport into the targeted side to treat the disease. There is different drug administration route such as internasal, ocular, oral, intravenous, rectal and intramuscular. These are the most common ways to treat many health issues. But they have some disadvantage such like unstable, uncontrolled release, side effects, poor absorption and many more.[1]

Controlled drug delivery system (DDS) are advanced systems for the transport of pharmaceutical compound inside the body, which have important significance to upgrade the efficacy of medication. It achieves the best accommodating effect by reducing medication side effects and increasing their bioavailability and dissolution [2] conventional drug delivery system shows many drawbacks, such as unfavourable pharmacokinetics and circulation, that may cause unwanted side effects, degradation of drug in blood and targeted of drug to the site can decrease. nanocarriers were investigated to beat the drawback related with standard prescription transport system [3]

Nano-carriers like liposomes, polymerase , micelles , polymer-based vesicles, and niosomes can give an perfect methodology to the transport of helpful experts to target objections .considering their advantage , experts stand apart to them ,by working on its components or creating a surface with various capabilities , nanocarriers , for instance ,can work on the half- life of medications in serum, prevent medications from being taken up by reticulo-endothelial system (RESs) and decrease vague adsorption. Also, they can in addition shield the medication from debasement away and in vivo steam. nanocarriers offer a couple of

advantage over standard medicine. Drug can change their shape, charge, properties and zeroing in the on component to control their take up, zeroing in on or end. It can be directed through various courses, e.g., nasal effective or oral courses [4]

Niosomes are bilayer vesicles made of different surfactants which are not ionic. Niosoms are initially introduced as a substitute to liposomes for controlled delivery of drug in order to address issues with sanitization, large-scale production, and dependability. In 1975, L'Oreal created and protected the first niosomes plans. Niosomes were used for the first time to deliver anticancer drug. [5]

The size range of the little lamellar plans of niosomes are between 10 to 1000 nm. Surfactant that were used for the formulation of niosomes are immunogenicity-free, biodegradable, and biocompatible. Niosomes have better advantage than liposomes and it have more engineered security of surfactants than phospholipids which are easily hydrolysed as a result of the ester bond and cost effective.[6] The capability to encapsulation both hydrophilic and lipophilic mixture is one of the benefits that niosomes share with liposomes. Also, it ca be formulated with fundamental techniques, require low creation cost and they are consistently showing long period, to overcoming the significant challenges of liposomes. Niosomes or non-ionic surfactants vesicles (NISVs) are commonly made by joining cholesterol and charged particles like diacetyl phosphate or stearyl amine with non-ionic surfactants like Span, Tween, Brij's.[7]

THE STRUCTURE OF NIOSOMES

Niosomes are cholesterol and non-ionic surfactants -based vesicular drug delivery vehicles. They are better than liposomes in terms of large-scale production, consistency and sterilization.[42] To form the bilayer structure non-ionic surfactant are self-aggregation on aqueous media. They are connected with significant sold areas for a surface strain among water. Niosomes have three types of unilamellar vesicles such as; small {SUV), large (LUV), and multilamellar (MLV).[8]

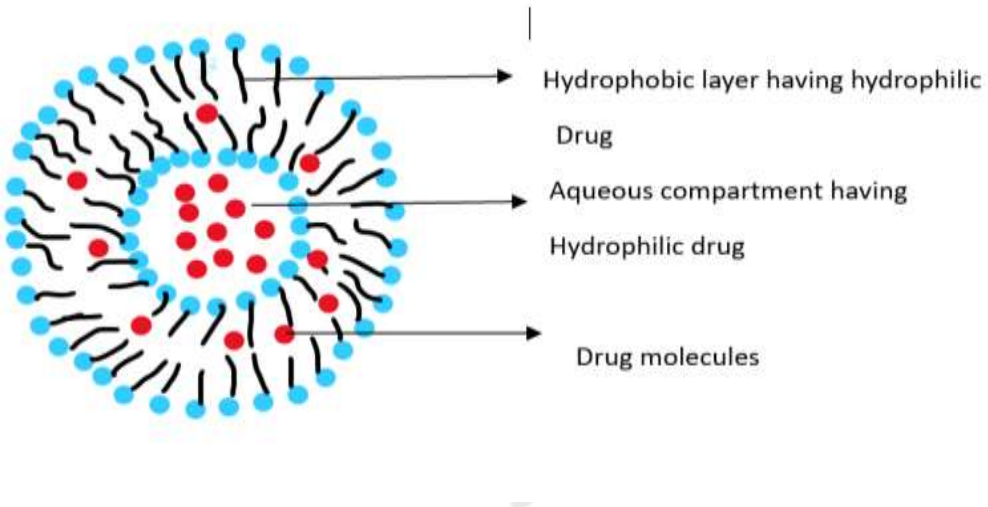


Fig 1: structure of niosomes

COMPENENTS OF NIOSOMES

Non-ionic surfactants

The polar or hydrophobic heads of a bilayer system developed by the non-ionic surfactants change challenging fluid-wide correspondences, whereas the hydrocarbon or hydrophobic head change so the planned exertion using the watery media would be less. To attained thermodynamic steadfast quality, all bilayer folds over themselves as unsurprising layer for example structure vesicles with the goal that the hydrocarbon/water content disappears.

There is various type of non -ionic surfactants which are used for the manufacture of niosomes. for example, Span (60,40,20,80), Tween (20, 60, 40, 80), Brij's (30,35,52,58,72).

Non- ionic surfactants have four classes such as; alkyl ethers; certain surfactants for creating of niosomes contain chemicals substances (surfactants-I, surfactants-II, surfactants -III) alkyl ester, alkyl amide (for example galactosidase and glycosides) are utilized to disturbed niosomes vesicles and easters of fatty acids.[36]

Charged molecules

Enhancing the niosomes stability through electrostatic repulsion, which prevents combination, a few charge molecules are introduced. The negatively charged particles that are utilized are phosphotidic destructive and diacetyl phosphate (DCP). The main role of these charged particles is to stop niosomes from aggregation. [9][40]

Cholesterol

Cholesterol is a significant added substances in the formulation of niosomes. although the cholesterols presence has an impact on a number of the niosomes properties, cholesterol itself is not necessary for its formulation. It can influence permeability and rigidity of the layer, capture effectiveness, security, time capacity and their harmfulness. When using low HLB surfactant with cholesterol, it may make the vesicles more stable. The used of cholesterol improve the thickness and rigidity of the formulation. [10][37]

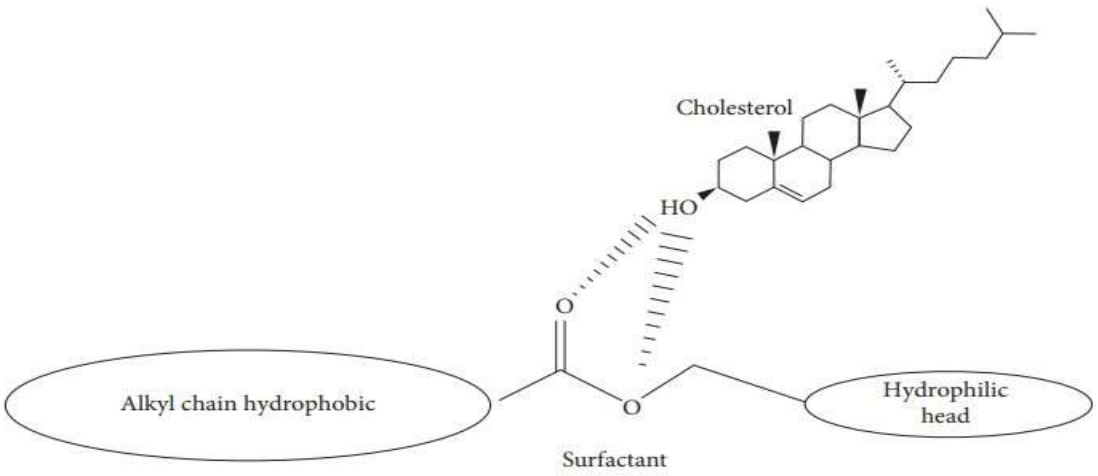


Fig 2: Interaction structure of cholesterol and surfactant [11]

Hydrophilic -lipophilic balance (HLB)

Relationship between hydrophilic and hydrophobic molecules of surfactants is objectively expressed by HLB. Higher HLB surfactants have greater water solubility than lower HLB surfactants. Niosomes size and the active ingredients EE were effect by the HLB values. HLB value of 4-8 with an surfactant can formulate niosomes. If the HLB values is 6 or more than cholesterol is required to form niosomes.[18]

Niosomes

- made of surfactant and cholosterol .
- size range from10 - 1000nm .
- unexpensive
- stable
- less toxic

liposomes

- made by bilayer of phospholipids
- size range from 10-3000nm
- expensive
- unstable
- more toxic

Types of unilamellar vesicles

Niosomes are divided into three classes based on their size;

a) small unilamellar vesicles (SUV) - 10 to 100nm.
b) large unilamellar vesicles (LUV) -100 to 3000 nm.
c) multilamellar vesicles (MLV) have more than one bilayer.

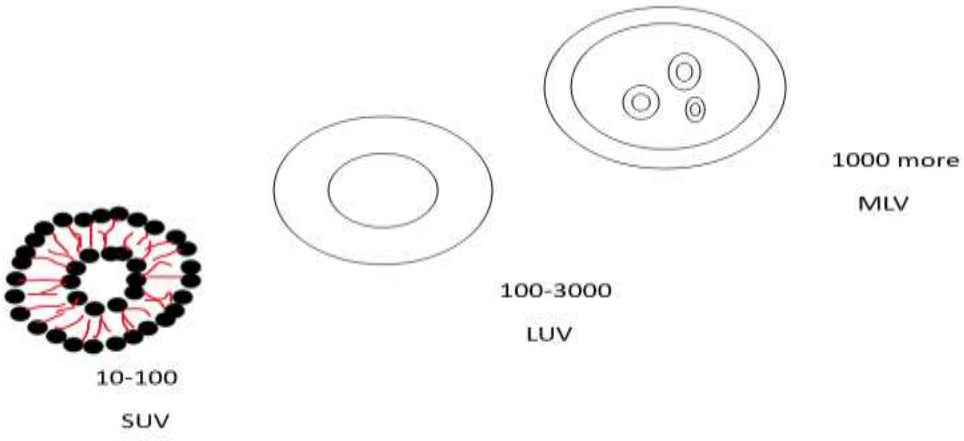


Fig 3; structure of bilayer vesicles

Proniosomes

Proniosomes are the types of niosomes arrangement it consist of water-soluble transporters and surfactant. The formulation of proniosomes is rehydrated before used and it help to overcome the drawbacks of niosomes like collection, combination and leakage of drug moieties.[38]

Discome

Cholesterol levels are low in structures with a large disk shape known as discomes. It was reported that spherical niosomes could be made by incubating them for one hour at 75°C in cholesteryl poly-24-oxyethylene ether (solution C24).[11] the development of discome formulation can used for sustained release in ocular delivery, 11-60 um are their size range.[38]

Apsasome

Apsasome are multi-layer vesicles that include charge lipid, like dihexadecyl phosphate. The formulation can further develop the transdermal drug-delivery and reduced the problems which set off utilizing responsive oxygen species.[39]

Elastic niosomes

The vesicles consist of a mixture of water, ethanol, cholesterol, and surfactant. The important advantage of this vesicles has high degree of versatility, it allows them to flow through opening that are less than the diameter of them.[46]

Bol- surfactant niosomes

These structures are prepared from mixture of span and cholesterol. Bola surfaces features has an advantage of a high micelle concentration and low critical surface tension. [12]

Transfersomes

Transfersomes are also the type of niosomes which are novel deformable vesicular transporter system, basically consisting of phospholipids. Which close to form a vesicle after self-assembling into lipid bilayer in a fluid environment. Both hydrophobic and hydrophilic moieties are present in transfersomes and hence hold drug particles including a verity of solubilities. They can carry both hefty and light molecular weight drug.[13][46]

PREPARATION METHOD FOR NIOSOMES

Ethanol injection method

In this techniques, Suitable weighed tween 80 was dissolved in an appropriate volume of distilled water and heated to 80 °C. A suitable volume of ethanol was used to dissolved span 60 and the mixture was placed to a five- minutes. 50°C a sonication a precise dosage of the medication was introduced to the tween solution. Then, using a 30-gauze syringe to agitate the tween solution at various rates at a fixed rate of one millilitre per minute, prepared span solution was added dropwise. About 30 minutes of agitation at 80 °C, again it required to stirring at room temperature for an additional half hour. lastly, distilled water was used to re-create the formulation to the appropriate volume.[14]

Sonication method

In this techniques the solution of drug and the mixture of cholesterol and surfactant are slowly added in the buffer solution. After that mixture of solution is probe – sonicated with a probe sonicator at 60 °C. To create vesicles with several layers, to deliver unilamellar vesicles, it could undergo additional ultrasonication. [15][31]

Thin film hydration techniques (hand shaking method)

The surfactant and cholesterol are mixed in a round bottom flask by using this approach in an organic volatile solvent (like chloroform or diethyl methanol). Utilising a rotating evaporator, organic solvent is removed at room temperature, leaving the solid mixture in a thin coating that is retained on the flak wall. multilamellar niosomes can be produced by rehydrating the aqueous phase at 0 – 60 °C to a dried surfactant film with mild stirring.[15][29][65]

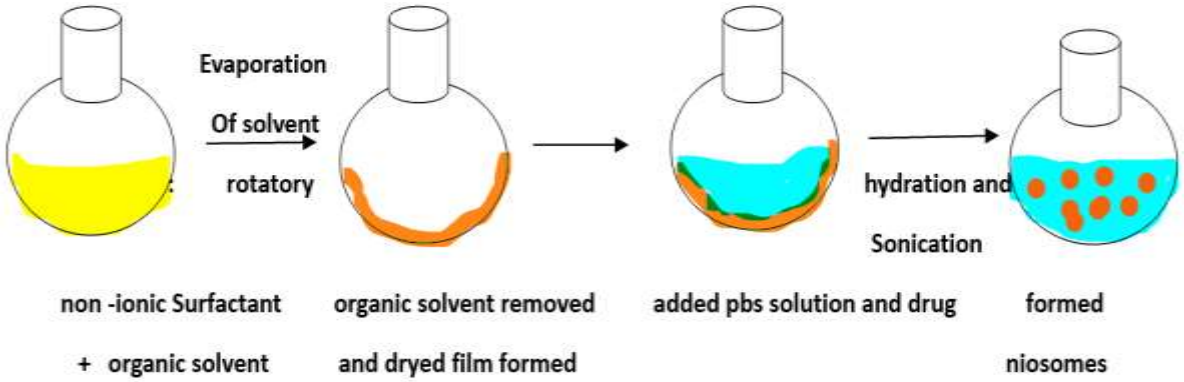


Fig 4; Thin film hydration techniques

Reverse phase evaporation method

In this process firstly drug is prepared in water- based system in one beaker, and surfactant and cholesterol are mixed in an organic solvent in another beaker. After that in the organic aqueous phase is added. and formed two -phase arrangement, this phase is homogenized under reduce pressure to remove organic phase, after removed organic phase the large unilamellar vesicles are formed.[16][45]

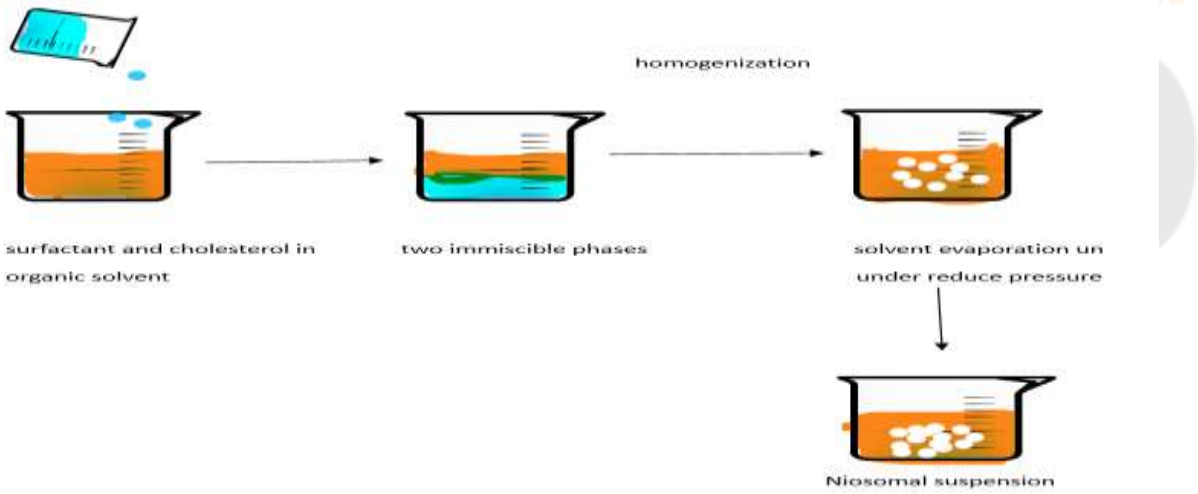


Fig 5; Reverse phase evaporation method

Emulsion method

In this techniques , cholesterol and surfactant are mixed in organic solvent in one beaker and aqueous drug solution are prepared in one beaker, after that mixture of organic solvent is added in an aqueous medication solution to create an emulsion of oil in water. After that, the evaporation of organic solvent occurs to get an aqueous medium containing niosomes suspension.[17]

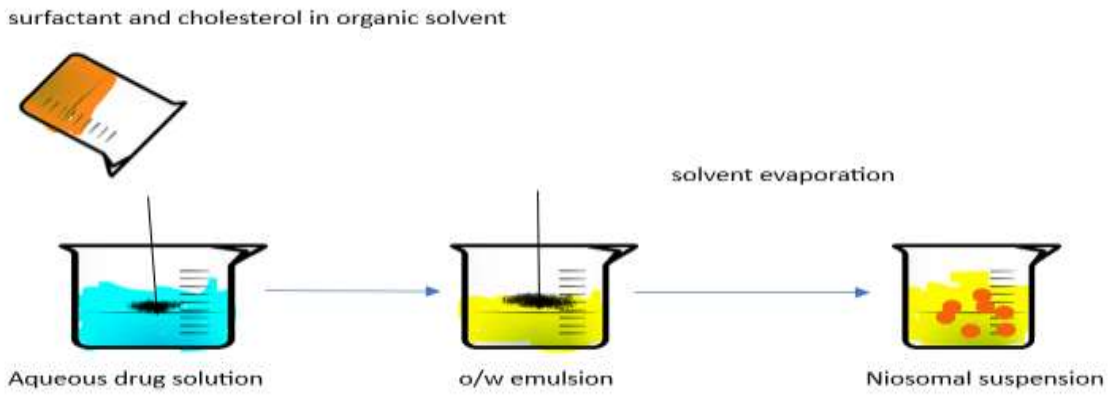


Fig 6; Emulsion method

Micro fluidization method

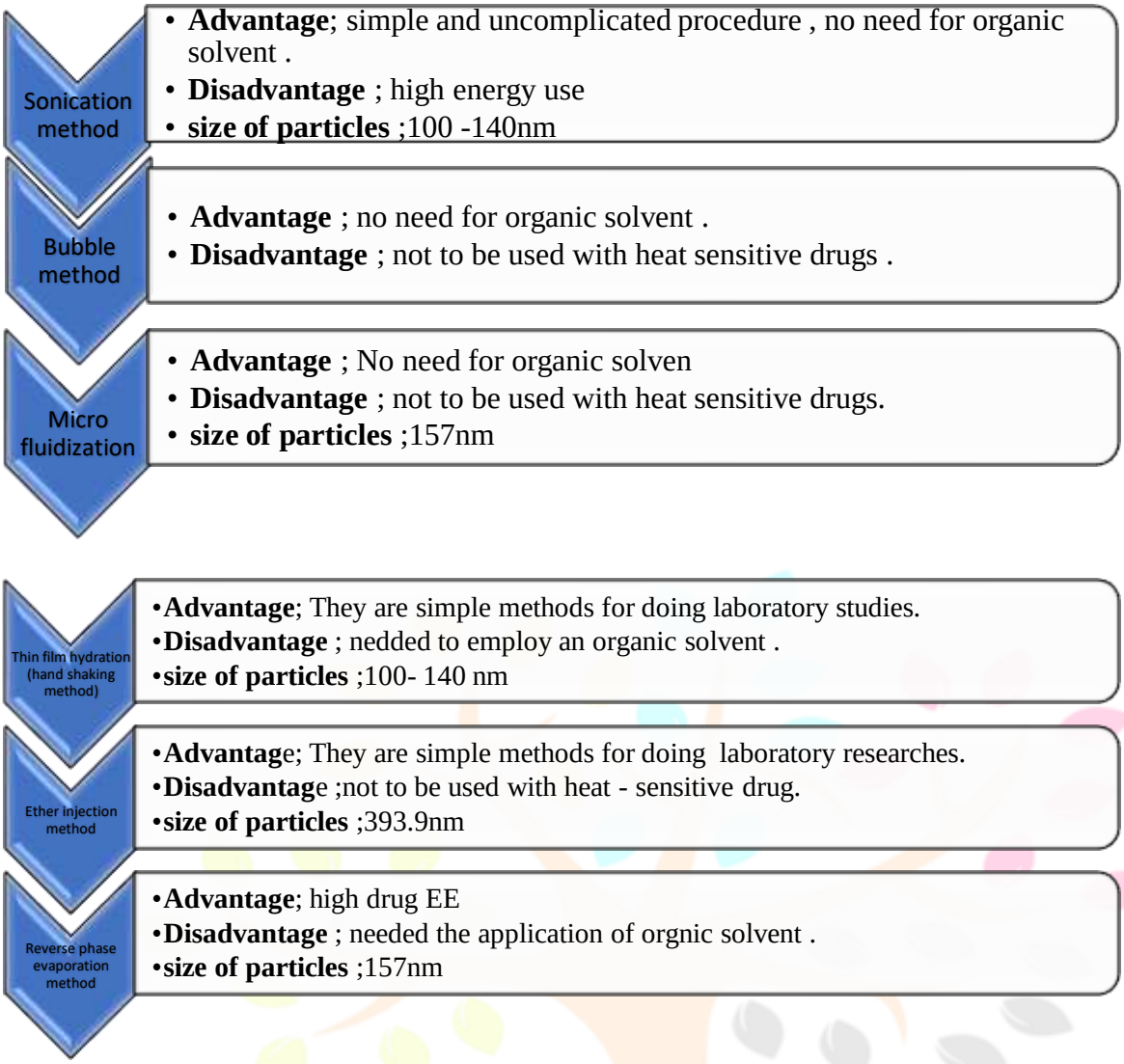
In this techniques , drug and surfactant are combined, then exerted pressure to create a reservoir, to an ice-filled communication chamber. To eliminate the heat produced throughout the procedure, the solution is run through a cooling loop. This process results in highly homogenous niosomes that are reduced in size.[41]

Lipid injection method

In this techniques, organic solvent are not necessarily used. cholesterol and surfactant both are melted and then injected to create a niosomes suspension into a highly watery phase containing drug particles that had dissolved.[18]

Ether injection method

In these techniques basic principle is to gradually dissolve a surfactant solution in diethyl ether in hot water that is kept at 60°C. The combination surfactant in ether is injected into aqueous solution using a 14 – gauge needle. Ether vaporization cause only one layer of vesicles to be arranged. The diameter of the vesicles ranges from 50 to 1000 nm, and the shape of the niosomes depends on the conditions used.[19]



NIOSOMES APPLICATION

Delivery of proteins and peptides

Protein and Peptides drugs which are orally administration was always change due to the destruction caused by GITs acidic medium and enzyme. However, these drugs are protected from the proteolytical proteins by niosomes. By the aided of modified light microscope, the definition was improved for stacking and discharged as a component of cholesterol to traverse 60M properties and used methyl organ to identify the location of protein in the vesicles. Niosomes of insulin coated with trimethyl chitosan is prepared for oral administration to improve insulin permeation.[43]

Delivery of vaccine and antigen

There are many surfactants which have been used as vaccine adjuvants because they have immunostimulatory properties. The adjuvant properties of 1-monopalmitoyl glycerol prepared niosomes; cholesterol; dicetyl phosphate (5;4;1) were shown in mice by given an ovalbumin or designed peptide bearing a recognized lymphocyte epitope and ox-like serum subcutaneously. In immune-reconstituted SCID- human mice, the formulation of same niosomes was also found to function as a vaccination adjuvant when administered intraperitoneally.[44][50]

Delivery of anticancer drug

Niosomes details can delivery different anticancer medications with less side effects. conventional chemotherapy is connected to reduced therapeutical effectiveness, a high rate if adverse effects, harm to normal cells, and an inability to target malignant cells specially. Colloidal niosomes system offer a potential approach for both passive and active drug delivery to tissues that pose a risk. Due to the blood-brain barrier low permeation, formulation of niosomes can deliver anticancer drug and control their

stability and low bioavailability and some side effects.[20][33] E.g.; The goal of this study was to examine whether artemether-loaded nano niosomes could have anti- breast cancer effects. Thin film hydration was used to create the niosomes using a mixture of cholesterol, tween and span at varying molar ratio. The formulation of the optimized niosomes was chosen for evaluation. The result of the 12-days trial shown that, in comparison to the control growth, nano-niosomes successfully inhibited tumors growth. [53]

Carrier of haemoglobin

Haemoglobin an also be carried by niosomes. niosomes suspension visible spectrum are appears to be superimposable the free haemoglobin. vesicles allow for the passage of oxygen and some way to non-encapsulation haemoglobin the haemoglobin dissociation curve can be change. The majority of drug used to treat antineoplastic diseases have severe side effects. The metabolism can be altered by niosomes; prolong the drugs half-life and circulation, thereby reducing its side effects. Niosomes are slower moving end segment that connect greater plasma levels and lowered cancer multiplication rate. [21][47]

Targeted drug delivery

Niosomes have ability to target medications that is one of the most advantage feature. When treating tumours in animals that are understood to spread to the spleen and liver, such placement of drug is employed. The liver problem caused by parasites can be treated with this medication restriction. Drug can be directed to organs other than the Res with the help of niosomes. Niosomes can be directed toward particular organs by attacking a carrier system, such as antibodies, to them [22][30]

Drug carrier as niosomes

Niosomes may serve as a neighbourhood station for the for the improved appearance of dermally dynamic constructs and as a solubilization matrix. As agents that improve the penetration or that act as rate limiting film obstructions to control the basic absorption of drug.[23] [28] E.g.; The goal of this work was to assess potential candidates and optimization the formulation of valacyclovir niosomes for long release of drug by using a three -factorial design of experiment. The medication valacyclovir is loaded in niosomes made by the ratio of cholesterol to span 60 in thin-film hydration process. The result shows the effectiveness of entrapment, effect on the vesicles size and the release of medication from the niosomes after the combination of surfactant and cholesterol.[52]

Brain targeting

Pentamidine clinical usefulness is limited because of unfortunate penetrability across blood mind obstruction and more hepatotoxicity. to overcome this problems pentamidine niosomes coated with chitosan -glutamate were ready for the intranasal medication administration to make it to the brain. The blood brain barrier and firs pass hepatic metabolism are passes by the intranasal route to the brain. [24][27][35]

Treatment of HIV-AIDS

Zidovudines have low potency and toxicity that make it unstable to treat AIDS patients in more case. The formulation of niosomes might decrease that significant challenges. They believed that zidovudine loaded niosomes would provide more potential to treat AIDS and supported drug delivery. [25][48] E.g.; The goal of this work to assess the develop carriers' anti-HIV effect. the PEGylated niosomes was loaded with Tenofovir to create a unique formulation using the cholesterol and span 60 surfactants in thin film hydration process. TAT peptide addition for improved cellular transit. The outcome might have shown the efficacy of the tenofovir-loaded PEGylate niosomes coupled with TAT peptide work to fight HIV or prevent the virus from replicating.[51].

Cosmetics

The first cosmetics production Niosomes was present in 1987. The advantage of niosomes in superficial and healthy skin and their application include the capacity to extend the strength of drug entrapped and furthermore develops bioavailability of substances with low absorption rates and enhance the penetration of skin. [26][49]

Table – 1

SEVERAL ROUTES ARE INVESTIGATED FOR NIOSOMES FOR EXAMPLES,

Route	Drug	Surfactant	Method	Reference
Oral	Celecoxib	Span 60	Proniosome derived niosomes method	**54**
	Ganciclovir	Span 60 and 40	Reverse phase evaporation	**55**
	Plasmid DNA for Hepatitis B	Span 60	Reverse phase evaporation	**56**
	Methotrexate	Tween 80	Thin film hydration	**57**
Ocular	Gatifloxacin	Span 60	Solvent injection method	**58**
	Naltrexone	Span 60	Reverse phase evaporation	**59**
	Plasmid pCMS-EGFP	Tween 80	Solvent emulsification evaporation	**60**
Dermal and transdermal	Acetazolamide	Span 60	Thin film hydration	**61**
	Artemisone	Span 60	Thin film hydration	**62**
	Moxifloxacin	Span 20and 60, Tween 20 and40,	Thin film hydration	**63**

LIMITATION AND CHALLENGES OF NANOCARRIER

Researchers and regulatory bodies encounter many difficulties when it comes to drug-loaded nanocarriers. Stability maintenance, scalable optimization techniques, robust characterization techniques and safety regulation are required to overcome these challenges.[64]

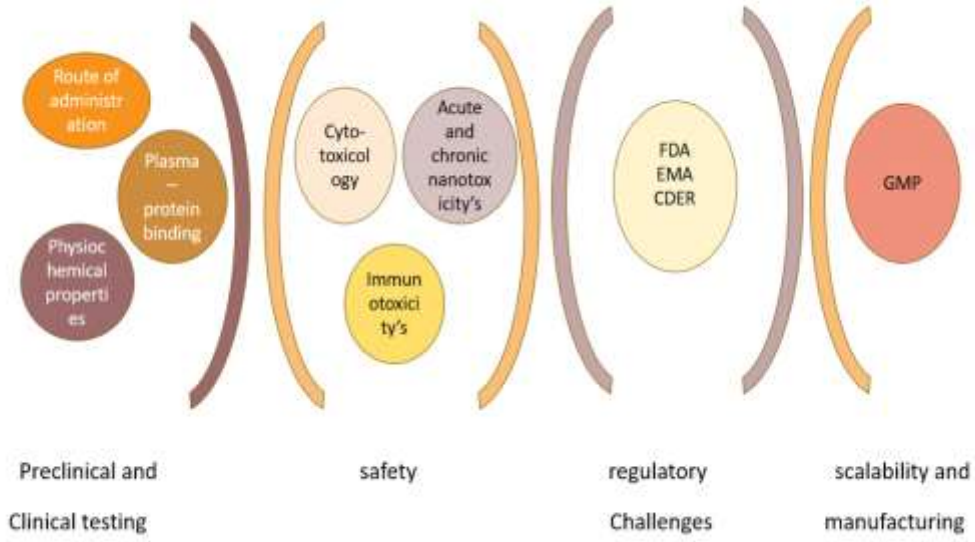


Fig 7; Pharmaceutical nanotechnology's present limitations and challenges.

CONCLUSION

Nanocarriers act as progressive stage to limit toxicity, further develop drug effectiveness and make it more targetable by novel preparation, formulation components and modification method. over the past few years, various nanocarriers details have be improved, presenting a variety of invitro and in vivo characterization methods. They are mostly made of cholesterol and surfactant at a buffer solution at proper pH. Niosomes have been broadly read up for various application for treatment of cancer, transdermal, skin, oral to brain specifically administered medication. Niosomes have been investigated as a liposomes substitute. Niosomes have a higher chemical stability than liposomes do, less toxic, low cost and osmotically active. Non-ionic surfactants vesicles have ability to change drugs metabolism, tissue distribution, plasma clearance energy and cell contact.

REFERENCE

1. Majumder J, Taratula O, Minko T. Nanocarrier-based systems for targeted and site-specific therapeutic delivery. Advanced drug delivery reviews. 2019 Apr 1; 144:57-77.
2. Hu J, Ni Z, Zhu H, Li H, Chen Y, Shang Y, Chen D, Liu H. A novel drug delivery system——Drug crystallization encapsulated liquid crystal emulsion. International Journal of Pharmaceutics. 2021 Sep 25; 607:121007.
3. Ge X, Wei M, He S, Yuan WE. Advances of non-ionic surfactant vesicles (niosomes) and their application in drug delivery. Pharmaceutics. 2019 Jan 29;11(2):55.
4. Alshawwa SZ, Kassem AA, Farid RM, Mostafa SK, Labib GS. Nanocarrier drug delivery systems: characterization, limitations, future perspectives and implementation of artificial intelligence. Pharmaceutics. 2022 Apr 18;14(4):883.
5. Abdelkader H, Alani AW, Alany RG. Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly, fabrication, characterization, drug delivery applications and limitations. Drug delivery. 2014 Mar 1;21(2):87-100.

6. Kaur D, Kumar S. Niosomes: present scenario and future aspects. Journal of drug delivery and therapeutics. 2018 Sep 6;8(5):35-43.
7. Wilkhu JS, Ouyang D, Kirchmeier MJ, Anderson DE, Perrie Y. Investigating the role of cholesterol in the formation of non-ionic surfactant-based bilayer vesicles: thermal analysis and molecular dynamics. International journal of pharmaceutics. 2014 Jan 30;461(1-2):331-41.
8. Aher P, Dandgavhal K, Bhandari D, Saindane H, Deore N, Amrutkar S. Niosomes as a potential drug delivery system. Int J Pharm Sci Rev Res. 2021 Jun;68(1):21-7.
9. Rajera R, Nagpal K, Singh SK, Mishra DN. Niosomes: a controlled and novel drug delivery system. Biological and Pharmaceutical Bulletin. 2011 Jul 1;34(7):945-53.
10. Bhardwaj P, Tripathi P, Gupta R, Pandey S. Niosomes: A review on niosomal research in the last decade. Journal of Drug Delivery Science and Technology. 2020 Apr 1; 56:101581.
11. Gharbavi M, Amani J, Kheiri-Manjili H, Danafar H, Sharafi A. Niosome: a promising nanocarrier for natural drug delivery through blood-brain barrier. Advances in Pharmacological and Pharmaceutical Sciences. 2018 Dec 11;2018.
12. Chen S, Hanning S, Falconer J, Locke M, Wen J. Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterization, pharmaceutical and cosmetic applications. European journal of pharmaceutics and biopharmaceutics. 2019 Nov 1; 144:18-39.
13. Thabet Y, Elsabahy M, Eissa NG. Methods for preparation of niosomes: A focus on thin-film hydration method. Methods. 2022 Mar 1; 199:9-15.
14. Sharma D, Ali AA, Aate JR. Niosomes as Novel Drug Delivery System: Review Article. PharmaTutor, 2018; 6 (3): 58-65.
15. Kumar GP, Rajeshwarrao P. Nonionic surfactant vesicular systems for effective drug delivery—an overview. Acta pharmaceutica sinica B. 2011 Dec 1;1(4):208-19.
16. Moammeri A, Chegeni MM, Sahrayi H, Ghafelehbashi R, Memarzadeh F, Mansouri A, Akbarzadeh I, Hejabi F, Abtahi MS, Ren Q. Current advances in niosomes applications for drug delivery and cancer treatment. Materials Today Bio. 2023 Oct 21:100837.
17. Puccetti M, Pariano M, Schoubben A, Giovagnoli S, Ricci M. Biologics, Theranostics, and Personalized Medicine in Drug Delivery Systems. Pharmacological Research. 2024 Jan 29:107086.
18. Chen S, Hanning S, Falconer J, Locke M, Wen J. Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterization, pharmaceutical and cosmetic applications. European journal of pharmaceutics and biopharmaceutics. 2019 Nov 1; 144:18-39.
19. Moghassemi S, Hadjizadeh A. Nano-niosomes as nanoscale drug delivery systems: an illustrated review. Journal of controlled release. 2014 Jul 10; 185:22-36.
20. Mahale NB, Thakkar PD, Mali RG, Walunj DR, Chaudhari SR. Niosomes: novel sustained release nonionic stable vesicular systems—an overview. Advances in colloid and interface science. 2012 Nov 15; 183:46-54.
21. Ag Seleci D, Seleci M, Walter JG, Stahl F, Scheper T. Niosomes as nanoparticular drug carriers: fundamentals and recent applications. Journal of nanomaterials. 2016 Oct;2016.
22. Sita VG, Jadhav D, Vavia P. Niosomes for nose-to-brain delivery of bromocriptine: Formulation development, efficacy evaluation and toxicity profiling. Journal of Drug Delivery Science and Technology. 2020 Aug 1; 58:101791.
23. Mazzotta E, Orlando C, Muzzalupo R. New nanomaterials with intrinsic antioxidant activity by surface functionalization of niosomes with natural phenolic acids. Pharmaceutics. 2021 May 21;13(6):766.
24. Muzzalupo R, Mazzotta E. Do niosomes have a place in the field of drug delivery? Expert Opinion on Drug Delivery. 2019 Nov 2;16(11):1145-7.
25. Bragagni M, Mennini N, Furlanetto S, Orlandini S, Ghelardini C, Mura P. Development and characterization of functionalized niosomes for brain targeting of dynorphin-B. European Journal of Pharmaceutics and Biopharmaceutics. 2014 May 1;87(1):73-9.
26. Abdelkader H, Ismail S, Hussein A, Wu Z, Al-Kassas R, Alany RG. Conjunctival and corneal tolerability assessment of ocular naltrexone niosomes and their ingredients on the hen's egg chorioallantoic membrane and excised bovine cornea models. International journal of pharmaceutics. 2012 Aug 1;432(1-2):1-0.

27. Muzzalupo R, Tavano L, La Mesa C. Alkyl glucopyranoside-based niosomes containing methotrexate for pharmaceutical applications: evaluation of physico-chemical and biological properties. International journal of pharmaceutics. 2013 Dec 15;458(1):224-9.
28. Murugesan N, Damodaran C, Krishnamoorthy S. Niosomal formulation of Quercetin and Resveratrol and in-vitro release studies. Journal of Integrated Science and Technology. 2022 Aug 10;10(2):134-8.
29. Yaghoobian M, Haeri A, Bolourchian N, Shahhosseni S, Dadashzadeh S. The impact of surfactant composition and surface charge of niosomes on the oral absorption of repaglinide as a BCS II model drug. International Journal of Nanomedicine. 2020 Nov 11:8767-81.
30. Gangwar M, Singh R, Goel RK, Nath G. Recent advances in various emerging vescicular systems: An overview. Asian Pacific Journal of Tropical Biomedicine. 2012 Feb 1;2(2): S1176-88.
31. Obeid MA, Khadra I, Aljabali AA, Amawi H, Ferro VA. Characterisation of niosome nanoparticles prepared by microfluidic mixing for drug delivery. International Journal of Pharmaceutics: X. 2022 Dec 1; 4:100137.
32. Alyami H, Abdelaziz K, Dahmash EZ, Iyire A. Nonionic surfactant vesicles (niosomes) for ocular drug delivery: Development, evaluation and toxicological profiling. Journal of Drug Delivery Science and Technology. 2020 Dec 1; 60:102069.
33. Sinico C, De Logu A, Lai F, Valenti D, Manconi M, Loy G, Bonsignore L, Fadda AM. Liposomal incorporation of Artemisia arborescens L. essential oil and in vitro antiviral activity. European Journal of Pharmaceutics and Biopharmaceutics. 2005 Jan 1;59(1):161-8.
34. SP ST, Mothilal M, Damodharan N, Jaison D. Screening and optimization of valacyclovir niosomes by design of experiments. International Journal of Applied Pharmaceutics. 2018 Jan 7:79-85.
35. Chahar RK, Tiwari C, Malik P, Jaiswal PK. Brain-Targeted Drug Delivery System: A Novel Approach. Journal of Drug Delivery and Therapeutics. 2022 Nov 15;12(6):171-8.
36. Al Qtaish N, Gallego I, Villate-Beitia I, Sainz-Ramos M, López-Méndez TB, Grijalvo S, Eritja R, Soto-Sánchez C, Martínez-Navarrete G, Fernández E, Puras G. Niosome-based approach for in situ gene delivery to retina and brain cortex as immune-privileged tissues. Pharmaceutics. 2020 Feb 25;12(3):198.
37. Witika BA, Bassey KE, Demana PH, Siwe-Noundou X, Poka MS. Current advances in specialised niosomal drug delivery: Manufacture, characterization and drug delivery applications. International Journal of Molecular Sciences. 2022 Aug 26;23(17):9668.
38. Aparajay P, Dev A. Functionalized niosomes as a smart delivery device in cancer and fungal infection. European Journal of Pharmaceutical Sciences. 2022 Jan 1;168:106052.
39. Ren Y, Nie L, Zhu S, Zhang X. Nanovesicles-mediated drug delivery for oral bioavailability enhancement. International Journal of Nanomedicine. 2022 Jan 1:4861-77.
40. Malik JA, Ansari JA, Ahmed S, Khan A, Ahemad N, Anwar S. Nano-drug delivery system: a promising approach against breast cancer. Therapeutic delivery. 2023 May;14(5):357-81.
41. Fainerman VB, Aksenenko EV, Kovalchuk VI, Mucic N, Javadi A, Liggieri L, Ravera F, Loglio G, Makievski AV, Schneck E, Miller R. New view of the adsorption of surfactants at water/alkane interfaces–Competitive and cooperative effects of surfactant and alkane molecules. Advances in Colloid and Interface Science. 2020 May 1;279:102143.
42. Verma A, Tiwari A, Saraf S, Panda PK, Jain A, Jain SK. Emerging potential of niosomes in ocular delivery. Expert opinion on drug delivery. 2021 Jan 2;18(1):55-71.
43. García-Manrique P, Machado ND, Fernández MA, Blanco-López MC, Matos M, Gutiérrez G. Effect of drug molecular weight on niosomes size and encapsulation efficiency. Colloids and Surfaces B: Biointerfaces. 2020 Feb 1;186:110711.
44. Mashal M, Attia N, Grijalvo S, Eritja R, Puras G, Pedraz JL. Stability of polymeric cationic niosomes and their plasmid DNA-based complexes as gene delivery carriers. Drug Delivery. 2023 Dec 31;30(1):2219420.
45. Fathalla D, Fouad EA, Soliman GM. Latanoprost niosomes as a sustained release ocular delivery system for the management of glaucoma. Drug development and industrial pharmacy. 2020 May 3;46(5):806-13.

46. Barani M, Paknia F, Roostaee M, Kavyani B, Kalantar-Neyestanaki D, Ajalli N, Amirbeigi A. Niosome as an effective nanoscale solution for the treatment of microbial infections. BioMed Research International. 2023 Aug 16;2023.
47. Ghaffari M, Kalantar SM, Hemati M, Dehghani Firoozabadi A, Asri A, Shams A, Jafari Ghalekohneh S, Haghiralsadat F. Co-delivery of miRNA-15a and miRNA-16–1 using cationic PEGylated niosomes downregulates Bcl-2 and induces apoptosis in prostate cancer cells. Biotechnology Letters. 2021 May;43:981-94.
48. Barani M, Mirzaei M, Torkzadeh-Mahani M, Lohrasbi-Nejad A, Nematollahi MH. A new formulation of hydrophobin-coated niosome as a drug carrier to cancer cells. Materials Science and Engineering: C. 2020 Aug 1;113:110975.
49. Li D, Martini N, Liu M, Falconer JR, Locke M, Wu Z, Wen J. Non-ionic surfactant vesicles as a carrier system for dermal delivery of (+)-Catechin and their antioxidant effects. Journal of Drug Targeting. 2021 Mar 16;29(3):310-22.
50. Al Qtaish N, Gallego I, Paredes AJ, Villate-Beitia I, Soto-Sánchez C, Martínez-Navarrete G, Sainz-Ramos M, Lopez-Mendez TB, Fernández E, Puras G, Pedraz JL. Nanodiamond integration into niosomes as an emerging and efficient gene therapy nanoplatform for central nervous system diseases. ACS Applied Materials & Interfaces. 2022 Mar 15;14(11):13665-77.
51. Yadavar-Nikravesh MS, Ahmadi S, Milani A, Akbarzadeh I, Khoobi M, Vahabpour R, Bolhassani A, Bakhshandeh H. Construction and characterization of a novel Tenofovir-loaded PEGylated niosome conjugated with TAT peptide for evaluation of its cytotoxicity and anti-HIV effects. Advanced Powder Technology. 2021 Sep 1;32(9):3161-73.
52. SP ST, Mothilal M, Damodharan N, Jaison D. Screening and optimization of valacyclovir niosomes by design of experiments. International Journal of Applied Pharmaceutics. 2018 Jan 7:79-85.
53. Mirzaei-Parsa MJ, Najafabadi MR, Haeri A, Zahmatkeshan M, Ebrahimi SA, Pazoki-Toroudi H, Adel M. Preparation, characterization, and evaluation of the anticancer activity of artemether-loaded nano-niosomes against breast cancer. Breast Cancer. 2020 Mar;27:243-51.
54. Nasr M. In vitro and in vivo evaluation of proniosomes containing celecoxib for oral administration. Aaps Pharmscitech. 2010 Mar;11:85-9.
55. Akhter S, Kushwaha S, Warsi MH, Anwar M, Ahmad MZ, Ahmad I, Talegaonkar S, Khan ZI, Khar RK, Ahmad FJ. Development and evaluation of nanosized niosomal dispersion for oral delivery of Ganciclovir. Drug development and industrial pharmacy. 2012 Jan 1;38(1):84-92.
56. Jain S, Singh P, Mishra V, Vyas SP. Mannosylated niosomes as adjuvant–carrier system for oral genetic immunization against Hepatitis B. Immunology letters. 2005 Oct 15;101(1):41-9.
57. Muzzalupo R, Tavano L, La Mesa C. Alkyl glucopyranoside-based niosomes containing methotrexate for pharmaceutical applications: evaluation of physico-chemical and biological properties. International journal of pharmaceutics. 2013 Dec 15;458(1):224-9.
58. Zubairu Y, Negi LM, Iqbal Z, Talegaonkar S. Design and development of novel bioadhesive niosomal formulation for the transcorneal delivery of anti-infective agent: In-vitro and ex-vivo investigations. Asian journal of pharmaceutical sciences. 2015 Jul 1;10(4):322-30.
59. Abdelkader H, Ismail S, Hussein A, Wu Z, Al-Kassas R, Alany RG. Conjunctival and corneal tolerability assessment of ocular naltrexone niosomes and their ingredients on the hen's egg chorioallantoic membrane and excised bovine cornea models. International journal of pharmaceutics. 2012 Aug 1;432(1-2):1-0.
60. Puras G, Mashal M, Zárate J, Agirre M, Ojeda E, Grijalvo S, Eritja R, Diaz-Tahoces A, Navarrete GM, Avilés-Trigueros M, Fernández E. A novel cationic niosome formulation for gene delivery to the retina. Journal of Controlled Release. 2014 Jan 28;174:27-36.
61. Zubairu Y, Negi LM, Iqbal Z, Talegaonkar S. Design and development of novel bioadhesive niosomal formulation for the transcorneal delivery of anti-infective agent: In-vitro and ex-vivo investigations. Asian journal of pharmaceutical sciences. 2015 Jul 1;10(4):322-30.
62. Dwivedi A, Mazumder A, Fox LT, Brümmer A, Gerber M, Du Preez JL, Haynes RK, Du Plessis J. In vitro skin permeation of artemisone and its nano-vesicular formulations. International Journal of Pharmaceutics. 2016 Apr 30;503(1-2):1-7.

63. Sohrabi S, Haeri A, Mahboubi A, Mortazavi A, Dadashzadeh S. Chitosan gel-embedded moxifloxacin niosomes: an efficient antimicrobial hybrid system for burn infection. International journal of biological macromolecules. 2016 Apr 1;85:625-33.

64. Alshawwa SZ, Kassem AA, Farid RM, Mostafa SK, Labib GS. Nanocarrier drug delivery systems: characterization, limitations, future perspectives and implementation of artificial intelligence. Pharmaceutics. 2022 Apr 18;14(4):883.

65. Kamboj S, Saini V, Bala S. Formulation and characterization of drug loaded nonionic surfactant vesicles (niosomes) for oral bioavailability enhancement. The scientific world journal. 2014 Jan 1;2014.