REVIEW ARTICLE

A Concise Literature Review on Niosome Drug Delivery from Ancient to Recent

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Abstract

About 50% of medications/drugs have obstacle of poor solubility, poor oral bioavailability, due to enzymatic/gastric degradation in the gastrointestinal tract pH, high pre-systemic intestinal and hepatic metabolism, permeability, small absorption window, and short residence duration at the absorption location. Niosomal drug deliveries have specific advantages over conventional dosage form with respect to improvement in bioavailability. Niosomes are colloidal particles created when non-ionic surfactants self-assemble in an aqueous solution to form closed bilayer structures. The various methods are reported until today for the preparation of niosomes; ether injection method, thin film hydration method, sonication method, microfluidization, multiple membrane extrusion method, reverse-phase evaporation technique, transmembrane Ph. Gradient drug uptake process (remote loading), the bubble method, freeze-thaw method, emulsion method, and formation of niosomes from proniosome. The current review article focused on the preparation and evaluation of niosome drug delivery and its advantages over conventional drug delivery. The niosomal drug delivery was found to be best for solubility and bioavailability enhancement of poorly water-soluble drugs.

Key words: Non-ionic surfactant, particle size, thin film hydration

INTRODUCTION

Oral route of administration is accepted to be the most convenient route for development of oral drug delivery system.[1] About 50% of medications/drugs have obstacle of poor solubility, poor oral bioavailability, due to enzymatic/gastric degradation in the gastrointestinal (GI) tract pH, high pre-systemic intestinal and hepatic metabolism, permeability, small absorption window, and short residence duration at the absorption location.[2] A variety of approaches can be used to modify the solubilization of drug and its bioavailability. Varied methods often used include micronation, chemical modification, pH adjustment, solid dispersion, complexation, cosolvency, micellar solubilization, and hydrotrophy.[3] The vesicles can operate as drug reservoirs and shield the drug from acidic and enzymatic degradation in the gastrointestinal tract. Niosomal drug deliveries have specific advantages over conventional dosage form with respect to improvement in bioavailability.[4] Niosomes are colloidal particles created when non-ionic surfactants self-assemble in an aqueous solution to form closed bilayer structures.[5]

FORMULATION COMPOSITION OF NIOSOMES[6,7]

Due to their lower irritant potential, non-ionic surfactants are preferred over cationic, anionic, and ampholytic.[6] Niosomes have a bilayer structure that is comparable to that of a liposome; however, they have more advantages over liposomes. Niosomes are tiny with size ranging from 10 nm to 100 nm. Niosomes contain both hydrophilic and lipophilic components, that is, amphiphilic nature. Niosomes have

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capacity to entrap both hydrophilic and lipophilic drugs [Figure 1]. Drugs which possess poor aqueous solubility and low bioavailability can be suitably used for the development on niosomes.[7]

Surfactant[8]

Non-ionic surfactants are a subclass of surfactants that lack charged groups in their hydrophilic heads. They are more stable, biocompatible than their anionic, amplified, or cationic cousins. They are consequently preferred for applications involving the creation of stable niosomes both *in vitro* and *in vivo* situations. Alkyl ethers, alkyl esters, alkyl amides, and fatty acids are the main non-ionic surfactant groups utilized in the processing of niosomes. The selection of surfactant molecules for niosome must take into account the hydrophilic-lipophilic balance and critical packing parameter values are important.

Cholesterol[9]

Cholesterol is used to enhance rigidity and orientational order. It can be assimilated at high molar ratios but does not contribute to the formation of the bilayer. As an amphiphilic molecule, cholesterol directs its OH group toward the aqueous phase and its aliphatic chain toward the hydrocarbon chain of the surfactant. By preventing the mobility of hydrocarbon carbon in the bilayer, rigid steroidal skeletons alternately positioned with surfactant molecules give rigidity. In addition, cholesterol has an added advantage to stop the transition from the gel to the liquid phase, which avoids leakage.

Additive[10]

To strengthen the physical stability of niosomes and prevent vesicle aggregation caused by electrostatic repulsive force, charge inducing chemicals are typically required. The widely used negatively charge inducer and positive charged inducers are diacetyl phosphate, phosphatide acid, and stearyl amine, stearyl pyridinium chloride, and cetylpyridinum chloride, respectively. Vesicle surface charges help to enhance the technical or biological properties of niosomes. When compared to conventional (uncharged) niosomes, negatively charged inducers like dicetyl phosphate (DCP) may also result in greater entrapment effectiveness, enhanced colloid stability.

TYPE OF NIOSOME[11]

According to size of niosomes:

a. Multiple lamellar vesicles (500–10000 nm)
b. Large unilamellar vesicles (100–3000 nm)
c. Small unilamellar vesicles (10–100 nm).

ANOTHER TYPE OF NIOSOME

Bola surfactant comprising niosome[12]

Bola-form amphiphilic are nonionic surfactants that have polar heads consisting of two identical aza-crown ether units joined by a lengthy alkyl chain.

Proniosome[12]

Proniosome is made using simple production procedures that can be avoided by preserving the composition and known characteristics of niosomes. They are actually carrier powders with surfactant coatings that can be hydrated in aqueous food matrices (milk, yoghurt, or functional beverages) to produce niosomes just before use.

Aspasomes[12]

Aspasomes are brand-new nanovesicles with one or more layers that are derived from ascorbyl palmitate (AP). These bilayer vesicles can increase transdermal medicine delivery's percutaneous absorption and consistency. AP, an amphiphilic ascorbic acid ester, was transformed into a double-layer vesicle in the presence of cholesterol (as a vesicle stabilizer) and DCP-charge inducer.

Discomes[13]

Discomes are potential drug carriers due to their low cholesterol levels and sustained release mechanism.

ADVANTAGES[14-20]

1. The infrastructure of hydrophilic, lipophilic, and amphiphilic moieties in niosomes allows for the accommodation of drug molecules with a wide spectrum of solubilities
2. Niosomes are naturally non-immunogenic, biodegradable, non-toxic, and biocompatible
3. They can release the drug in a sustained/controlled manner, for example, glimepiride
4. Oral bioavailability is increased for the poorly soluble drug, for example, as griseofulvin, paclitaxel, levofloxacin, and repaglinide
5. Niosomes are capable of encasing a variety of solubilized medicines
6. They do not need any particular handling or storage condition
7. They attempted to use oral, parenteral, and current routes to get to the site of action
8. Prevents acidic and enzymatic breakdown of drug improves stability
9. Simply by limiting the influence of the entrapped drug on the target cells and lowering the drug's clearance, they enhance its therapeutic performance

10. Niosomes increase the stability of an entrapped medication and they are osmotically active, for example, zidovudine and piroxicam
11. They might perform the function of a depot formulation, enabling a regulated release of the drug, for example, – acyclovir and metronidazole.

DISADVANTAGES[21]

1. Physical instability
2. Aggregation
3. Fusion
4. Entrapped drug leakage
5. Drugs that are encapsulated hydrolyze, reducing the shelf-life of the dispersions.

DRUG SELECTION FOR ORAL NIOSOMAL PREPARATIONS[22]

Poor drug permeability through the GI mucosa and/or low water solubility is two of these variables that are crucial. Poor water solubility and intrinsic dissolution rates are the main causes of decreased bioavailability for medications classified under biopharmaceutical classification systems II or IV. Poor GI permeability is another issue that greatly affects many people's oral bioavailability.

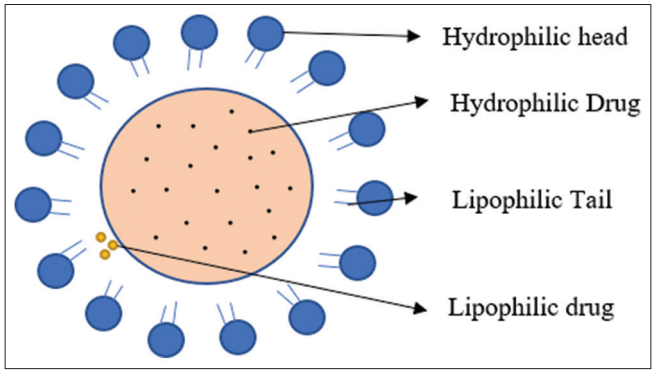

Figure 1: Amphiphilic structure of niosome

FACTORS INFLUENCING FOR PREPARATION OF NIOSOMES[23]

Drug

Drug entrapment in niosomes occurs most likely through interaction of the solute with the head groups of the surfactant, which increases the charge and mutual repulsion of the surfactant bilayers and increases vesicle size coated with PEG. Drug interaction with surfactant head groups results in the development of a charge that causes mutual repulsion between surfactant bilayers, increasing vesicle size. The charge generation on the bilayer prevents the vesicles from aggregating.

Amount and type of surfactant[23]

The surface free energy lowers as the hydrophobicity of a surfactant increases, the mean size of niosomes rises correspondingly as hydrophilic lipophilic balance (HLB) surfactants like Span 85 (HLB 1.8) to Span 20 (HLB 8.6) are used. According on temperature, lipid or surfactant type, and the presence of other elements like cholesterol, and the bilayers of the vesicles can either be in the so-called liquid state or in the gel state. The efficacy of entrapment is also influenced by the surfactant's phase transition temperature (TC), with Span 60 having a higher TC offering better entrapment.

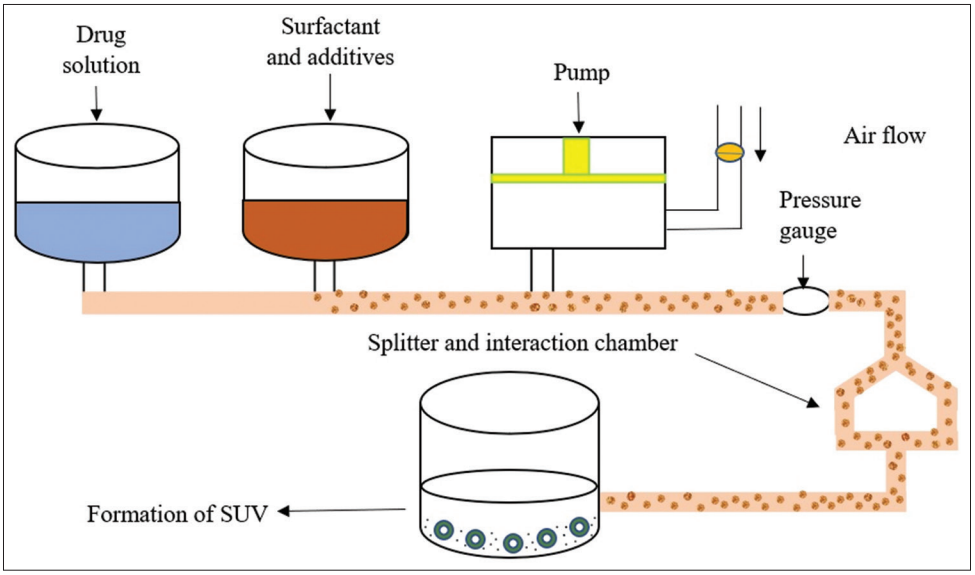

Figure 2: Microfludization method

Hydration temperature[24]

The size and shape of the vesicles during niosome formation could be influenced by temperature and hydration. The hydration temperature should be higher than the surfactant's transition phase temperature. The shape of vesicles can alter if the temperature is lower as that of surfactant TC. When the incorrect hydration temperature, volume of hydration medium, and time are chosen for the production of the niosomes, drug leakage problems are created. It also produces delicate niosomes.

Cholesterol content[25]

Cholesterol's inclusion into the niosomes bilayer structure results in the activation of membrane stabilizing enzymes. Therefore, adding cholesterol to the bilayer improves drug loading.

Membrane composition[26,27]

Stable niosomes can be produced by mixing various ingredients with surfactants and other chemicals. Niosomes permeability and stability characteristics can be modified by modifying membrane characteristics with different additions.

For example, the shape of the polyhedral niosomes created from C16G2 is unaffected when a small amount of Solulan C24 (cholesteryl poly24-oxyethylene ether) is added, preventing aggregation due to the development of steric hindrance, enoxacin.

Resistance to osmotic stress[28,29]

Niosomes in suspension experience a reduction in diameter in a hypertonic salt solution are added. Faster release may be caused by mechanical loosening of the vesicle structure under osmotic stress after an initial slow release with minor vesicle enlargement in the hypotonic salt solution, for example, salicylic acid.

Charge[30]

The presence of charge causes the interlamellar distance between succeeding bilayers in a multilamellar vesicle structure to rise. Greater overall volume is entrapped as a result.

METHOD OF PREPARATION

1. Ether injection method
2. Thin film hydration method (TFH)
3. Microfluidization method
4. Sonication method
5. Multiple membrane extrusion method
6. Reverse-phase evaporation technique (REV)
7. Transmembrane pH gradient drug uptake process (remote loading)
8. The bubble method
9. Freeze-thaw method
10. Emulsion method
11. Formation of niosomes from proniosome

Ether injection method[31]

The surfactant/cholesterol solution is dissolved in diethyl ether and gently injected into the aqueous phase at 60°C using a needle. During the ether's evaporation, large unilamellar vesicles are created [Table 1].

TFH (Handshaking method)[38]

This process involves dissolving the surfactants, cholesterol, and some additives − such as charged molecules − in an organic solvent in a flask with a circular bottom. A thin coating is then produced on the inside wall of the flask by removing the organic solvent using a rotary vacuum evaporator. The dry film is hydrated for a predetermined amount of time above the surfactant's TC while being continuously shaken. The drug-containing aqueous solution is added. This results in the formation of multilamellar niosomes [Table 2].

Microfluidization method[46,47]

By applying the microfluidization technology, it is possible to produce niosomes with more uniformity, smaller size, unilamellar vesicles, and improved reproducibility. This technology makes advantage of the submerged jet principle, in which two fluidized streams contact at extremely high-speed velocities in well-calibrated microchannels inside the interaction chamber. The arrangement of the impingement of a thin liquid sheet along a common front ensures that the energy supplied to the system stays within the region of niosome formation [Figure 2].

For example − The literature data for the drug (Topotecan) are available for preparing of niosomal formulation by microfluidization method. The niosomes were prepared using span 60, cholesterol. The entrapment efficiency (EE) (%) for the formulation was found to be 39.30–37.50% and Z was found to be –27.80 mV.

Sonication method[48]

The mixture of surfactant and cholesterol is distributed during the sonication in the water phase that also contains the drug in the flax. The mixture is then exposed to probe-assisted sonication for 3 min at 60°C, resulting in the production of multilamellar vesicles [Table 3].

Table 1: Literature for noisome prepared using ether injection method

Drug	Excipient	Outcome	Characterization	References
Griseofulvin (Oral route)	Span-20, Span-40, Span-60, cholesterol, and dicetyl phosphate (DCP)	Improved oral bioavailability and prolonged drug released.	Entrapment efficiency (EE) (76.8%)	[32]
Ofloxacin	Span 60, cholesterol, chloroform, and methanol	Improve therapeutic effect of drug.	Vesicle size (VS) (100–300 nm), Entrapment efficiency (EE) (78.4%)	[33]
Fluconazole (Oral route)	Cholesterol and Span 60	Achieve maximum therapeutic response with minimum side effect.	Entrapment efficiency (EE) (92.71±0.43%)	[34]
Carvedilol (Oral route)	Span 20, Span 60, Span 80, chloroform, DCP, and cholesterol	Improve bioavailability of drug (having fold 2.3 to 1.7).	Zeta potential (Z) (−27.7±3.4 mV), Entrapment efficiency (EE) 96.0±0.22%)	[35]
Aceclofenac	Cholesterol, methanol, and diethyl ether	Shows better therapeutic response of drug.	Vesicle size (VS) (4.22±0.47 μm to4.83±0.35 μm), Entrapment efficiency (EE) (90%)	[36]
Resveratrol (Topical route)	Cholesterol, methanol, and chloroform	It shows Prolonged therapeutic action.	Particle size (PS) (214.0–331.9 nm), entrapment efficiency (EE) 67.2±1.17%).	[37]

Table 2: Literature for niosome prepared using thin film hydration method

Drug	Excipient	Outcome	Characterization	References
Paclitaxel (Intravenous route)	Cholesterol, DCP, Span 40, and chloroform	Increase mean residence time (1.66±0.133 h).	Elimination half-life (7.63±0.380 h), the mean residence time (11.0±0.6 h)	[39]
Fluconazole (Cutaneous route)	Span 20, Span 40, Span 60, and DCP	It gives higher entrapment efficiency and shows sustain release effect.	PS (0.378±0.022 μm, 0.343±0.063 μm, 0.287±0.12 μm EE (>41%)	[40]
Doxycycline (Ophthalmic)	Span 60 and cholesterol	It shows sustain drug release.	PS 756±2.1 nm	[41]
Trans-Ferulic acid	Span 60, cholesterol, methanol, and chloroform	It shows high penetration to the skin.	PS (158.7 nm), EE (21.64%)	[42]
Lacidipine	Cholesterol and Span 60	EE (82.77±4.34%).	VS 676.98±10.92 nm, EE (82.77±4.34%)	[43]
Timolol malate	Span 20, Span 40, Span 60, Tween 40, and chloroform	Increase the bioavailability of drug.	PS 0.6nm to 3 micron, EE (94.6% and 98.8%)	[44]
α-lipoic acid	Span 20, Span 40, Span 60, Tween 20, Tween 40, and Tween 60	Improve bioavailability and penetration of the drug into CNS.	EE (94.5±0.2, 59.27±5.6%)	[45]

Table 3: Literature for niosome prepared using sonication method

Drug	Excipients	Outcome	Characterization	References
Rifampicin	Span 60 and cholesterol	Improve the drug release profile of a poorly soluble drug.	Size 190–893 nm, EE (75.37%)	[49]
Propylthiouracil	Tween, Span, cholesterol, and DCP	It shows controlled release of drug.	Drug release 75–94%	[50]
Vildagliptin	Cholesterol and Span 60	It shows sustain release of drug up to 13 h.	PS (179–250.9 nm), Z range between (33.5 mV±−50.4mV), EE (86.82–92.32%)	[51]
Rifampicin and ceftriaxone (dual therapy)	Span 60 and DCP	It shows high entrapment efficiency.	PS (165±893 nm), EE 96% for ceftriaxone and 99% for rifampicin	[52]

Table 4: Literature for niosome prepared reverse-phase evaporation technique

Drug	Excipients	Outcome	Characterization	References
Acetazolamide (Ophthalmic route)	Span 60, Span 40, and cholesterol	It shows higher EE (%) of drug.	EE (16.81–18.49%)	[56]
Isoniazid (Oral route)	Span 20, Span 60, cholesterol, chloroform, and diethyl ether	It shows target specific drug delivery.	Z 23Mv	[57]
Lansoprazole	Span 60, cholesterol, diethyl ether, and chloroform	Improve the therapeutic effect of drug.	EE (57.2%)	[58]
Vincristine	Span 60 and cholesterol	It improves drug penetration.	Z (−18.8mV)	[59]
Galangin (Oral route)	Span 60, Span 40, Span 20, cholesterol, and DCP	Increase the bioavailability of drug.	VS (−173.7±12.6 nm, 355.6±17.9 nm), EE (45.13±0.35, 77.69±0.45%)	[60]
Ellagic acid (Transdermal route)	Span 60, Tween 60, and cholesterol	It enhances permeability of the drug.	VS (124–752 nm), EE (1.35%, 26.75%)	[61]

Multiple membrane extrusion method[53,54]

A thin layer is created by evaporating a mixture of surfactant, cholesterol, and DCP in chloroform. The film is hydrated with aqueous drug polycarbonate membranes, solution, and the resulting suspension extruded through which are inserted in succession for up to eight passages. It is an effective technique for regulating noisy size.

For example − The literature data for the drug (Doxycycline hyclate) are available for preparing of niosomal formulation by multiple membrane extrusion method. The niosomes were prepared using Span 20, Span 60, Span 80, and cholesterol. The EE (%) for the formulation was found to be 92.33 ± 1.2.

REV[55]

Chloroform is used to dissolve surfactant and cholesterol. Then, an aqueous phase containing the drug is added, the two phases are combined, sonicated at 4–5°C, and the chloroform is then evaporated under reduced pressure. The mixture creates a gel, which is then hydrated to produce vesicles [Table 4].

Transmembrane pH gradient drug uptake process (remote loading)[62]

To create a thin lipid film on the wall of a round-bottomed flask, surfactant and cholesterol are dissolved in chloroform and evaporated under decreased pressure in equal parts. Using vortex mixing, an acidic chemical solution (often citric acid) is used to hydrate the film. After undergoing freeze-thaw cycles, the final product is added to an aqueous drug solution, and the mixture is vortexes. The sample's pH is then increased using a disodium hydrogen phosphate solution to 7–7.2 [Table 5].

The bubble method[66,67]

It consists of a flask with a round bottom and three necks that are heated in a water bath. The first neck and second neck are used to situate the water-cooled reflux and thermometer, while the third neck is used to provide nitrogen. In this buffer (pH 7.4) at 70°C, cholesterol and surfactant are combined. The dispersion mechanism generates and introduces a steady stream of nitrogen gas bubbles that result in the formation of niosomes.

For example − The literature data for the drug (Diclofenac sodium) are available for preparing of niosomal formulation by bubble method. The niosomes were prepared using Span 60-cholesterol. The particle size for the optimized formulation was found to be 311.6 nm and EE (%) is 92.33 ± 1.2.

Freeze-thaw method[68,69]

This method typically prepares a thin coating of nonionic surfactant. The thin film is then frozen in liquid nitrogen for 1 min and thawed in an aqueous solution for 60 s. This method is mostly used to create and melt multilamellar vesicles (FAT-MLVs).

For example − The literature data for the drug (Naltrexone hydrochloride) are available for preparing of niosomal formulation by freeze-thaw method. The niosomes were prepared using span 60, cholesterol. The particle diameter of drug was found to be 22.41 ± 1.40 and 5.37 ± 1.40.

Emulsion method[70,71]

Another approach for making niosomes is the emulsion method, which employs an oil-in-water emulsion created from an organic solution of surfactant, cholesterol, and aqueous drug solution. To get the finished product, the organic solvent is evaporated. In contrast, the lipid injection

approach involves melting a mixture of lipids and surfactant and injecting it into a heated aqueous phase that contains the medication.

For example − The literature data for the drug (Anthocyanins) are available for preparing of niosomal formulation by emulsion method. The niosomes were prepared using Tween 20, dichloromethane, and diethyl ether. The EE (%) for the formulation was found to be 40%.

Formation of niosomes from proniosome[72,73]

A surfactant can be used to coat a water-soluble carrier, such as sorbitol, to create niosomes. It creates a dry formulation through the coating process. There is a small layer of dry surfactant on top of each water-soluble particle. It is called "Proniosome" this preparation. Aqueous phase is added at T > T m, and then after a brief period of agitation [Figure 3].

T = Temperature, niosomes are produced.
Tm stands for the average phase TC.

The literature data for the drug (Felodipine) are available for preparing of niosomal formulation by proniosome method. The niosomes were prepared using span 60, cholesterol, and chloroform. The EE (%) was found to be 72.35%.

EVALUATION OF NIOSOME

Surface morphology, vesicle size, and zeta potential[74]

The size of the niosomes can be determined by various techniques. Mostly dynamic laser scattering particle size analyzer used for size distribution and polydispersity index. Morphology of the niosomes is determined by SEM, TEM, and AFM.

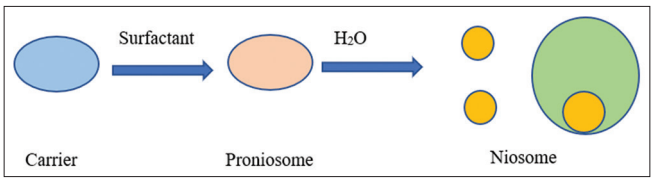

Figure 3: Conversion of proniosome to noisome

Phase behavior[75]

Thermal analysis methods, such as thermogravimetric analysis and differential scanning calorimetry and crystallographic analysis methods, like X-ray diffraction (XRD), are the two methods most frequently employed to study the phase behavior of niosomes (XRD). With the use of these techniques, it is possible to characterize and monitor the quality of niosomal formulations by examining the thermal behavior and crystallinity of such a system.

Freeze fractured microscopy[76]

Niosome size and shape were discovered to be influenced by drug entrapment, drug type, and surfactant type. Vesicles are typically freeze-thawed observed and measured for size using a freeze-fractured electron EE amount of drug total amount added microscope.

Drug release[77]

Through the use of isothermal titration calorimetry and dialysis, the drug release from the niosomes needed to be investigated.

In vitro release studies[78]

Dialysis tubing, reverse dialysis, and the Franz diffusion cell method are all methods for *in vitro* drug release. An approach that is frequently used to study *in vitro* release is one that uses dialysis tubing. A dialysis bag is cleaned and given distilled water to soak in. After 30 min, the drug-loaded niosomal suspension is added to this bag. The vesicle-containing bag is submerged in buffer solution and vigorously shaken at a temperature of 25°C or 37°C. Samples were taken out of the outer buffer (release medium) at predetermined intervals and replaced with the same volume of brand-new buffer. An appropriate assay method is used to determine the drug content in the samples.

In vivo behavior[79]

Niosomes have been found to be equivalent to liposomes *in vivo* for enhancing the therapeutic effectiveness of pharmaceuticals,

Table 5: Literature for niosome prepared using trans membrane pH gradient drug uptake process (remote loading)

Drug	Excipients	Outcome	Characterization	References
Mupirocin (Topical route)	Cholesterol, Span 80, and Tween 80	It shows controlled release of drug.	PS (2.21–6.83 μm), EE (99.97%)	[63]
Turmeric oil	Span 20, Span 60, Span 80, cholesterol, and DCP	It gives good stability of drug.	Z (−41.7–58.4 mV), PS (491.09 nm)	[64]
Ciprofloxacin	Tween 40, Tween 60, Span 40, Span 60, and cholesterol	High encapsulation efficacy and stability of drug.	EE and stability (61.9% 1.0, 77.9±2.8)	[65]

Table 6: Current research in formulation of niosomal dosage forms

Drug	Excipients	Method of preparation	Evaluation	Result	References
Cefixime	Tween 80 and cholesterol	TFH Method	VS (159.76±6.54 nm), EE (71.39±3.52%)	Increase solubility and bioavailability of drug.	[81]
Candesartan cilexetil	Span 60, cholesterol, DCP, and Tween 80	Film Hydration Method	EE (%) 99.06±1.74–36.26±2.78	Enhance stability of drug.	[82]
Levofloxacin	Tween 80 and cholesterol	TFH Method	VS (190.31±4.51 nm), PDI 0.29±0.03, EE (68.28±3.45%)	Improve bioavailability of drug.	[83]
Repaglinide	Span 20, Span 40, Span 60, Tween 20, Tween 60, Tween 80, and cholesterol	TFH Method	EE (52.8%, 77.1%)	Enhancing the bioavailability of the drug.	[84]
Gliclazide	Cholesterol and Span 60	Lipid Film Hydration Method	EE (%) 67.86±4.32–86	Improved bioavailability and prolong drug release profile.	[85]
Ginkgo Bilbo extract	Tween 80, cholesterol, Mannitol, and dichloromethane	TFH Method	EE(%) 75	Improve the bioavailability of the drug.	[86]
Glutathione	Span 20, Span 40, Span 60, Span 80, Tween 20, Tween 40, Tween 60, Tween 80, chloroform, and methanol	TFH Method	PS (688.5±14 (−26.47±0.158 mV), and (EE) (66±2.8%)	Increase the bioavailability of the drug.	[87]
Cyclosporine	Tween 60, Span 60, Tween 80, Span 80, and Span 20	TFH Method	EE (optimized batch 77.29 and 89.31%)	It shows sustain release of the drug.	[88]
Vinca rosea	Span 60 and cholesterol	TFH Method	PS (400–800 nm), EE (74.02%)	Increase the bioavailability of the drug.	[89]
Temozolomide	Cholesterol, Span, and stearyl amine	TFH Method	EE (79.09+1.56%), PDI (0.15±0.031), Z (3.26 mV)	Improve stability and enhanced permeation of the drug into the brain.	[90]
Acyclovir	DCP, Span 60, and cholesterol	TFH Method	VS 0.95 μm	Enhance the bioavailability of drug and prolong drug release.	[91]
Clarithromycin	Chloroform, methanol, cholesterol, and DCP	TFH Method	PS (4.67 μm)	It shows sustained release of drug and improves its bioavailability	[92]
Gabapentin	Cholesterol, Tween 60, Span 60, methanol, and chloroform	TFH Method	EE (76.34%)	It gives prolonged release of the drug.	[93]
Paclitaxel	Cholesterol, Span 60, Span 20, Span 40, Tween, Tween 60, and Tween 80	TFH Method	Z (229.3 nm and 588.2 nm) EE (12.1±1.36% and 96.6±0.482%.)	Increasing the bioavailability of drug.	[94]
Tenofovir disoproxil fumarate	Cholesterol, chloroform, Span20, Span 40, Span 60, and Span 80	TFH Method	VS (2.95–10.91 μm)	Enhance the bioavailability and prolong release of drug.	[95]
Letrozole	Span 20, Span 60, Span 80, cholesterol, and DCP	TFH Method	EE (Optimize Batches 98.4772±0.2063%)	Enhance the stability of the drug.	[96]

(Contd...)

Table 6: *(Continued)*

Drug	Excipients	Method of preparation	Evaluation	Result	References
Glimepiride	Cholesterol, chloroform, and methanol.	TFH Method	(E.E. %) 98.70	Enhance the bioavailability of drug, sustained and prolong effect.	[97]
Simvastatin	Span-60 and cholesterol	Film Hydration Method	PS (137 nm), EE (98.21%)	Improve the stability, bioavailability, and therapeutic efficacy.	[98]
ROSUVASTATIN CALCIUM	Span 20, Span 60, Span 80, chloroform, and methanol	TFH Method	VS (150 nm in diameter)	Enhancing the dissolution of drugs.	[99]
Celecoxib	Chloroform, Tween 80, Span 80, and methanol	TFH Method	VS (209–322 nm)	It improves therapeutic activity and bioavailability of the drug.	[100]
Diacerein	Cholesterol, Span 20, and Span 60	TFH Method	PS (0.5–2.6μm)	Increase the bioavailability and solubility of drug.	[101]
Oxcarbazepine	Cholesterol and Span	TFH Method	Cmax (49.54 μg.h/mL)	Increase mean residence time and shows Sustained drug release profile.	[102]
Stavudine	Span 60, cholesterol, chloroform, and methanol	Ether injection method	Z (24.8–29.54 Mv)	Prolonged release and longer duration of action.	[103]
Allopurinol	Span 20, Tween 20, and cholesterol	Ether injection method	Z (22.2 m 79.44±0.02%,	The better antigout activity display and sustain release of drug and high solubility.	[104]
Pioglitazone	Cholesterol and Span 20	Ether injection method	PS (145.3 nm), EE (83.44%), Z (−29.1 mV)	Prolonged systemic availability of the therapeutic drug and better patient compliance.	[105]
Cefdinir	Span 60, Span 40, and cholesterol	Sonication method	Z (190 nm–1140 nm), EE (74.56%)	Improve oral bioavailability and controlled drug release profile.	[106]
Ganciclovir	Span 20, Span 60 cholesterol, and ethanol	REV Technique	VS (144±3.47nm) [PDI] =0.08, Z (−27.9±1.5), EE (Optimized batch 89±2.13%)	Enhance the bioavailability of drug.	[107]
Metformin	Cholesterol, DCP, and Span 40	REV Technique	Z (optimized batche-26.9±1.0mV), EE (MN1batche 92.62%),	Prolonged and improve hypoglycemic effect can be obtained.	[108]
Doxorubicin	Cholesterol, Span 40, and Span 60	REV Technique	EE (57.8±1.8%)	To give stable nanosized vesicles to improve brain delivery.	[109]
Tetanus toxoid	Cholesterol, Tween 20, Span 60, and diethyl ether	REV Technique	EE (42.1±2.1)	It enhanced stability of dosage form.	[110]

and their body distribution mimics that of other colloidal drug delivery systems, while the primary portion of the niosome is disposed of by the extravasation tissues of the liver, lung, spleen, and bone marrow.

STABILITY AND TOXICITY OF NIOSOMES[80]

The surfactant used in niosomes is non-toxic and has not been shown to have any adverse effects in animal experiments when niosomes were utilized as medication carriers. Niosomes have a stable structure, which is why they are referred to as stabilized niosomes. The composition of the surfactants utilized in its development is the only factor that could cause niosome instability; however, there has not been any research on how niosome toxicity *in vivo* is correlated with the quantity of ether or ester surfactant used to prepare the vesicle.

FACTORS AFFECTING NIOSOME STABILITY AND TOXICITY

- The type of surface-active agent we used.
- Storage
- Temperature
- Detergent
- Drug nature in encapsulation.

DRUGS USED DEVELPOMENT AND EVALUATION OF NIOSOMAL DOSAGE FORM USING VARIOUS TECHNIUES

The following table highlights for the excipient used various methods of preparation of niosomal dosage forms and outcome of the research work carried out by various researchers [Table 6].

CONCLUSION

Niosomes drug delivery is an effective approach toward novel drug delivery system. Niosomes may be prepared by various methods such as handshaking method, sonication method, and ether injection method. Niosomal drug deliveries have specific advantages over conventional dosage form with respect to improvement in bioavailability. The current review article focuses on the preparation and evaluation of noisome drug delivery and its advantages over conventional drug delivery. The niosomal drug delivery was found to be best for solubility and bioavailability enhancement of poorly water-soluble drugs.

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