WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 3, 1760-1783. Review Article ISSN 2277–7105

COMPREHENSIVE REVIEW ON NIOSOMES A TOOL IN NANOTECHNOLOGY

***A. Sirisha**

Assistant Professor, Nirmala College of Pharmacy, Kadapa, India.

Article Received on 05 Jan. 2025,
Article Revised on 25 Jan. 2026,
Article Published on 04 Feb. 2026,

https://doi.org/10.5281/zenodo.18481188

***Corresponding Author**

A. Sirisha

Assistant Professor, Nirmala College of Pharmacy, Kadapa, India.

How to cite this Article: A. Sirisha. (2026). Comprehensive Review on Niosomes A Tool In Nanotechnology. World Journal of Pharmaceutical Research, 15(3), 1760–1783.

ABSTRACT

Novel Drug Delivery System (NDDS) have emerged as a trans-formative approach to overcoming the limitations of conventional drug delivery, particularly for chronic and Life threatening diseases such as cancer, diabetes, and hypertension. Traditional formulation often suffer from poor solubility, rapid metabolism, off-target toxicity, and inadequate therapeutic efficacy. NDDS aim to deliver the right dose of a drug to the targeted site while maintaining optimal plasma levels for the required duration. Among various advanced carriers vesicular system especially niosomes have gained substantial attention due to their bio-compatibility, structural stability, and ability to encapsulate both hydrophilic and lipophilic drugs. Niosomes, composed primarily of non-ionic surfactants and cholesterol, offer advantages such as improved bio availability, reduced toxicity, prolonged circulation time, controlled drug release, site-specific delivery. Their application span trans-dermal, ocular, oral, pulmonary, and even blood-brain barrier delivery, making them valuable in chemotherapy, immunology, vaccine delivery, and gene delivery. Various preparation techniques, including thin film hydration, ether injection, microfluidization, and pro niosomes conversion, allow precise control over vesicle size lamellarity, and entrapment efficiency. Nanocarrier-based systems further enhance therapeutic outcomes by improving pharmacokinetics reducing systemic toxicity and enabling ligand-mediated targeting. Overall, NDDS particularly niosomal systems represent a promising platform for achieving effective, safe, and targeted drug therapy, addressing the critical challenges associates with conventional drug delivery.

KEYWORDS: Novel drug delivery system, conventional drug delivery system, vesicular drug delivery system, niosomes, non ionic surfactants, targeted drug delivery system.

1. INTRODUCTION

The main aim of novel drug delivery system (NDDS) is to ensure that the right amount of a drug reaches the correct site in the body and maintain its concentration for the required duration. In other words, such a system should release the drug at a rate that matches the body' needs throughout the treatment period.[1]

Before the development of novel drug delivery system (NDDS), conventional approaches were used, including immediate-release formulation, sustained-release dosage forms (mostly through oral administration), and long-acting injectable preparations.[2]

However, chronic and life-threatening diseases such as cancer, diabetes and hypertension present significant challenges when treated with traditional delivery method. Limitation such as extensive metabolism, poor solubility of certain drugs, interactions with food and digestive enzymes, and off-target adverse effects on healthy tissues reduced therapeutic efficiency.

This highlights the importance of advanced delivery systems capable of transporting drugs directly to the diseased site and releasing them in a controlled manner.[3] Such novel system often rely on carrier that respond to internal or external stimuli to archive site specific and time-specific release.

Many drugs especially anticancer agents, have a very narrow therapeutic range, which means the safe and effective dose is very close to the toxic dose. Their clinical use is often limited by serious side effect. By designing advanced drug delivery methods, the therapeutic efficiency of these medicines can be improved. Over the last few decades, a lot of research has been directed towards the development of NDDS.[4] These system aim not only to maintain controlled drug release but also to specially target the active compound to the desired site of action something conventional and even prolonged release dosage forms fail to achieve.

In recent times, vesicular carrier have gained significant important in drug delivery. Lipid based vesicles have proven useful in fields like immunology, membrane biology, diagnostic method, and genetic engineering. They are especially valuable in mimicking cell membrane and in transporting and targeting drug. Traditional chemotherapy often fails against infection

because the drugs cannot easily penetrate cells. This challenge can be addressed through vesicular drug delivery systems. Encapsulating drug inside vesicles helps them remain longer in circulation and can lower toxicity if targeted uptake is achieved. When taken up by phagocyte cells, drug- loaded vesicles can directly reach infection sites resulting in effective treatment with minimal adverse effects.

1.1 Advantages of vesicular drug delivery system[5,6]

- Provide a target approach by delivering the drug directly to the site of infection.
- Minimize drug toxicity and reduce the risk of side effects
- Enhance drug bio-availability, which can lead to lower treatment costs.
- Capable of carrying both water soluble (hydrophilic) and fat soluble (lipophilic) drugs
- Extend the circulation time of drugs that are rapidly broken down in the body
- Offer controlled or sustain drug release over time.
- Address issues related to poor drug solubility, instability and quick degradation.

1.2. Types of vesicular systems[7]

Various types of vesicular system are as follows

a. Liposomes

b. Niosomes

c. Transferosomes

d. Pharmacosomes

e. Enzymosomes

f. Virosomes

g. Emulsomes

h. Discomes

i. Aquasomes

j. Erythrosomes

k. Hemosomes

l. Proteosomes

m. Vesosomes

n. Archaeosomes

o. Apsasomes

p. Colloidosomes

q. Cubasomes

1.3. Present scenario of ndds

1. Liposomes based system
2. Niosomes
3. Nanoparticles
4. Transdermal drug delivery system
5. Implantable system
6. Advanced oral drug delivery systems
7. Microencapsulation techniques/ microcapsules
8. Use of polymer in drug delivery

Future of ndds

1. Personalized medicine
2. Smart drug delivery system
3. Gene and RNA based drug delivery
4. Nanorobotics and targeted delivery
5. Sustain drug green drug delivery system
6. Regenerative medicine and NDDS
7. 3D printing of drug delivery system

1.4. Merits of novel drug delivery system[8]

Enhanced management of chronic diseases by maintaining consistent drug level in the blood stream, reducing break through symptoms.

Examples: Asthma, Arthritis.

Improved bio availability allows a larger fraction of the active drug to reach the systemic circulation.

Reduced frequency and intensity of adverse side effects, by avoiding high effects, by avoiding high pick plasma concentrations.

Sustained therapeutic effect, including during periods without dosing (e.g overnight), ensuring continuous symptoms control.

Protection of the drug from first-pass metabolism and degradation in the gastrointestinal tract enhancing drug stability and efficacy.

Targeted drug delivery to specific tissues or organs, minimizing exposure to healthy tissues and thereby reducing systemic toxicity.

1.5. Limitations of novel drug delivery system (NDDS)

Risk of localized drug accumulation: Some delivery systems may remain intact and become lodged at specific sites in the body. This can lead to a slow release of the drug in that area, potentially resulting in high local drug concentration that may cause irritation or tissues damage.

Unsuitability for drugs with very short half-lives: Drugs with a biological half life of one hour or less are generally challenging to incorporate into sustained or controlled release formulation, as they may require frequent dosing to maintain therapeutic levels.

Caution with highly potent drugs: Including drugs with narrow therapeutic windows or very high potency in such delivery system can be risky. A slight deviation in release rate could lead to toxic effects or sub therapeutic outcomes.

1.6. Targeted drug delivery system

Paul Ehrlich was the first to introduce the concept of targeting in 1902, defining targeted drug delivery as a mechanism in which a drug carrier complex or conjugate specifically transports the drug to predetermined target cells.[9] Later, in 1981, Gregoriadis referred to drug targeting through novel drug delivery system as “old drugs in new clothes,” highlighting the innovative application of existing drugs using advanced delivery methods.

Targeted drug delivery refers to the precise and efficient delivery of a pharmacologic ally active substance to specific, pre identified targets within the body at therapeutic concentration.

At the same time it minimizes exposure to healthy, non target tissues, there by reducing side effects and enhancing the drug’ therapeutic effectiveness.

1.7. Ideal characteristics of drug carrier

Specificity and Selectivity: The carrier should be recognized specifically by the target cells and maintain high affinity and specificity through its surface ligands.

Stable drug ligand linkage: It bond between the drug and its targeting ligand should remain stable in plasma, interstitial fluid, and other biological fluids.

Bio compatibility and safety: It bond between the drug and its targeting ligand should remain stable in plasma, interstitial fluid and other biological fluids.

Ability to cross barriers: The carrier should efficiently transverse anatomical barriers such as the tumor vasculature in cancer therapy.

Passive targeting capability: It should enable effective delivery of drugs to organs like the liver, spleen and bone marrow through passive targeting mechanisms

1.8. Carrier systems for targeted drug delivery

A. Colloidal carriers

Vesicular system

Liposomes

Niosomes

Pharmacosomes

Virosomes

Immunoliposomes

B. Microparticulate system

Micropartricles

Nanoparticles

Magnetic microspheres

Albumin microspheres

Nanocapsules

C. Cellular carriers

1. Released erythrocytes
2. Serum albumin
3. Antibodies
4. Platelets
5. Leucocytes

D .Supramolecular delivery system

1. Micelles
2. Reverse micelles
3. Mixed micelles

4. Liquid micelles
5. Lipoproteins (Chylomicrons, LDL, VLDL)

E. polymer based system

1. Signal sensitive
2. Muco-adhesive
3. Biodegradable
4. Bioerodible
5. Synthetic soluble polymeric carriers

F. Macromolecular carriers

1. Neoglycoproteins
2. Artificial viral envelopes(AVE)
3. Glycosylated water soluble polymers(poly-L-lysin)
4. MABs
5. Immunological fab fragments

1.9. Levels of Drug Targeting

Passive Targeting

In passive targeting, the drug-carrier system relies on the body's natural physiological and biochemical process to accumulate in specific tissues. The targeting is primarily driven by the physicochemical properties of the drug and its carrier.

Examples: Histoplasmosis : Amphotericin B Gaucher's disease: Glucocerebroside.

Inverse targeting

This approach is designed to prevent the drug or carrier system from being taken up by the reticulo endothelial system (RES) thereby altering the usual distribution pattern. It aims from sites of passive uptake.

Active targeting: Active targeting involves modifying the drug carrier with specific ligands or homing devices that bind to receptor-mediated localization improves drug delivery to the intended site.

Dual targeting In dual targeting the carrier itself possesses intrinsic therapeutic activity (e.g: antiviral), which works in synergy with the loaded active drug .this combined action enhances the overall therapeutic effect.

1.10. Advantages of novel drug delivery system[10,11]

Improved drug properties

Enhanced solubility and dissolution rate

Increased oral bio availability

Better adhesion to biological tissues

Targeted drug delivery

Improved targeting capability allows for delivery to specific tissues or cells

Greater potential to reach sub cellular sites of action

Optimized dosing

Requires lower drug doses

Reduce side effects

Enhanced therapeutic outcomes

Convenient dosage forms

More patients-friendly delivery methods

Potential for controlled and sustained release

Versatility as a drug delivery vector

Ideal for cancer targeted therapies

Facilitates drug delivery across the blood brain barrier

Enables effective oral delivery of peptides

Acts as a vaccine adjuvant to boost immune response

Useful in gene therapy applications

1.11. Applications of novel drug delivery systems

Pharmaceutical research & drug delivery discovery

Used in identifying and developing new therapeutic compounds and understanding disease mechanisms.

Protein interaction mapping

Helps in studying and visualizing interaction between proteins to better understand cellular functions.

DNA structure analysis

Utilized to explore and analyze the structure and behavior of DNA molecule

Biomolecule& cell separation

Support efficient separation and purification of cells,proteins,and biological molecules

Tissues engineering

Applied in the development of artificial tissues and scaffolds for regenerative medicine.

Non viral gene delivery

Offer a safer alternative to viral vector for delivering genes into target cells.

Forensic applications

Used in detecting narcotics and analyzing fingerprint in criminal investigation

1.12. Nanocarriers in drug delivery

Nanocarriers are nanoscale colloidal systems, generally ranging between 50-500 nm in size. They serve as vehicles for incorporating active substance such as drugs, proteins and other biological agents to delivery them to specific sites within the body. In recent years, research on nanocarrier-based drug delivery system has grown significantly due to their remarkable potential in improving the treatment and management of various diseases, including cancer, bacterial and viral infection and neurodegenerative disorders.

The effectiveness of nanocarriers primarily stems from their high surface area to volume ratio and their capability to modify essential drug characteristics like bio-activity[12] Key benefits of nanoocarrier-based system include:

- Enhanced pharmacokinetics and better bio distribution of therapeutics agents
- Reduce toxicity and minimized adverse side effects;
- Improved solubility and stability of drugs;
- Controlled or sustained drug release;
- Site specific drug delivery, helping to bypass first-pass metabolism and prevent dose dumping.

Additionally, the physicochemical feature of nanocarrier can be tailored through functionalization techniques and structural modifications enabling the design of advances, intelligent delivery system. Some strategies include.[13]

- Adjusting their composition using organic, inorganic or hybrid material
- Designing nanocarriers in various sizes and shapes such as spheres, rods, or cubes.

- Modifying surface properties by changing surface charge, introducing functional groups applying PE Gylation or other coatings and attaching targeting ligands for precise delivery.

In conclusion, the main objectives of using nanocarriers in drug delivery is to achieve effective treatment of diseases while minimizing adverse effects. Conventional drug delivery system often face numerous limitations such as low specificity, high systemic toxicity, development of drug resistant, poor patient compliance with complex treatment regimens and prolonged therapy duration. These issues frequently result in treatment failure, relapse or the emergence of secondary complains.[14]

Nanocarrier-based delivery system address these challenges by exploiting the unique tissues micro environments associated with various diseases, there by significantly enhancing therapeutic outcomes. Furthermore, the over expression of specific receptors on diseased cells enables targeted delivery using ligand or other functional groups leading to improved selectivity and efficacy.[15]

Drug-loaded nanocarriers exhibit prolonged circulation time in the blood stream, ensuring controlled and sustained release of the encapsulated drug in precise doses. This characteristic reduces plasma release of the encapsulated drug in precise doses. This characteristic reduces plasma concentration fluctuations and minimizes drug related toxicity. Additionally, their nanoscale size allows them to easily penetrate tissues, promoting faster and more efficient drug accumulation at the target site.

Compared to larger particles in the micrometer range (1-10 µm) nanocarriers demonstrate significantly higher cellular uptake enabling direct interaction with target cells. This feature not only enhance therapeutic efficiency but also results in reduced or even negligible side effects.[16]

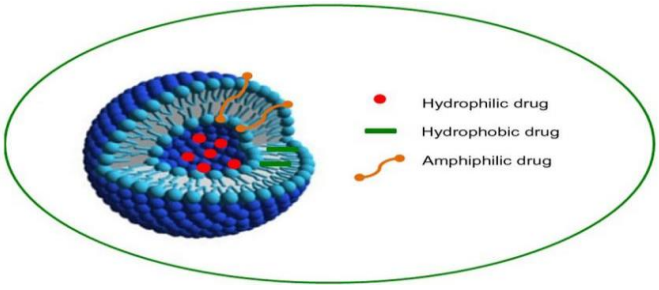

Figure 1: Niosomes as a drug delivery nanocarrier Mahmoud Gharbavi *et., al.*

1.13. Niosomes in drug delivery

Niosomal drug delivery has wide potential in improving the action of many pharmacological agents against various diseases. It also serves as an effective vehicles for drugs with poor absorption making it useful in designing novel drug delivery system. By crossing the gastrointestinal barrier through transcytosis of M cells in Peyer's patches of intestinal lymphatic tissues,[17] niosomal enhance drug bio availability. Once administered, the vesicles are taken up by the reticuloendothelial systems which allows localised drug accumulation useful in diseases like leishmaniasis, where parasites infect liver and spleen.[18] cells. Additionally, certain non-reticuloendothelial systems, such as immunoglobulin, can recognise the lipid surface of niosomes.[19]

Encapsulation of anticancer drugs in niosomes has been shown to reduce toxic side effects while maintain or even improving anti-tumour activity.[20] For instance doxorubicin ,through effective, causes dose-dependent irreversible cardiotoxicity.[21] when delivered through niosomes in mice with S-180 tumours, improved survival and slowed tumour growth. Similarly methotrexate-loaded niosomes led to complete tumours regression in mice, while prolonging plasma levels and slowing elimination. Niosomes also provide controlled drug release which is particularly beneficial in treating brain malignancies.

Beyond chemotherapy, niosomes are being studied in immunology as antigen carriers and even as haemoglobin carriers.[22,23] since their vesicles allow oxygen permeability and can alter haemoglobin's dissociation curve similar to free haemoglobin. For transdermal drug delivery.[24] where slow skin penetration is a drawback, niosomes improve effectiveness of drug like flurbiprofen, piroxicam, estradiol and levonorgestrel. Moreover, they enhance drug concentration at target sites orally, when administrated orally or topically. Their sustained-release action makes them valuable them valuable for drugs with low solubility and a narrow therapeutic index.

Because of their size and limited penetration through epithelial and connective tissues, niosomes allow localised drug action. This increases drug potency while reducing systemic toxicity. For examples, antimonials in niosomes are selectively taken up by mononuclear cells, resulting in localisation, higher potency, reduced dosage and lower toxicity.

Niosomes are bilayer vesicular system structurally similar to liposomes, consisting of outer lipophilic layer and an internal hydrophilic core (refer to failure 2.1 and 2.2). These vesicles

have emerged as effective carriers for controlled, sustained and targeted drug delivery.[25] Recently, there has been a growing shift in reserch interest towards niosomes due to their superior ability to address several limitations associated with conventional drug delivery systems.[26]

Niosomes are primarly composed of non-ionic surfactant, cholesterol or its derivatives and sometimes charged molecules molecules. Cholesterol serves as a lipid component that enhances the rigidity and stability of the bilayer membrane. The inclusion of charged molecules helps stabilize polar interactions and contributes to the overall structural integrity of the vesicle.

Unlike traditional liposomes, lies in the use of non ionic surfactants as span and tweens, which impart amphiphilic properties and neutrality to the vesicles. This amphiphilic enhances both the stability of the vesicles and their drug-carrying capacity. Due to more precise control over charge distribution and core composition, niosomes are capable of encapsulating both hydrophilic and more efficiently than liposomes. Niosomes have proven effective in delivering drugs through several routes of administration

Ocular delivery (e.g., Tacrolimus, Naltrexons HCL)

Transdermal delivery (e.g Gallidermin, clomipramine)

Pulmonary delivery (e.g Cefdinir, Lornoxicam)

Crossing the blood-brain barrier (e.g temozolomide)

Notably, the cosmetic industry like **L'Oreal** being a pioneer, was the first to utilize niosomes in various applications. Since then, many pharmaceutical companies have adopted this versatile technology.[27]

Beyond conventional drugs, niosomes are also capable of encapsulating genes, proteins and vaccines, owing to their well-defined bilayer structure. Hydrophillic molecules are either encapsulated within the aqueous core or adsorbed onto the bilayer surface, while lipophilic compounds are incorporated into lipophilic regions of the bilayer membrane.

The formation of niosomes involves the hydration of thin lipid films, leading to swelling and the eventual development of vesicular structures. Subsequent agitation facilitates the detachment and self-assembly of hydrated into closed bilayer membrane.[28]

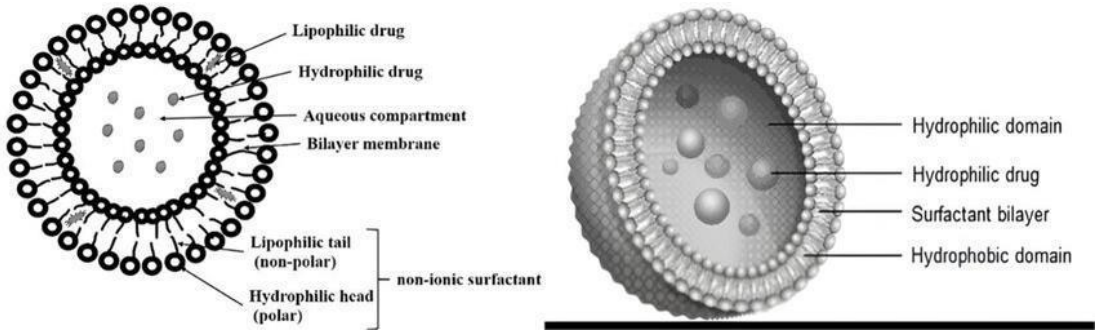

Figure 2: A schematic diagram showing the cross section of a niosome. Prachi Pandey *et., al.*

1.14. Formulation aspect of niosomes

The formulation of niosomes involves various parameters that influence the creation of niosomal vesicles. These vesicles are made from excipients such as non-ionic surfactant, polar lipids and charge inducers, which are used in different concentration. Key factor that affect niosomal vesicles formation include **Hydrohilic-lipophilic balance (HLB), Critical packing parameters (CPP),and transition temperature[29] (TC).**

Surfactant which are typically amphiphilic molecules, have two distinct region:a hydrophilic head and a hydrophobic tail. The hydrophobic region consist of chains made from alkanes, fluorocarbons, aromatic compound, or other non-polar groups, while the hydrophilic head includes functional groups that are highly solvated, such as phosphonates, ammonium, sulfonates, carboxylates, and their derivatives. Surfactants are classified based on the nature of their polar head groups into cations, anionic, amphoteric, or non-ionic surfactant. For example, surfactants with a negatively charged head group like fatty acid salts (soaps), phosphate esters, sulfates and ether sulfates are termed anionic surfactants, while amphoteric (zwitter ionic) surfactants have a head group, with two oppositely charged moieties.[30]

It is worth noting that cationic surfactants are often regarded as irritating and sometimes toxic, which limits their application compared to other types of surfactants. on the other hand, non ionic surfactants**,** which lack any charge on their head groups, are particularly suitable for niosomal formulations. When these surfactant are dispersed in aqueous solution, they spontaneously form structure where the hydrophilic heads face the aqueous phase, and the hydrophobic tails align with the organic phase. This self-assembly process leads to the formation of niosomes. Non-ionic amphiphiles used in niosomal formulations are typically categorized into four types: alkyl esters, amides, ethers and fatty acid esters.[31]

The toxicity of niosomal formulation has been investigated to assess their impact on cell proliferation and to understand the influence of factors such as cholesterol content non-ionic surfactants and alkyl chain length on cellular behavior.[32] The findings indicated that these formulations generally exerted minimal inhibitory effects on cell proliferation. However, the nature of the bond linkage between the surfactant and the polyoxyethylene head group significantly influenced cell growth. Specifically, surfactants containing ether linkages were found to inhibit cell proliferation by approximately 50%, in contrast to only 10%inhibition observed with ester-linked surfactants, likely due to the increased susceptibility of ester bonds to enzymatic degradation. Additionally, variations in cholesterol concentration with in the bilayer structure did not appear to significantly affect cell proliferation.[33,34]

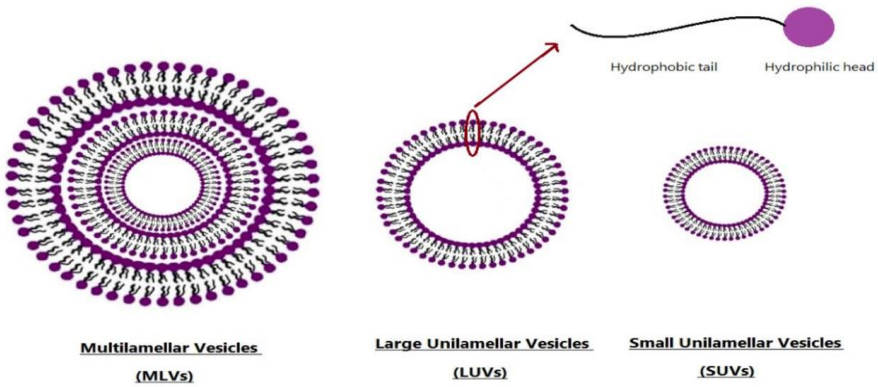

Figure 3: Different vesicles morphology of niosomes- Multiamellar (MLV), Oigolamellar (OLV) and Unilamellar (ULV) vesicles (H.Abdelkader *et., al.)*

1.15. Types of Niosomes

Niosomes can be categorized based on either the number of bilayer (lamellarity) or their particles size.

Based on lamellarity

Multillamellar vesicles (MLVs[35,36] These have multiple lipid bilayers (lamellarity)and typically range from 1to 5µm in diameter.

Large Unilamellar Vesicles (LUV): These consist of a single vesicles with diameter between 25 to 500 nm.

Small Unilamellar Vesicles (SUVs): These are single-layer vesicles with diameter between 25 to 500 nm.

Based on size

Small niosomes: 100-200 nm

Large niosomes: 800-900 nm

Very large niosomes: 2-4 μm

1.16. Preparation of niosomes

Niosomes are synthesized using non-ionic surfactants, and their properties such as number of bilayers, vesicles size, encapsulation efficiency and membrane permeability are significantly influenced by the method of preparation. Typically a surfactant- lipid mixture is hydrated at elevated temperatures to form a colloidal dispersion. Unentrapped drug is then separated by techniques such as centrifugation, gel filtration or dialysis. While several lab scale production, such as the **Novasome® Method and heating method.**

Below are the key techniques used for niosomes preparation.

1. Ether injection method

This techniques involves the slow injections of an ether based solution (containg surfactants and cholestrol mixture dissolved in 20 ml of ether is injected into 4 ml of ether is injected into 4ml of aqueous solution using a14-gauge needle. This process yield large unilamellar vesicles (LUVs).[37,38]

2. Thin film hydration method (film method)

In this method, a mixer of surfactant and cholesterol is dissolved in an organic solvent (e.g., chloroform or diethyl ether) in a round-bottom flask. The solvent is evaporated under vacuum to form a thin film. Upon hydration at 50-60^0 C with constant agitation, multilamellar vesicles (MLVs) are produced.

3. Sonication

The aqueous phase is added to the surfactant-cholesterol mixture and sonicated using a probe or bath sonicator. This process result in small unilamellar vesicles (SUVs) compared to liposomal SUVs niosomal SUVs are typically larger (>100nm).

4. Rev1erse phase evaporation techniques

In this approach, surfactants are dissolved in chloroform, and phosphate -buffered saline (PBS) is added to form a water-in-oil (w/o) emulsion. After sonication, the chloroform is

removed under reduced pressure, leading to gel formation, which then hydrates into niosomes. Additional agents like protamine may be added before centrifugation for phase separation.[39]

5. Heating method

Non ionic surfactant, cholesterol, and optional charge-inducing agents are mixed in an aqueous medium (e.g: buffer or water) with a poly like glycerol. The mixture is stirred and heated under low shear until niosomes are formed.

6. **Microfluidization**

This modern techniques uses high-velocity fluid stream that interact in micro channels. The method ensure controlled mixing and energy distribution, resulting in unilamellar vesicles with uniform size and improve reproducibility.

7. **Multiple membrane extrusion method**

Here, surfactant, cholesterol and dicetyl phosphate dissolved in chloroform are dried into a thin film. After hydration with a drug solution, the suspension is passed through polycarbonate membranes (up to 8 times) to achieve controlled vesicles size.[40]

8. **Bubble method**

A solvent-free, one-step method where cholesterol and surfactants are mixed in buffer (pH 7.4)and heated to 70^0 C. After high-shear mixing, the solution is bubbled with nitrogen gas to form niosomes. The setup includes a three-neck flask, water bath reflux condenser and thermometer.[41]

9. **Emulsion method**

The oil-in water (o/w) emulsion is created by mixing an organic solution containing surfactant, cholesterol and the drug in an aqueous solution. The organic solvents is then removed through evaporation, resulting in the formation of niosomes dispersed in the water phase.[42,43]

10. Lipid injection method

The lipid injection method eliminates the need for costly organic phases. In this approach a mixture of lipids and surfactant is first melted and then injected into a vigorously stirred heated aqueous phase that contains the dissolved drug. The drug can be dissolved in the molten lipid, and this mixture is then added to the heated, agitated aqueous phase containing the surfactant.[44]

10. **Formation from proniosomes**[45]

Niosomes can also be derived from proniosomes, which are dry formulation made by coating a water-soluble carrier (e.g., sorbitol) with a thin layer of surfactant. Upon adding water at a temperature above the surfactant's phase transition temperature (T>Tm)and brief agitation, the surfactant hydrates to form niosomes.

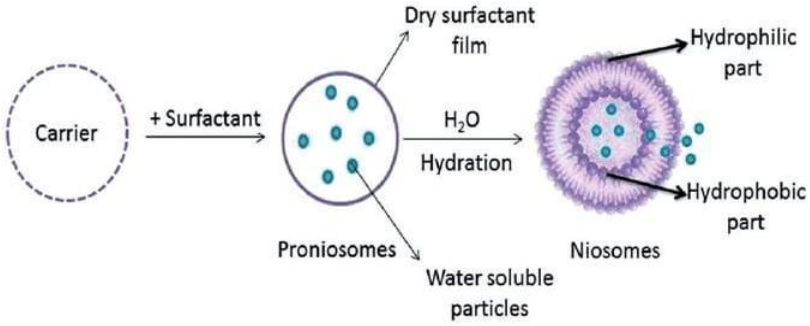

Figure 4: Niosome form proniosome (Venkata Ramesh Yasham *et., al.).*

1.17. Characterization of Niosomes

Entrapment Efficiency

After preparing a niosomal dispersion, the free (unentrapped) drug is seperated using techniques like dialysis, centrifugation, or gel filtration. To measure the amount of drug that remains inside the niosomes, the vesicles are broken open using either 50% n-propanol or 0.1% Triton X-100. the drug content in disrupted solution is then analyzed using a suitable assay. The Entrapment Efficiency (EE) is calculated using the formula.[46]

EE (%)=Entrapment drug/total drug added) x 100

Vesicle Diameter

Niosomes are spherical, similar to liposomes, and their size can measured using techniques such as

a) Light microscopy
b) Photon correlation spectroscopy (Dynamic light scattering)
c) Freeze-fracture electron microscopy

Freeze-thaw cycling (freezing at- 20^0C for 24 hours followed by thawing at room temperature) may increase vesicles size, likely due to fusion of vesicles during the process.

In-vitro Drug Release

To study drug release from niosomes, a dialysis method is used. A dialysis bag containing the niosomal suspension is immersed in 200 ml of buffer in a beaker and stirred continuously at either 25^0C or 37^0C. At predetermined time points, the buffer is sample and analyzed for drug content using appropriate assay.[47,48]

Osmotic Shrinkage

This property is evaluated by observing a decrease in vesicle size after adding a hyper tonic salt solution to the niosomes suspension. Niosomes made from pure surfactant are more sensitive to osmotic shrinkage compared to those containing cholesterol.

Physical stability at Different temperatures

The stability of niosomes over time is assessed by measuring change in vesicle size using laser light scattering. Vesicles are stored in glass containers at room temperature or refrigerated at 4^0C for up to 3 months. Morphological changes, include vesicles aggregation or fusion, are evaluated under an optical microscope. The retention of the encapsulated drug is measured at 72 hours, and again after 1,2, and 3 months.

Turbidity measurement

Niosomes are diluted with distilled water to final lipid concentration of 0.312 mm. After sonication for 5 minutes to ensure uniform mixing, turbidity is measured by recording absorbance using a UV-visible diode array spectrophotometer.

1.18. Applications of niosomal drug delivery

Niosomes are versatile carriers with several pharmaceutical and biomedical applications including

1. Targeted drug delivery -Direct the drug to specific tissues or cells, improving therapeutics effectiveness and reducing side effects.

2. Anti- infective therapy -Enhances the delivery and efficacy of antimicrobial drugs

3. Brain drug delivery- Facilitates the transport of drugs across the blood-brain barrier.

4. Topical delivery- improves drug penetration and retention in the skin for dermatological treatments.

5. Ocular delivery - Used for sustained and localized drug delivery to the eyes.

6. Niosomes vaccines- Can serve as carriers for antigens, enhancing immune response

CONCLUSION

Novel drug delivery system (NDDS) have significantly advanced pharmaceutical therapy by addressing the major limitations of conventional drug delivery, including poor solubility, rapid metabolism, off-target toxicity, and reduced therapeutic efficacy. These system are particularly beneficial in the treatment of chronic and life threatening diseases such as cancer, diabetes, and hypertension, where precise dosing and sustained drug action are essential. By ensuring targeted drug delivery and maintaining optimal plasma concentrations, NDDS enhance therapeutic effectiveness while minimizing adverse effects.

Among the various advanced delivery carrier, vesicular system especially niosomes have gained considerable importance due to their bio compatibility, structural stability, and versatility in encapsulating both hydrophilic and lipophilic drugs. Niosomes, composed of non-ionic surfactant and cholesterol, offer several advantages including improved bio availability, prolonged circulation time controlled drug release and site specific targeting. Their applicability across multiple route of administration, such as trans dermal, ocular, oral, pulmonary and blood brain barrier delivery, highlight their broad therapeutic potential in chemotherapy, immunology vaccine delivery and gene therapy.

Furthermore, advanced preparation techniques enable precise control over vesicle characteristics, while nano carrier based strategies improve pharmacokinetics and reduce systemic toxicity through ligand mediated targeting. Overall, NDDS, Particularly niosomal systems, mediated targeting. overall, NDDS, particularly niosomal systems, represent a promising drug therapy, offering substantial potential for future pharmaceutical and clinical applications.

REFERENCES

1. Florence AT, New drug delivery systems. chem. ind, 1993; 12: 1000-1004.
2. Todd, J. A., Modest, E. J., Rossow, P. W, Tokes, Z. A. Biochem. Pharmacol, 1982; 456(34): 5: 41-54.
3. D. Patra, S. Sengupta, W. Duan, H. Zhang, R. Pavlick, A. Sen, Intelligent, Self- powdered, drug deliverysystem, Nanoscale, 2013; 5: 12731283, https;//doi.org/10.1039/c2nr32600k.
4. Horbett TA, Ratner BD, Kost T, Singh M. Recent Advances in Drug delivery system,1 st ed. Plenum press, New york, 1984. DOI 10.1177/088532829701100402.
5. Welling PG, Dobrinska MR, in Robinson JR, Lee VHL, Controlled Drug delivery system 2nd ed. Marcel Dekker, Newyork, 1987.

6. Jani p, Halbertt GW, Langridge J, florence AT, The uptake and translocation of latex nanospheres and microsperes after oral administration to rats, J. Pharma. Pharmacol, 1989; 41: 809-812. DOI :10.1111/j.2042-7158.1989.tb06377.x
7. Elder JH, Stass JK, Meulbroek JA Mc Ghee JR, Tice TR, Gilley R Biodegradable microspheres as vaccine delivery system, Mol. Immunol, 1991; 28: 287-294. DOI 10.1016/0161-5890(91)90076-v
8. Jain, S., Jain V., & Mahajan, S. C., Lipid based vesicular drug delivery system, Advances in pharmacuetics, 2014. https://doi.org/10.1155/2014/574673
9. Kumar Khanna, V, Targeted delivery of nanomedicines, ISRN pharmacology,2012 ISRN Pharmacol Apr 10 2012; 571394 DOI: 10.5402/2012/571394.
10. Parhi, P., Mohanty, C., & Sahoo, S.K, Nanotechnology-based combinational drug delivery: an emeging approches for cancer therapy, Drug discovery today, 2012; 17(1718): 1044-1052 DOI :10.1016/j.drudis.2012.05.010.
11. Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., del Pilar Rodriguez-Torres, M., Acosta-Torres, L. S., Diaz-Torres., L. A, Grillo, R., Swamy, M. K., Sharma, S., and Habtemariam, S, Nano based drug delivery system : recent developments and future prospects, Journal of nanobiotechnology, 2018; 16(1): 71. DOI: 10.1186/s12951-018-0392-8.
12. Sahoo, SK., & Labhasetwar, V. (2003). Nanotech approches to drug delivery and imagine. Drug discovery today, 2003; 8(24): 1112-1120. 2003 dec. DOI: 10.1016/s 1359-6446 (03)02903-9.
13. Zhang, L., Gu, F. X., Chan, j. M., Wang, A. Z., Langer, R. S., & Farokhzad, O. C. Nanoparticles in medicine: Therapeutic application and developments. Clinical pharmacology & therapeutics, 2008; 8(5): 761-769. DOI: 10.1038/sj.clpt.6100400.
14. Chamundeeswari, s, M., Jeslin, J., & Verma, M. L, Nanocarriers for drug delivery applications, Environmental chemistry Letters, 2019; 17(2): 849-865. DOI:10.1007/s10311-018-00841-1.
15. Allen, T. M., & Cullis, P. R. Drug delivery system: Entering the mainstream. Science, 2004; 303(5665): 1818-1822. DOI :10.1126/Science. 1095833.
16. Din, F., Aman, W., Ullah, I., Qureshi, O., Shafique, S., & Zeb, A, Effective use of nanocarrier as drug delivery system for the treatment of selected tumors, International journal of nanomedicine., 2017; 12: 7291. DOI:10.2147/IJN.S146315.

17. Shirsand SB, Para MS, Nagendra kumar D, Kanani KM, Keerthi D. Formulation and evaluation of ketaconazole niosomal gel drug delivery system.Int J Pharma Investig. 2012; 2(4): 201-207. DOI:10.4103/2230-973X.107002.
18. Rogerson A, Cummings J, Willmott N, Floresence AT. The distribution of doxorubicin in mice following administration in niosomes.J Pharm Pharmacol. 1988; 40: 337-42. DOI 10.1111/j.2042-7158.1988.tb05263.x.
19. Okore VC, Attama AA, Ofokansi KC, Esimone Co, Onuigbo EB. Formulation and evaluation of niosomes. Indian. J Pharma Sci., 2011; 73: 323328. DOI: 10.4103/0250-474X.93515.
20. Ruckmani K, Sankar V. Formulation and optimization of zidovudine niosomes. AAPS Pharma SciTech., 2010; 11(3): 1119-27. DOI: 10.1208/s 12249-010-9480-2.
21. Azeem A, Anwer MK, Talegaonkar S. Niosomes in sustained and targeted drug delivery : Some recent advances J. Drug Target. 2009; 17(9): 671-89. DOI: 10.3109/10611860903079454.
22. Ibrahim MMA, Sammour OA, Hammad MA, Megrab NA. In vitro evaluation of pro niosomes as a drug carrier for flurbiprofen. AAPS Pharma Sci Tech. 2008; 9(3): DOI:10.1208/s12249008-9114-0.
23. Attai IA, EI-Gizawy SA, Fouda MA, Donia AM. Influence of a niosomal formulation on the oral bioavailability of acyclovir in rabbits. AAPS Pharma Sci Tech., 2007; 8(4): 206-12. DOI:10.1208/pt0804106.
24. Jain CP Vyas SP, Dixit VK.Niosomal syatem for delivery of rifampicin to lymphatics. Indian J. Pharma. Sci., 2006; 68(25): 575-578. DOI:10 4103/0250-474X.29622.
25. Khandare JN, Madhavi G, Tamhankar BM. Niosomes novel drug delivery system. East Pharmacist. 1994; 37: 61-4.
26. Malhotra M, Jain NK. Niosomes as drug carriers. Indian drugs, 19194; 31; 81-6.
27. Udupa N. Niosomes as drug carriers. In: Jain NK, editor. Controlled and novel drug delivery. 1st edition. New Delhi: CBS Publishers and Distributors, 2002.
28. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of niosomes -Non ionic surfactant vesicles.J Pharm Pharmacol, 1985; 37; 863-8. DOI;10.1111/j.2024-7158.tb 04990.x.
29. Prachi Pandey et., al Advancement and characteristics of non -ionic surfactant vesicles (niosomes) and their application for July 2024 International Journal of Pharmaceutical Investigation, 14(3): 616-632. DOI:10.5530/ijpi.14.3.74

30. Hunter CA, Dolan TF, Coombs GH, Baillie AJ. Vesicular system (Nioisome and Liposomes) for delivery of sodium stibogluconate in experimental murine viseral leishmaniasis. J pharma pharmacol, 1988; 40: 161-5. DOI: 10.11.1111/j.2042-7158.1988.tb05210.
31. Cumming J ,Status JF, Calman KC. Determination of adriamycin, adriamycinol and their 7-deoxyaglycones in human serum by high- performance liquid chromatography. J Chromatogr, 1984; 11: 125-33. DOI; 10.1016/So378-447(00)84698-8
32. Suzuki k, Sokan. The Application of liposomes to cosmetics.Cosmetic and Toiletries, 1990; 105: 65-78.
33. Brewer JM Alexander J. The adjuvant activity of non ionic surfactant vesicles (niosomes)on the BALB/c humor response to bovin serum albumin. immunology, 1992; 75: 570-5.
34. Moser P, Marchand-Arvier M, Labrude P, Handjain-vila Rm, Vignerson C.Hemoglobin niosomes.I.Preparation, Function and physico-chemical properties and stability. Pharma Act Helv., 1989; 64: 192-202.
35. Uchegbu IF, Vyas SP. Non ionic surfactant based vesicles (niosomes) in drug delivery. int J Pharma. 1998; 172: 33-70.
36. Hao Y, Zhao F, Li N, Yang Y, Li K. Studies on a high encapsulation of colchicines by a niosomes system.Int J pharma., 2002; 244: 7-80. DOI:10.1016/s0378-517(02)00301-0
37. Naresh RA, Chandrashekar G, Pillai GK, Udupa N. Antiinflammatory activity of niosomes encapsulated diclofenac sodium with Tween-85 in Arthitic rats. IndJ Pharmacol, 1994; 26: 46-8.
38. Kaur IP, Garg A, Singla AK, Aggarwal. D. Vesicular system in occular drug delivery: an overview. Int J Pharma., 2004; 269: 1-14. DOI
39. Hu C, RHODES DG. Proniosomes: A. Novel Drug Carrier Preparation. Int J Pharm., 1999; 185: 23-35. DOI:10.1016/s0378-5173(99) 00122-2.DOI
40. Alcantar N, Dearborn K, Van Anker M, Toomey R, Hood E. Niosomehydrogel drug delivery. US 2008/0050445A1.2008.
41. Hao Y, ZhaoF, Li N, Yang Y, LiK. Sstudies on high encapsulation of colchicines by a niosomes system. Int J Pharm. 2002; 244: 73-80. DOI 10.1016/s0378-5173(02)00301-0
42. Uchegbu IF, Vyas SP. Non ionicsurfactant based vesicles (niosomes) in drug delivery. int J Phram., 1998; 172: 33-70.

43. Moser P, marchand-Arvier M, Labrude P, Handjani-Vila RM, Vignerson C Hemoglobin niosomes.I.Preparation, functional and physico-chemical properties and stability.Pharma Acta Helva., 1989; 192-202.
44. Jayaraman SC, Ramachandran C, Weiner N. Topical delivery of erythromycin from various formulation; an in vivo hairless mouse study.J Pharma Sci., 1996; 65: 82-92. DOI:10.1021/js960040u.
45. Balasubramaniam A. Kumar VA, Pillai KS. Formulation and in vivo evaluation of niosomes encapsulated daunorubicin hydrochloride. Drug dev Ind Pharm., 2002; 28; 1181-93. DOI: 10.1081/DDC-120015351.
46. Yoshika T, Stermberg B, Florence AT. Preparation and properties of vesicles (niosomes) of sobitan monoesters (span 20, 40, 60, and 80) and a sorbitan triester (span 85) Int J Pharma., 1994; 105: 1-6. https://doi.org/10.1016/0378-5173(94)90228-3
47. Karki R, Mamatha GC, Subramanya G, Udupa N. Preparation,characterization and tissues disposition of niosomes containg isoniazid.Rasayan J Chem., 2008; 1: 224-7.
48. K Ruckmani; B Jayakar; sk Ghosal. Drug Development industrial pharma., 2000; 26: 217. DOI:10.1081/DDC-100100348.
49. Majid T, Naser T, Mahmoud RJ, Saeid D. Enhancement of follicular delivery of finastide by liposomes and niosomes. Int. J. Pharm., 2006; 323(1-2): 1-10. DOI:10.1016/j.ijpharm.2006.05.041.
50. Abbas P, Jaleh V, Abdolhossein, Rouholamini.Invitro study of polyoxyethylene alkyl ether niosomes for delivery of insulin. J. Pharma., 2006; 328(2): 130-41. DOI: 10.1016/j.ijpharm.2006.08.002.
51. Samar M, Guinedi AS, Nahed D. Preparation and evaluation of reverse phase evaporation and mulati lammellar niosomes as ophthalmic carriers of acetazolamide. Int. J. Pharm 2005; 306(12): 7182. DOI:10.1016/j.ijpharm.2005.09.023.
52. Mullaicharam AR, Murthy RSR. Formulation, optimization and stability of Rifampicin niosomes. The Indian Pharmacist. 2004; (4): 54-58. DOI:10.1016/j.jddst.2020.101763.
53. Agarwal S, Vasundhra, Bakshi, Vitta P, Raghuram AP, Pandey S, Udupa N. Efeect of cholestrol content and surfactant HLB on vesicles properties of niosomes. Indian J. Pharma Sci., 2004; (10): 121-123.
54. Yongmei H, Fenglin Z, Na L, Yanhong K, Li. Studies on high encapsulation of colchicines by a niosome system. Int. Pharma., 2002; 244(1-2): 73-80. DOI:10.1016/S0378-5173(02)00301-0.

55. Manconi M, Sinico C, Valenti D, Loy G, Fadda AM. Niosomes as carriers for tretinion I. Preparation and properties. Int. J. Pharm., 2002; 234(1-2): 237-248. DOI:10.1016/s0378-5173(0)00971-1.
56. Ravichandran V, Velrajan G, Raghuraman S. Preparation and In vitro release of diclofenac sodium niosomes. The Eastern pharmacist, 2001; 113-116.
57. Khandare JN, Jiwandas BH, Uppal R. Preparation and evaluation of nimesulide niosomes for topical application. Indian drugs, 2001; 38(4): 197-202.
58. Arunothayanum P, Bernard MS, Craig IF, Uchegbu, Florence AT. The effect of processing variables on the physical characteristics of non ionic surfactants vesicles (Niosomes) formed from a hexadecyl diglyecrol ether. Int. J. Pharm., 2000; 201: 7-9. DOI:10.1016/s0378-5173(00)00362-8
59. David T.Wong, Kenneth W. Perry, Frank P Bymaster. The discovery of Fluoxetine Hydrochloride (Prozac). Nature Reviews Drug Discovery., 2005; 4: 765-774.
60. Andrea Rossi, Alessandra Barraco, Pietro Donda. Fluoxetine: a review on evidence based medicine. Annals of General Hospital Psychiatry. 2004; 3(2). DOI:10.1186/1475-2832-3-2
61. Avisek Mukhopadhyay, Krishanta Kumar Pradhana et.al., Development and validation of an UV-spectrophotometric method for the estimation of fluoxetine in pure and tablets dosage forms, International Journal of Pharmaceutical Sciences and Research, 2014; 5(8): 3418-3424. DOI: http://dx.doi.org/10.13040/IJPSR.0975-8232.5(8).
62. Rubesh kumar s,p gayathri et al., simultaneous estimation of fluoxetine hcl and olanzapine in bulk drug and pharmaceutical formulation by using uv visible spectroscopy method, international journal of pharmaceutical sciences and drug research, 2011; 3(1): 52-55. DOI https://doi.org/10.25004/IJPSDR.2011.030113
63. Syed Ayaz Ali, Sonali Nerkar et., al., Determination of fluoxetine and Zonisamide by UV Spectrophotometric method, Journal of Medicinal Chemistry and Drug Discovery, 2015; 438-444. https:// pubchem.ncbi.nlm.nih.gov/compound/Fluoxetine
64. Rajera R, Nagpal, K, Kumar S, Mishra DN et., al., Niosomes: A controlled and novel drug delivery system. Biol. Pharma Bull. 2011; 34(7): 945-953. DOI:10.1248/bpb.34.945.