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Advances In Nanoparticle-Based Drug Delivery Systems: A Pharmaceutics Perspective

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Abstract

Inquisitions made in the field of new delivery system leads to prevent various problem and difficulties associated with conventional therapy and could led to the development of several vesicular systems. Advancements in this field have led to the emergence of nanorange delivery system among which Nanosome have achieved the prime importance as they are not taken up by the RES by which the rapid clearance of the drug is inhibited, the major drawback associated with other vesicular systems. A Nanosome is a phospholipids Bilayer vesicle that is nanometer in size and made up of one or more lipid bilayers. Because they share molecular traits with mammalian cell membranes, they are generally non-toxic, non-antigenic, and biodegradable. The current review deals with the classification, properties, method of preparation, and mode of transport and characterization parameters of Nanosome with an overlook on its applications.

Key Words:

Reticuloendothelial cells, Nanosome, Microparticle, Microcapsule, Liposomes, Niosomes, Pharmacosomes

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. Introduction

Conventional therapy faces major drawback such as poor specificity of the drug , increase adverse effects , and reduced therapeutic efficacy, to overcome these problem. A new drug delivery system has come in existence in which various carrier system are introduced such as Microparticle microcapsule, Liposomes, Niosomes, pharmacosomes, and many more, but these system may also have some problems for example in case of liposome the major problem associated with this are there stability, leakage and greater uptake of this vesicular system by the reticuloendothelial system, and may rapidly cleared off from such system[1].

To overcome these problems nanorange delivery system has come in existence in which Nanosome have got the major attention, because of their nano range they are not easily recognize by the RES system

and due to this rapid clearance of the drug is inhibited , which was the major drawback of other vesicular system[2]. For fabricating nano scale delivery devices nanotechnology has been employed which combine the diagnostic and therapeutic action for immediate application of therapy [3].

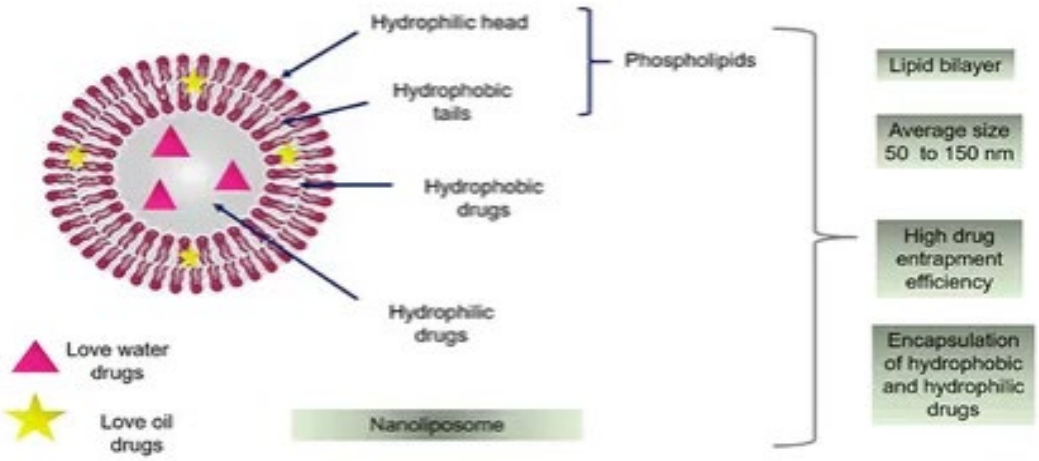

Fig.1. Diagrammatic illustration of the amphiphilic nature of nanoliposomes' bilayer structure enabling trapping of hydrophilic and hydrophobic medicines.

[4]Nanosome are the primary carrier mediated therapeutic agents,[5,6] which are nanosized lipid vesicle[7]. Nanosome are the small uniform lipid vesicular system has a grain size between 10 to 100nm utilizing phospholipids for their preparation. The ultimate goal of Nanosome is to eliminate the drawbacks of all other vesicular system like stability, solubility, rapid clearance and bioavailability[2].

Structure of Nanosome comprised of aqueous core which is encapsulated by phospholipids Bilayer. Phospholipids forms planner Bilayer sheets by aligning themselves closely in aqueous media to reduce the unnecessary interaction amongst bulk aqueous phase and fatty acyl chain of long hydrocarbons. By totally removing the aforementioned interaction, these sheets fold over themselves to create a closed, sealed concentric vesicle, creating the ultimate structure of a Nanosome with an aqueous center.[1]

Because of their hydrophilic polar head and hydrophobic tail, phospholipids are amphiphathic molecules. Phosphoric acid is primarily attached to a water-soluble molecule at the polar end of the molecule. When exposed to solvents, the hydrophilic and hydrophobic segments in the amphiphilic lipid's molecular geometry align and self-organize into an ordered supramolecular structure.

2. Classification

2.1. Classification on the basis of stability[2, 8-10]

2.1.1. Stabilized Nanosome

2.1.2. Non-stabilized Nanosome

Stabilized Nanosome further classified on the basis of stabilizing agent

(1) Protein stabilized

- Bovine serum albumin
- Tissue type plasminogen activator

(2) Carbohydrate stabilized

- Galactose
- Fructose
- Mannose

(3) Polymer stabilized

- PEGyleted Nanosome

2.2. Classification of Nanosome on the basis of phospholipids used[1]

2.2.1. Conventional or simple phospholipids used:

(a) Synthetic:

- Dioleoylphosphatidylcholine(DOPC)
- Dioleoylphosphatidyl ethanolamine (DOPE)
- Distearoylphosphatidylcholine(DSPC)
- Distearoyl phosphatidylethanolamine(DSPE)

(b) Natural

- Egg lecithin

2.2.2. Sphingolipids[11]

A Synthetic

(a) Sphingosine

- Sphingomyelin
- Sphingosine-1-phosphate
- Glycosylated sphingosine

(b) Omega labeled sphingosine

- Omega biotinyl - sphingosine
- Omega biotinyl D-erythro-sphingosine-1-phosphate

(c) Ceramide derivatives

- Ceramides
- Glycosylated Ceramide

(d) Sphinganine (dihydrosphingosine)

- Sphinganine-1-phosphate
- Sphinganine(c20)

B Natural

(a) Sphingosine derivatives (egg,brain and milk)

- D-erythro-sphingosine
- Sphingomyelin
- Cerebrosides

(b) Gangliosides

- Gangliosides-ovine brain
- Gangliosides-porcine brain

(c) Sphingesine derivatives (soy bean)

- Glucosylceramide

(d) Phytosphingosine derivatives (yeast)

- Phytosphingosine

3. Properties of Nanosome

Lipid bilayers make up nanosomes, which are self-contained structures that retain some of the surrounding solvent inside. The special qualities of these nanosomes are covered below.

3.1. Amphiphilic nature

One of the unique properties of Nanosome is their amphiphilic character due to the presence of phospholipids, which make them suitable for drug delivery. Amphiphiles are used in many different applications such as food and pharmaceutical preparations. They have the special power to self assemble into a variety of structures that enables them to be useful in a wide range of areas. Amphiphiles spontaneously self assemble to form a variety of structures because of their dual choice for solvent. One component of any amphiphile is soluble in non-polar solvents, while the other component is soluble in polar ones. This indicates that very polar or very non-polar solvents, such as water, encourage self-assembly.[12,13,14].

Hydrocarbon chains make up the hydrophobic portion of Amphiphiles, whereas polar head groups make up the hydrophilic portion.[13]The Amphiphiles first dissolve as monomers in water solution, but they self-assemble spontaneously at a particular concentration to reduce unfavorable hydrophobic interactions. Increased system entropy typically accompanies this self-organization. When the Amphiphiles are freely suspended as monomers, the water-hydrocarbon interactions that drive the water molecules into an ordered structure around the hydrophobic portion are the source of the increased entropy.[1]

3.2. Surface charge

The hydrocarbon chain that is attached to the head group of phospholipids used in Nanosome preparation can be charged (positively or negatively), zwitterionic, or neutral. The charge on the phospholipids surface can change the properties of the Nanosome preparation. For instance, phospholipids like phosphotidylcholines are zwitterionic at all relevant PH and can therefore form lamellar structures regardless of the pH in the solution.

Phospholipids with PH-dependent phase behavior include phosphatidylethanolamine. They have zwitterionic head groups and cannot create lamellar structure at physiological pH; however, beyond PH 9, the head groups become charged and can form lamellar structure.

3.3. Phase behavior of Nanosome

Phospholipids composition and temperature are the factors which is responsible for the major changes in phase behavior of Nanosome. The Bilayer is forced into a gel state at low temperatures or high saturation levels, where the hydrocarbon chains show close packing and a more or less frozen shape. A Bilayer of a liquid crystalline (fluid) state, where the chains are disordered and have high mobility, is produced by raising the temperature or adding unsaturated acyl chains. The chemical makeup of the bilayers, particularly the acyl chains, determines the temperature at which the gel to liquid crystalline phase change takes place.[15]

Since the double bond causes kinks in the chain that prevent close packing, the temperature of an unsaturated phosphotidylcholines lipid will be substantially lower than that of its saturated counterpart. The phase transition temperature

provides useful information on permeability, nanosomes stability, and whether the medication is trapped in the aqueous compartment's bilayer[1,15-18]

Table: 1.Transitional Temperature Value of Some Phospholipids

LIPIDS	CHARGE	TRANSITION TEMP.
Dilauryl phosphatidylcholine (DLPC)	0	0
Dimyristoyl phosphatidylcholine (DMPC)	0	23
Dipalmitoyl phosphatidylcholine (DPPC)	0	41
Distearoyl phosphatidylcholine (DSPC)	0	58
Dilauryl phosphatidylglyserol (DLPG)	-1	04
Dioleyl phosphatidylglycerol (DOPG)	-1	18
Dipalmitoyl phosphatidylglycerol (DPPG)	-1	41
Distearoyl phosphatidylglycerol (DSPG)	-1	55

3.4. Membrane permeability

A phospholipids membrane obviously forms a very tenuous barrier for molecules with high solubility in both organic and aqueous media, while polar solutes and high molecular weight compounds pass through the membrane very slowly. For this reason, nanosomal membranes are semi-permeable, meaning that the rate of diffusion of molecules and ions across the membrane varies significantly. The most common way that polar solutes leak is through membrane flaws or transient holes (pores).[14,16].

In order to improve the Bilayer packing order and produce a lipid membrane with decreased permeability, cholesterol is utilized in the Nanosome manufacturing process.[1]. The preparation of the membrane is significantly altered when sterols are added to the Nanosome Bilayer. Cholesterol can be integrated into phospholipids membranes at very high concentrations, but it cannot create a Bilayer structure on its own. With its hydroxyl group facing the aqueous surface and its aliphatic chain parallel to the acyl chains in the middle of the Bilayer, cholesterol enters the membrane.[1,17,18].

3.5. Stability

3.5.1 Chemical stability

Stability of lipid vesicular system is one of the most important issues in their application. Nanosome are prepared by the use of phospholipids, these lipid are undergoes various Deterioration process among them typical degradation pathway is oxidation and hydrolysis. Nanosome preparation consists of highly purified lipids which minimizes the oxidation of these preparations[14]. When lipids are hydrolyzed, the rate of hydrolysis depends on both pH and temperature. This can be minimizing by maintaining the ph of the system to 6.5. It is expected that, the hydrolysis of lipid is much more in both higher ph and lower ph. Temperature is also an important factor for the hydrolysis of the system, and can be described by the Arrhenius relation.

$$K=Ae\times p\ (\Psi Ea/RT)$$

Where,

k is the hydrolysis rate, A is frequency factor, Ea is the activation energy and RT is the thermal energy, this means that the rate is significantly slower at lower temperature[19,20,21].

3.5.2 Biological stability

Nanosome are different than other conventional lipid vesicular system, the Nanosome preparation are more stable inside the body due to their nano size range, which can be further stabilized by the coating of Nanosome with PEG, which prevent the RES uptake of Nanosome, resulting in increasing residence time inside the body[21].

4. Method of preparation for Nanosome

4.1. Super fluids phospholipids manufacturing process

Super fluids at the right temperature and pressure are used in an apparatus known as the super fluids CFN apparatus to solvate phospholipids, cholesterol, and other Nanosome raw materials in the super fluids phospholipids synthesis process.[7] The choice of SFS is a crucial process parameter because this manufacturing method is entirely dependent on its capacity to dissolve the Nanosome raw material under specific temperature and pressure conditions. In order to guarantee adequate mixing of the SFS and Nanosome source material in an upper high pressure loop, the super fluid CFN equipment includes a circulation pump. The resultant combination is decompressed using a back pressure regulator (valve) as it passes through a dip tube with a nozzle into a decompression chamber (vessel B) that holds phosphate buffer saline or another biocompatible solution after a certain amount of time.[22,23].

When the bubble separates from the nozzle into the aqueous solution, it ruptures, causing bilayers of phospholipids to peel off, encasing solute molecules and spontaneously sealing themselves to form phospholipids nanosomes. In this technique, bubbles will form at the injection nozzle tip due to SFS depressurization and phase conversion into a gas, and the solvated phospholipids will deposit out at the phase boundary of the aqueous bubble.[22,23]

4.1.1. SFS cocktail method

In certain cases, the targeted chemicals and the phospholipids are solvated at the same time in an SFS "cocktail" that is continually dissolved in an aqueous medium. The target molecule is trapped by the unstable phospholipids Bilayer fragments that collide and quickly seal to form a Nanosome as the process stream decompresses. This system's primary benefits are its concentrated product recovery and excellent trapping efficiency.[22]

4.1.2. SFS-CFN method

SFS-CFN is a special method that can be used to encapsulate extremely hydrophobic compounds, such as powerful anti-cancer medications. This method involves injecting the phospholipids and the hydrophobic medications into a phosphate buffer saline or another biocompatible solution after they have been immediately solvated in the SFS. The SFS evaporates after decompression through a nozzle, leaving behind an aqueous solution of nanosomes that have hydrophobic

molecules trapped within their lipid bilayer.[22,23]

4.2. Heating method

To create a nano range lipid vesicular system, "Mozafari" provides a heating approach that entails hydrating phospholipids in an aqueous solution with 3 vol% glycerol and raising the temperature to 60°C or 120°C. Glycerol is used because it is a medically acceptable, water-soluble substance that can function as an isotonizing agent and improve lipid vesicle stability by inhibiting sedimentation and coagulation. Since a high temperature was used in the fabrication of the nanosomes, there was no documented lipid breakdown and no requirement for sterilization.[24,25]

Using the heating approach, one can incorporate the drug to the solution at various points, such as at the beginning, when the temperature was higher than the lipid's transition temperature, or at room temperature following the manufacture of nanosomes for materials that are heat-sensitive[24,25].

4.3. Thin film hydration technique

A lipid phase was created in the thin film hydration process by dissolving varying amounts of the active ingredients, cholesterol, and phospholipids in a 95:5 chloroform-methanol mixture in a 250 ml round-bottom flask. A thin layer of lipids was obtained on the flask wall by rotational evaporation at 40±C, which separated the solvent mixture from the lipid phase. To speed up the annealing process, the dry lipid film was moistened with saline solution and allowed to sit at room temperature for five hours. The preparation of small unilamellar vesicles (SUV) involved 60 minutes of sonication (at a temperature higher than the Tc of the lipids) in a Grant bath-type sonicator, followed by 5 minutes of probe sonication using a Branson B-12 probe-type sonicator set to 70 W. To get rid of any titanium shards, the suspension was sonicated, allowed to stand at 37±C for 10 minutes, quickly cooled in an ice bath, and then centrifuged for 10 minutes at 10,000 rpm. SUV were produced using a Mini Extruder device after five extrusions through a specific polycarbonate membrane (200 nm), corresponding to a mean diameter of 100–200 nm.[12].

5. Mode of Transport

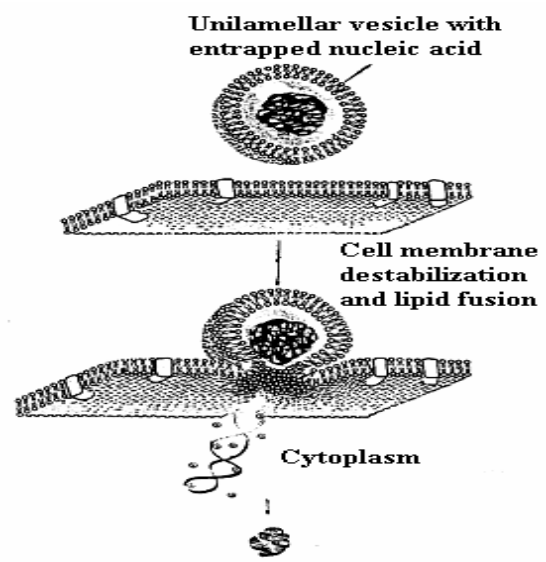

Fig.2. Transport mechanism of Nanosome inside the cell

Through a variety of processes, including the penetration of individual lipid components, which allows phospholipids to diffuse into the stratum corneum, nanosomes can improve medication delivery through cutaneous channels. Additionally, the lipid mixing of Nanosome phospholipids with the lipid bilayers of the skin is the basis for the interactions and enhancer impact of nanosomes on the stratum corneum. The stratum corneum's bilayers fluidity can be disrupted by phospholipids in Nanosome systems, lowering the skin's barrier qualities.[26,27].

Additionally, some researchers have shown that phospholipids in nanosomes may combine with lipids in the stratum corneum to create a lipid-enriched environment. Lipophilic medicines prefer this lipid depot in the skin, which leads to improved skin uptake.

In certain instances, phospholipids themselves may act as solubilizers to make lipophilic medications more soluble.

When organic solvents like propylene glycol, tetra glycol, and ethanol are present, phospholipids ought to show their skin-enhancing properties. Another significant element influencing the transdermal flow of medications is the concentration of phospholipids and the content of unsaturated fatty acids in phospholipids.[27,28]

6. Characterization Parameter for Nanosome

After formulation and processing for a designated purpose, nanosomal formulations are assessed to guarantee consistent in vitro and in vivo performance.

6.1. Vesicle shape and lamellarity

Numerous electron microscopic techniques can be used to evaluate the form and lamellarity of vesicles, and these methods can be expanded to calculate the vesicle's average size. Nuclear magnetic resonance analysis and freeze-fracture electron microscopy are used to count the number of bilayers in the Nanosome.

6.1.1. Freeze facture electron microscopy:

The shape, lamellarity, and surface morphology of the Nanosome can all be evaluated using freeze-fracture electron microscopy. Because the vesicles in this approach are randomly positioned in the frozen state, the fracture plan may not always pass through the mid plane, which could lead to non-mid plane fracture and inaccurate measurements. Thus, the distance between the vesicle center and the plane of fracture determines the observed dispersion profile. Additionally, a diverse population necessitates close observation prior to evaluating the outcomes.[29]

6.1.2. Nuclear magnetic resonance analysis:

One of the most precise and straightforward methods for figuring out a nanosomes lamellarity is nuclear magnetic resonance analysis. By adding an impermeable paramagnetic shift or a nanopermeable broadening agent, like Mn++, to the external medium, the technique investigates nuclear magnetic resonance monitoring. This reduces the intensity of the initial NMR signal by a proportional amount to the fraction of lipid exposed to the external medium.

A 50% decrease in NMR signal strength implies a unilamellar vesicular preparation, but a subsequent reduction shows a multilamellar one, as the maganenese ion interacts with the outermost bilayers leaflets.

6.2. Vesicle size and size distribution

When it comes to the in vitro characterization of the nanosomal product, the average vesicle size and size distribution are crucial parameters. This is due to the fact that they affect the entrapped materials' and nanosomes physicochemical characteristics and biological destiny following in vivo delivery.

The literature describes a variety of methods for determining size and size distribution. This covers, among other things, laser light scattering, photon correlation spectroscopy, electron microscopy, light microscopy, fluorescence microscopy, and freeze fracture microscopy.

6.2.1. Freeze fracture electron microscopy:

The primary purpose of freeze fracture electron microscopy is to evaluate surface features and lamellarity; it can also be used to determine the actual vesicle width.[1, 15]

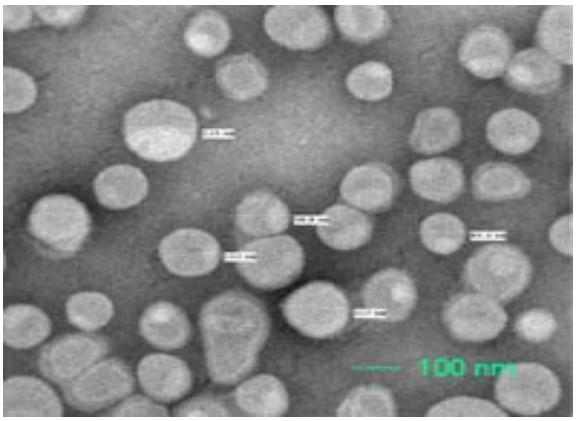

Fig.3. Nanosome having size range 100nm

6.2.2. Scanning electron microscopy:

The use of scanning electron microscopy is less common. One explanation for why scanning electron microscopy is not a suitable evaluation method is the distortion that occurs during sample preparation.[30]

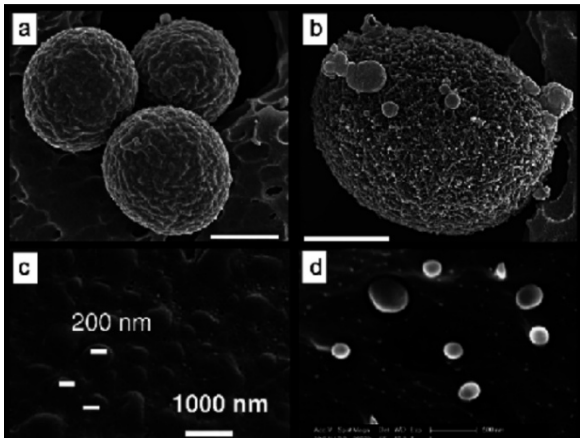

Fig: 4. Electron microscopy image of small unilamellar nanosome[31]

6.2.3. Diffraction and scattering technique:

(a) Laser light scattering:

The homogenous colloidal particle population can be analyzed with the use of quasi-elastic light scattering techniques, especially those based on lasers. The method is used on unimodel systems and is based on the time-dependent coherence of light dispersed by a vesicle.[1]

(b) Photon correlation spectroscopy:

The primary method based on laser scattering analysis that takes use of the time dependence of intensity fluctuations in scattered laser light caused by various particle Brownian movements in nanosomal dispersions is photon correlation spectroscopy. The rate of fluctuations of scattered light intensity, which is a function of the mean hydrodynamic radius of the particles as established by the Strokes-Einstein equation, is influenced by the differential diffusion profile of the particles of small and larger dimensions.

6.3. Surface Charge

Studying the charge on the vesicle surface is essential since nanosomes are made with charge-transferring constituent lipids. Typically, there are two ways to evaluate the surface charge.[1]

(a) free-flow electrophoresis

(b) Zeta potential

6.4. Encapsulation Efficiency The percentage of the aqueous phase and, consequently, the percentage of water-soluble medication that is eventually trapped in nanosomes are known as the encapsulation efficiency. Two methods are used to evaluate encapsulation efficiency: the protamine aggregation method and the micro column centrifugation method.[1,15]

Mini column centrifugation is commonly used to analyze the dispersion of nanosomes to ascertain the efficacy of encapsulation as well as to purify and separate nanosomes on a tiny scale.

For both negatively and neutrally charged nanosomes, the proton aggregation approach can be applied. A protamine solution can be used to precipitate the nanosomal dispersion, and the supernatant and nanosomal pellet can then be centrifuged.

6.5. Phase Response and Transitional Behavior

For their functions in stimulus-mediated fusing of nanosomal constituents with the target cells or prompted drug release, lipid bilayers display a variety of phase changes. By choosing the right lipids, the temperature of thesis phase transitions can be adjusted. Lipid bilayers can exist in a solid ordered phase at low temperatures and in a fluid disordered phase above a specific temperature.

The production and use of nanosomes depend on the phospholipids membrane's phase transition and fluidity. Properties including permeability, fusion, aggregation, and protein binding are all determined by the phase behavior of a nanosomal membrane.

Differential scanning calorimetry (DSC) analysis and freeze-fracture electron microscopy have been utilized to evaluate the phase transition.[1,15]

7. Advantages

Greater solubility, extended exposure time, targeted distribution of the entrapped drug to the site of action, improved therapeutic index, and the potential to overcome resistance linked to conventional anticancer agents are the putative benefits of the nanosomal drug delivery system. A few instances are [2]

1. With an average diameter of roughly 10 to 100 nm, nanosomes are comparatively small. Their size allows extravasations through the endothelial gaps in the target tumor's capillary bed and best balances the drug carrying capacity and circulation time.[2]
2. The way that nanosomal and non-nanosomal anticancer drugs behave and penetrate tumors indicates that the former have a longer systemic half-life and extravasate into solid tumors through the tumor neovasculature's capillaries.[2]
3. The solubility problems with the majority of camptothecin analogues, the preservation of the medications in

active lactone form, and the possibility of sustained exposure following a single dose make nanosomal encapsulation of some medications, such as camptothecin, an appealing formulation.[32]

4. Nanosomal form protects the active agents from its premature metabolism[32].
5. Nanosomal formulation reduced the toxicity by reducing the frequent dosing of active agents especially anticancer agents[1].
6. Nanosome utilize phospholipids for their preparation which are amphiphathic having affinity for both hydrophilic as well hydrophobic active agents so they are able to encapsulate both the hydrophilic as well as hydrophobic therapeutic agents[33,34].

8. Applications

8.1. Nanosome for the encapsulation and targeting of antitumor agents

It is a little mysterious how nanosomes can efficiently localize to malignancies. Nanosomes will localize to tumors even if they do not have ligands specific to tumor cells affixed to their surfaces. In this regard, it is well acknowledged that nanosomal tumor targeting is a passive process that is mostly dependent on how frequently a single Nanosome traverses the vascular network inside a tumor. Significant anatomical and functional abnormalities cause the blood vessels in a tumor to leak abnormally. The extravasations and retention of Liposomes within the tumor interstitium are explained by this leakiness as well as the concurrent absence of a completely functional lymphatic drainage system. Therefore, the capacity of nanosomes to stay in circulation can be changed by changing their physicochemical properties.

The advertised propensity of nanosomal carriers to localize in the tissues of the mononuclear phagocytic system (MPS), specifically the liver and spleen, has limited their use in some applications. Therefore, MPS cells frequently remove classical nanosomes and the medications they are linked with from circulation prior to effective delivery. The creation of nanosomes with surface carbohydrates like monosialoganglioside or polymers like PEG can address the drawbacks of classical nanosomes. More time is spent in circulation by these nanosomes than by conventional ones. In the reticuloendothelial system, conjugated nanosomes remain in circulation for a comparatively longer amount of time because they are not easily absorbed by the macrophages.

PEG is particularly helpful due to its controlled molecular weight, ease of synthesis, affordability, and ability to attach to lipids or proteins, including the antibody, using a number of different techniques. It has been demonstrated that these nanosomes preferentially aggregate in the tumor tissue because of the longer circulation duration of the PEG-containing Nanosome and the leaky microvasculature in the solid tumor tissue. Therefore, only tiny nanoparticles with a circulation half-life of 100 nm or less have more chances to extravasate through irregular capillaries under physiological tumor conditions. They also have a better chance of escaping the spaces between neighboring endothelial cells and openings at

the vessel termini during tumor angiogenesis.[35]

8.2. Nanosome in gene delivery

Successful nucleic acid transport into cells in vitro and in vivo is essential for recombinant DNA technologies, gene function research, and gene therapy. For introducing genes into cells, numerous physical, chemical, and biological techniques have been devised. The two most popular forms of gene delivery vehicles are non-viral and viral, such as retrovirus.[1]

Among the non-viral vector systems, lipid complexes and particularly tailored nanosomes like ph-sensitive, cationic, and genosomes—have been studied for their ability to transfer genes. The majority of non-viral gene vectors used for transfection that are sold commercially are cationic Nanosome-DNA complexes. The cationic charge provides a template for lipid-DNA complexation and electrostatic DNA adsorption on the surface. According to reports, the technology can actually use electrostatic compression to consolidate the DNA molecule. By delivering the content through likely membrane fusion, the cationic Nanosome prevents DNA from being broken down by lysosomes and nucleoli.

8.3. Nanosome in antimicrobial, antifungal and antiviral therapy

Intracellular pathogens harbor in the liver and spleen and thus therapeutic moieties can be targeted to these organs using conventional Nanosome as a carrier system. Due to their intrinsic passive vectorization to RES-predominant organs, conventional Nanosome offers enormous potential and opportunities for targeted drug delivery to intracellular pathogens like leishmanissis, candidiasi, girardiasis, malaria and tuberculosis. Conventional Nanosome mediated treatment of fungal, viral, bacterial and protozoal infections take the advantage of natural targeting of nanosome to the RES-predominant organs. The drug of first choice is the pentavalent antimonials, meglumine antimonite and sodium stibogluconate, and the second choice of drug amphoterecin B. [1, 36].

On administration of these nanosomal forms of drugs exceptional hepatosplenic accumulation of encapsulated drug was observed with minimal toxic side effects. Similarly, the existence of malaria parasite in the hepatocytes and possibly the kupffer cells in its tissue stage resulted in investigation on use of the conventional Nanosome in the treatment of malaria.

8.4. Nanosome in dermatology and cosmetology

Nanosomes imitate the lipid composition and structure of human skin, making them a model for biological membranes in biological and medical research. To improve skin penetration, stratum corneum lipid-containing nanosomes have been explored. The following are some benefits of topical nanosomes in dermatology and cosmetics:

- They are capable of navigating water-soluble and lipophilic compounds in various phases and domains, much like biological membranes.
- Mimic the structure and content of the epidermis, which allows them to more deeply penetrate the epidermal barrier than conventional delivery methods.

- Because nanosomes are nontoxic and biodegradable, they can prevent hazardous or systemic side effects.
- It is believed that nanosomes serve as both drug localizers and transporters, preventing systemic absorption and the ensuing negative effects.

Nanosomes are utilized in topical anti-aging compositions in cosmetics; their interactions with corneocytes and intercellular lipids minimize skin roughness, resulting in smoother, softer skin [1].

9. Future Aspects

Future nanosome generations will include thermo sensitive nanosomes, immunonanosomes, and single nanosomes containing two anticancer drugs. Immunonanosomes are intended for target cell internalization and intracellular drug release, including doxorubicin, vincristine, and others. They combine antibody-mediated tumor identification with nanosomal delivery.

By rapidly releasing the medicine when hypothermia is introduced to the tumor location, thermo sensitive nanosomes may offer a way to improve the tumor-specific delivery of anti-cancer drugs.

Future research on nanosomes must also assess how they are cleared and determine the variables linked to the pharmacokinetic and pharmacodynamic variability of nanosomal anticancer drugs in patients, and in particular, in malignancies. Furthermore, phenotypic probes that may be utilized to forecast this variability and customized treatment with nanosomal drugs must be developed for future research.

10. Conclusions

The nanometer-sized vesicles of phospholipids bilayers, known as nanosomes, are made up of one or more lipid bilayers. In general, phospholipids and cholesterol make up nanosomes. In order to reduce the unfavorable interactions between the bulk aqueous phase and the long hydrocarbon fatty acyl chain, the phospholipids in the nanosomes structure align themselves closely in aqueous media to form planer bilayers sheets that enclose the aqueous core. Protein macromolecules, nucleic acids, and other hydrophilic medications, as well as hydrophobic treatments including anti-cancer and anti-HIV medications, can be better delivered and encapsulated using nanosomes.

Because of their nanorange size, nanosomes are typically used as a carrier for parenteral and transdermal medication delivery. In general, stability and stabilizing agents are employed to classify nanosomes; occasionally, phospholipids may also be used.

Nanosome can be prepared by various methods like super fluid phospholipids manufacturing process, thin film hydration technique, heating method etc. which can be already discussed in the thesis. These Nanosome posses' unique properties such as amphiphilic nature, nano size range etc, which make them suitable carrier for drug delivery especially for tumor targeting.

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