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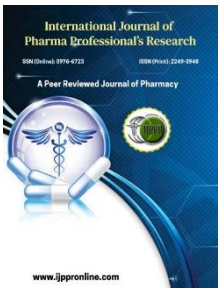

Sphingosomes: A Novel Vesicular Drug Delivery System

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ABSTRACT:
Sphingosomes are bilayer vesicles, primarily made of natural or synthetic sphingolipids, that completely surround an aqueous volume. Sphingosomes address the main issues with vesicle systems (liposomes, niosomes), including their lack of stability, short in vivo circulation times, and poor tumour loading efficacy in cancer therapy. Sphingosomes are a promising vesicular drug delivery system that can transport therapeutic chemicals for a variety of potential applications, according to the review's findings. The development of novel medication delivery systems has received a lot of attention in recent decades (NDDS). To begin, it should administer the medication at a pace determined by the body's requirements throughout the course of therapy. Second, it must direct the active entity to the action location. None of these can be met by conventional-dose forms, including extended-release dosage forms. No existing drug delivery system now acts optimally, although genuine efforts have been made to accomplish them via different new drug delivery methods.[1-5]

Introduction:

The creation of innovative drug delivery systems (NDDS) has received a lot of attention during the last few decades. Idealistically, the NDDS should meet two requirements. The medicine should first be delivered over the course of treatment at a rate determined by the body's needs. Second, it ought to direct the active entity to the area of impact. None of these can be met by conventional dosage forms, including delayed-release dosage forms. Although no perfect drug delivery system is currently available, earnest efforts have been made to obtain them using a variety of new drug administration techniques.[6-10] In recent years, several carrier systems and technologies have undergone substantial research with the goal of regulating medication release and increasing the formulation's effectiveness and selectivity.

Nowadays, vesicles are the preferred method for delivering drugs, and lipid vesicles have also proven useful in the fields of immunology, membrane biology, diagnostics, and, most recently, genetic engineering.[11-12] Vesicular delivery systems offer a reliable way to deliver medication to the infection site, which reduces drug toxicity without causing any negative side effects. Vesicular drug administration lowers therapy costs by increasing the medication's bioavailability, particularly in the case of poorly soluble medicines. They can combine with both hydrophilic and liophilic medications.. Liposomes, niosomes, sphingosomes, transferosomes, and pharmacosomes are some of the novel ways utilised to transport the medicine by vesicular system. Thus, the primary goal of this review paper is to describe various vesicular drug delivery systems together with their commercial formulation and limitations for students, teachers, and researchers who would be interested in learning more about these systems. [13-15]

Definition

"Concentric, bilayered vesicle in which an aqueous volume is completely enclosed by a membranous lipid bilayer primarily composed of natural or synthetic sphingolipid" is one definition of sphingosine. When compared to alternative formulations, liposomal cholesterol based on sphingomyelin provides a number of benefits.[16-18] The Sphingosomes have better drug retention properties and are significantly more resilient to acid hydrolysis. There are several ways to give sphingosine, including intravenous, intramuscular, subcutaneous, and intra-arterial routes. In most circumstances, it will be taken intravenously, though there are few exceptions.

General structure of sphingolipid

Oral or transdermal administration of sphingosomes is an option (Webb et al., 1996). The sphingolipid (sphingomyelin) and cholesterol that make up sphingosomes have an acidic intra-liposomal pH ratio that ranges from 75 to 25 mol%/mol% (but 55 to 45 mol%/mol% is preferred).

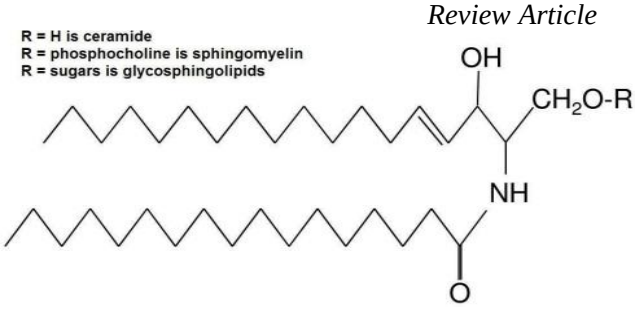

Figure 1: Structure of Sphingolipid

Composition The main lipid compositional difference among liposomal preparations is found in sphingosomes. They have one or more membranes that are made of cholesterol and sphingolipids. The polar head groups of the neighboring molecules tend to associate and interact with those of the nearby molecules, and the sphingolipid and cholesterol are normally present at a percentage molar ratio of 75:25 to 30:50. As sphingolipids, in general have a predilection for partitioning into ordered domains, sphingosomes are creating ordered membranes. Naturally occurring sphingolipids come in a wide variety of head group configurations and acyl chain compositions. The partitioning of sphingolipids into organised membrane domains is encouraged by the ceramide moieties with the long-chain base and long saturated N-acyl chains. It is likely that the polar head group, which can range from a single hydroxyl in ceramide and a phosphocholine group in sphingomyelin to huge assemblies of carbohydrates for the complicated glycol sphingolipid, will also have an impact on how these lipids are distributed.[19-23]

General advantages of sphingosomes

a) Choose tumour tissue for passive targeting. Improve the therapeutic index and efficacy.

b) Boost stability through encapsulating a decrease in the encapsulated agent's toxicity.

c) Increased circulation time will improve the pharmacokinetic effect.

d) The ability to combine with ligands that are unique to a given location to achieve active targeting:

e) Systems for vesicular drug delivery are becoming more common, having applications in the pharmaceutical, cosmetic, and food industries. Their direct drug delivery to the infection site reduces drug toxicity with no negative side effects. By giving the medicine greater biological qualities, it also lowers the cost of therapy, leading to increased bioavailability, especially for medicines that are not easily soluble. Various non-steroidal anti-inflammatory drugs, proteins, cardiovascular, anti-neoplastic, anti-glucoma, and anti-diabetic medications that are integrated with vesicular system are now readily available in the commercial market and are playing a vital role in the treatment of diseases, thereby enhancing human health. Below is a list of some of the new vesicular drug delivery systems. [24-25]

Method of preparation of Spingosomes

A. Lipid film formation (Handshaking method*).* Diethyl ether was used to dissolve the surfactant/cholesterol mixture in a round bottom flask, and the ether was then extracted at room temperature under decreased pressure using a rotary evaporator. A lipid solution in diethyl ether was slowly added to warm water to hydrate the dried surfactant film at 50–60°C. Typically, the lipid mixture was then injected into an aqueous solution of the material to be encapsulated (using a syringe-type infusion pump) at 55–65°C and under reduced pressure. Single-layered vesicles (SLVs) are produced when ether vaporizes; the diameter of the vesicles varies depending on the conditions. This procedure results in multilamellar vesicles (MLVs) with a high diameter.[26]

B. Micro fluidization. This method of preparing miniature MLVS is quite new. The fluid is pumped through a screen using a microfluidizer at a very high pressure (10,000 psi). The fluid is then driven along predetermined microchannels, causing two streams of fluid to meet at right angles and transfer energy very effectively. You can add the lipids to the fluidizer. Reusing the collected fluid through the pump will provide vesicles with spherical dimensions. This results in greater uniformity, small size and better reproducible niosomes.[27]

C. Reverse phase evaporation. The evaporation of a solvent from an emulsion is the method's inventive key. A two-phase mixture is bath-sonicated to create a water-in-oil emulsion, which is subsequently dried under decreased pressure in a rotary evaporator to a semi-solid gel. The next stage is to use a vortex mixture and a forceful mechanical shake to cause a fraction of the water droplets to collapse. In such cases, the lipid monolayer that surrounds the collapsing vesicles is added to the lipid monolayer of neighbouring intact vesicles to create the outer leaflet of the bilayer of enormous unilamellar niosomes. Unilamellar vesicles with a diameter of 0.5 m are produced.[28]

Classification of Sphingolipids

1) Sphingoid bases

a) Sphing-4-enines (sphingosines)

b) Sphinganines.4-Hydroxysphinganines (phytosphingosines)

c) Hexadecasphinganine (Sphingoid base homologs and variants)

d) Sphingoid base 1-phosphates

e) Lysosphingomyelins,and lysoglycosphingolipids

f) *N*-Methylated sphingoid bases

g) Sphingoid base analogs Ceramides

2) Ceramides

a) N-Acylsphingosines (ceramides)

b) N-Acylsphinganines (dihydroceramides)

c) N-Acyl-4 hydroxysphinganines (phytoceramides)

3) Neutral glycol sphingolipids

a) Simple Glc series (GlcCer, LacCer, etc.)
GalNAcβ1-3Galα1-4Galβ1-4Glc-(globoseries)
b) GalNAcβ1-4Galβ1-4Glc- (ganglio series)
c) Galβ1-3GlcNAcβ1-3Galβ1-4Glc- (lacto series)
d) Galβ1-4GlcNAcβ1-3Galβ1-4Glc- (neolactoseries)
e) GalNAcβ1-3Galα1-3Galβ1-4Glc- (isoglboseries)
f) GlcNAcβ1-2Manα1-3Manβ1-4Glc- (molluseries)
g) GalNAcβ1-4GlcNAcβ1-3Manβ1-4Glc- (arthro series)

4) Acidic glycosphingolipids

a. Gangliosides
b. Sulfoglycosphingolipids (sulfatides)
c. Glucuronosphingolipids
d. Phosphoglycosphingolipids
e. Other Amphoteric glycosphingolipids

Transport mechanism of sphingosomes

Small unilamellar sphingosomal vesicles (SUSVs) interact with cells in a variety of ways at the cellular level, including through multiple transport mechanisms. These include lipid transfer, persistent adsorption, endocytosis, and fusion (Jain, 2001).- Stable adsorption: The interaction of whole vesicles with the cell surface is referred to as stable adsorption. Such a process is mediated at the vesicle or cell surface by non-specific electrostatic, hydrophobic, or other forces or components. Endocytosis is the process of vesicle ingestion into endocytotic vesicles, which is thought to lead to the transfer of the vesicles to the lysosomal apparatus. [29-30]

Other Therapeutic Applications of Sphingosomes [31]

a) Sphingosomes in antimicrobial, antifungal and antiviral (anti- HIV) therapy
Examples: Ciprofloxacin, Ofloxacin, Vancomycin, Amoxicillin Amphotericin B., Iodoxuridine.
b) Spingosomes in antifungal therapy
c) Spingosomes in cosmetics
d) Spoingosomes in ocular drug delivery
e) Sphingosomes may be used in gene delivery
f) Sphingosomes may be used in gene therapy
g) Sphingosomes may be used in enzyme immobilization

Future Aspects

Researchers from all around the world are still working to improve vesicular systems by making them stable in nature to stop content from leaching, oxidising, and being absorbed by natural defence mechanisms . The genetic engineering component can be combined to offer the current cellular drug carrier notion a novel dimension. Their possible uses in medicine include the treatment of drug overdoses, immobilisation of enzymes, disguising medication flavours, improving gastrointestinal absorption, and serving as carriers for sustained release and transdermal drug delivery. With the development of numerous innovative preparation, stabilisation, and characterisation strategies, these systems can function as potential drug carriers.[32-34]

Conclusion

Sphingosomes are bilayer vesicles, primarily made of natural or synthetic sphingolipid, that completely surround an aqueous volume. The chosen category of cations to be encapsulated is lipophilic.Clinical uses of sphingosomes include the delivery of chemotherapy drugs, diagnostic procedures, and the cosmetics sector. Sphingosomes are widely recognised as secure delivery mechanisms.

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